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Efficient real-space representations for the electronic structure of heavy elements

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In this talk we will discuss how real-space numerical representations can be used to overcome the shortcomings of the traditional Gaussian AO numerical technology for the electronic structure computations of heavy elements. As recently demonstrated by some of us, efficient real-space solvers can be developed for treatment of single-particle (Dirac-Fock) and many-body (MBPT) electronic structure with controlled precision. We will discuss our initial efforts to extend these efforts to general MCSCF and correlated methods for heavy elements.

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Heavy element FPD composite method: Applications to ionization energies and electron affinities

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The Feller-Peterson-Dixon (FPD) composite thermochemistry method, modified for heavy element calculations, is based on complete basis set (CBS) extrapolations at the scalar relativistic (DKH3 or X2C) CCSD(T) level of theory using all-electron correlation consistent Gaussian basis sets. In addition to the usual contributions of outer-core electron correlation and zero-point vibrational corrections, spin-orbit coupling effects, both molecular and atomic, are accurately recovered using 2- or 4-component all-electron methods, as well as small contributions due to the leading term in quantum electrodynamics, the Lamb shift. As in calculations involving light elements, electron correlation beyond CCSD(T) is also considered when computationally feasible, i.e., CCSDT and CCSDT(Q) or CCSDTQ. Recent work using this approach that will be highlighted will include atomic and molecular ionization energies, including high ionization energies of several lanthanide and actinide atoms, electron affinities of early actinide atoms, as well as current efforts to interpret recent anion photodetachment spectra of various thorium-oxide, thorium-gold, and thorium-platinum anions.

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Understanding the Electronic Structure and Spectroscopic Properties of *f*-block Complexes in +2 and +3 Oxidation States: An *ab-initio* Study

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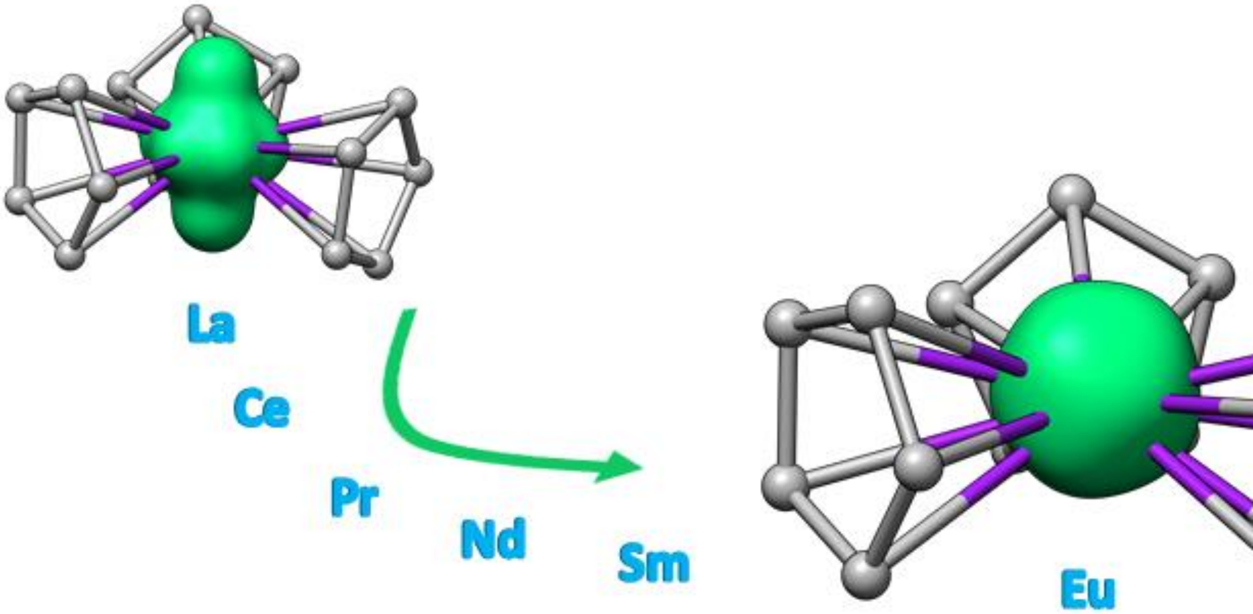
For years, the oxidation state of the *f*-block was considered to be simple and mostly limited to the +3 oxidation state. Until late sixties, Eu^{2+}, Sm^{2+},Yb^{2+}, Tm^{2+}, Dy^{2+} and Nd^{2+} were the only known divalent ions whose existence was explained because of their less negative redox potentials. Recently, research conducted by William Evans and collaborators demonstrated that Ln^{2+} ions are accessible in soluble molecules for all of the lanthanides excepting promethium in a tris(trimethylsilylcyclopentadienyl), $[LnCp'_3]^-$, environment. Further developments led to the synthesis and characterization of some actinides such as U^{2+}, Pu^{2+} and Th^{2+}. Experimental and Density Functional Theory (DFT) studies have shown that Ln^{2+} complexes exhibit variable ground state configurations: $4f^n$ for Sm^{2+}, Eu^{2+}, Tm^{2+}, Yb^{2+}, $4f^n5d^1$ for La^{2+}, Ce^{2+}, Pr^{2+}, Gd^{2+}, Tb^{2+}, Ho^{2+}, Er^{2+}, or both for Dy^{2+} and Nd^{2+} depending on the ligand environment. Structural and spectroscopic properties have also been reported to change going from one configuration to another. Despite these intricacies have been addressed in several works, there is still no clarity about what is the driving force behind the variable nature of the ground states. We have studied the $[LnCp'_3]^-$ series using *ab-initio* multiconfigurational methods which allowed us to obtain the electronic structure, spectroscopic properties and ground state densities of each system. We have overcome several difficulties in the correct prediction of the ground state and explored different avenues in order to provide a more insightful explanation to these experimental observations. In this context, we have proposed that the shape of the ground state density is related to its nature which is directly linked to the electron-electron repulsion. This offers a predictive and intuitive tool that can be applied in the analysis of new lanthanide(II) systems and its actinides analogues.



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Using electronic structure and implicit solvent calculations to model the effect of the organic solvent on liquid-liquid extraction of lanthanides

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As the demand for pure lanthanides continues to rise in the technology sector, efficiently and responsibly obtaining them continues to be a topic of great concern. Specifically, separating lanthanides from one another in mixtures is a challenging and costly process. Liquid-liquid solvent extractions are often employed to separate lanthanide mixtures. This study sheds light on the effects of the organic phase in liquid-liquid solvent extractions by modeling the interactions of trivalent lanthanides (Ln = La, Lu) with different extractants and acids. Explicit lanthanide-ligand molecular complexes in implicit solvents served as models of three ligand-lanthanide-organic solvent extraction systems. To determine the computational models with maximum correlation to experiments, the relative free energy of the complexation reactions was computed for different organic phases. The polarizable continuum model (PCM) and the conductor-like screening model (COSMO) both produce energy values that correlate with the

experimental results for the diphosphine oxide/nitric acid systems. There was no correlation when using the self-consistent reaction field (SCRF) implicit solvation model. For the diglycolamide ligand extraction of lanthanides from hydrochloric acid, COSMO and PCM provide qualitative accuracy when modeling systems with a 1:1 ligand-to-metal ratio but break down in systems with higher ligand-to-metal ratios. For systems with diglycolamide ligand extraction from nitric acid, none of the computational models reproduce the experimentally observed trend, the possible reasons will be discussed.

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Long Time-scale Quantum Molecular Dynamics Simulation of Actinides in Solution

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Actinide chemistry in solution is very intricate in nature. There is a pressing need to develop molecular dynamics (MD) methods that can describe quantum mechanical behavior, such as bond breaking and forming, at long timescales. Current first-principle MD methods can only reach to tens of picoseconds, and this is not adequate for actinide chemistry, while the classical force fields cannot deal with bond breaking and forming. To achieve this goal, we developed the first density functional theory tight-binding (DFTB) parameters for uranium chemistry to enable MD simulations at long time scales that will be instrumental in understanding actinide speciation, reaction mechanisms, and kinetics. In this talk, we will demonstrate the transferability of our DFTB model on prediction of molecular structural parameters of various molecular clusters and a variety of chemical reaction free energies. Reaching the first nanosecond quantum MD simulations allows us to study the kinetics and dynamics of potential reaction mechanisms of uranium speciation in aqueous solution.

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Core-level spectroscopy of actinide compounds

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Properly interpreted, the core-level spectra obtained with X-Ray Photoelectron Spectroscopy, XPS, and X-Ray Absorption Spectroscopy, XAS, can provide invaluable information about the properties and the chemical bonding in actinide compounds. In this presentation, we demonstrate how XPS and XAS can show the covalent character of the bonding in different compounds and the contributions to this bonding of different

atomic shells of the actinide. We will show how the spectra change for different oxidation states of the actinide with an emphasis on relating these changes to shell occupations and to chemical bonding. We will compare $L_{2,3}$ XAS edges with $M_{4,5}$ edges to show the difference between the involvement of the actinide 5f and 6d orbitals in the bonding. We will also examine the extent to which the angular momentum coupling of the open shell electrons can be described with Russell-Saunders multiplets and how structure in the XPS and XAS can be related to the stronger selection rules for Russell-Saunders coupling than for j-j coupling. The results presented here are based on the properties of atomic, molecular, and cluster model wavefunctions. These wavefunctions are solutions of appropriate Dirac-Coulomb Hamiltonians and include scalar and spin-orbit relativistic effects. Angular momentum coupling of the open shell electrons is treated rigorously which is necessary to allow selection rules to be applied

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Variational Relativistic Multireference Methods for Heavy-Element Chemistry

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As the relativistic corrections become stronger for late-row elements, the fully perturbative treatment of spin-orbit coupling and dynamic correlation may become inadequate for accurate descriptions of chemical properties. In this talk, I will discuss the development of variational relativistic multiference methods, including CASSCF, MRCI, MRPT2, and MCPDFT. Benchmark studies of atomic fine structure splitting show that variational approaches outperforms the fully perturbative CASPT2-SO for heavier atomic species (>4th row). This observation suggests that as the strength of the spin-orbit coupling increases, the coupling between relativistic corrections and dynamic correlation also increases and cannot be treated as separate perturbations. I will also discuss how the correlation space affect various heavy element properties.

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Lanthanide and actinide spectroscopy: Improving the use of the ligand-field theory

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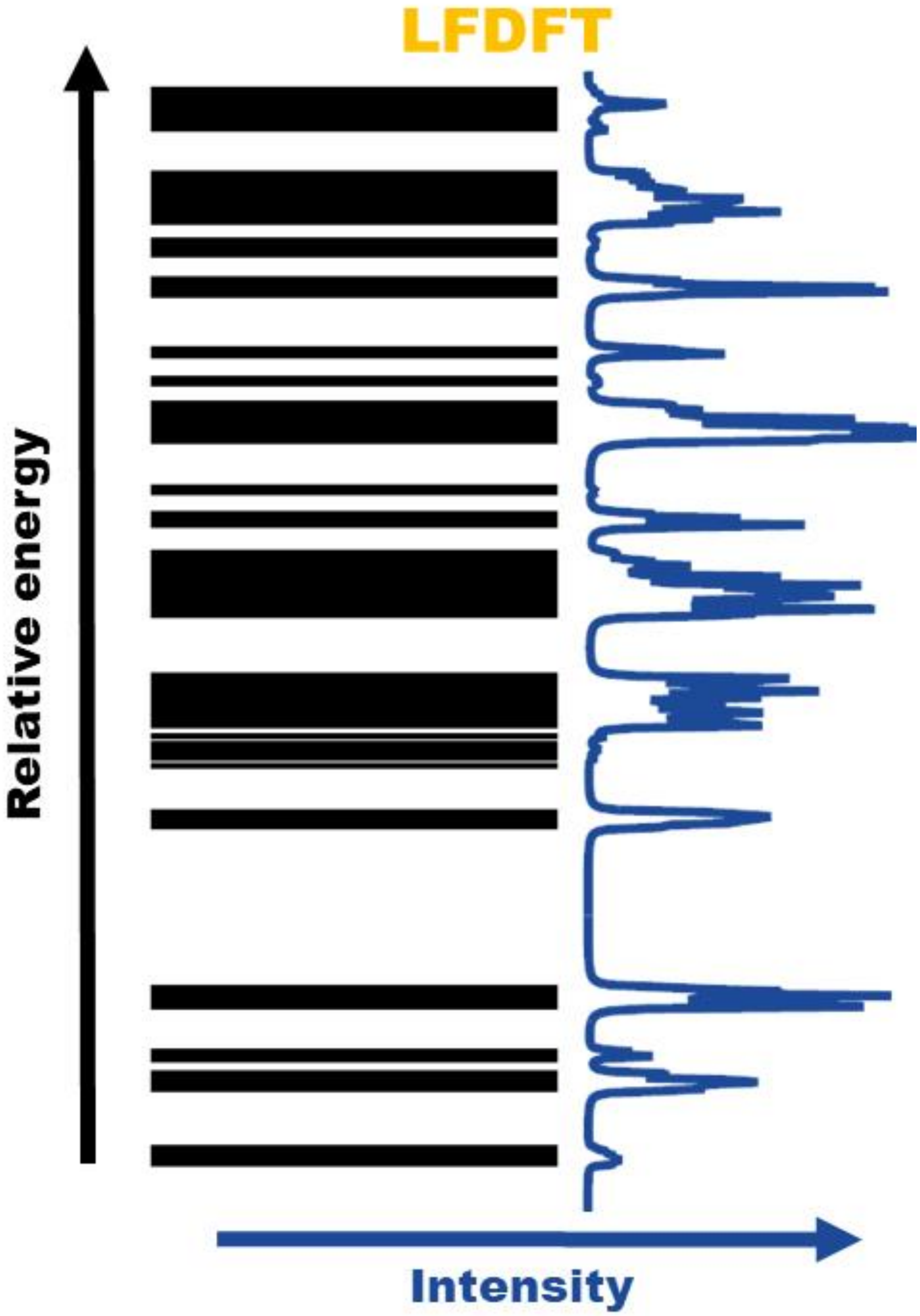
Reproducing and predicting optical spectra of f-block compounds is crucial to understand the nature of the complex transitions involved. However, the intricate interplay between relativistic, ligand field, and electron correlation effects makes this task rather elusive. Semi-empirical ligand field models have been used in the past to interpret f-block absorption and emission spectra, but limited by the lack of experimental

data. Non-empirical methods have been proposed based on Density Functional Theory (DFT), the Ligand Field DFT (LFDFT) approach and the wavefunction-based ab-initio LF theory (AILFT). The accuracy of the predicted multiplet structure strongly depends on the corresponding orbital set used to calculate the interelectronic repulsion (F^k), spin-orbit coupling (ζ_{SO}), and ligand field (B^k_q)parameters. We have studied the reliability of Kohn-Sham orbitals within the LFDFT approach and explored new avenues to improve its performance. We have implemented a new feature to LFDFT to predict the absorption and emission intensities accounting for electric and magnetic dipole, and electric quadrupole contributions. This paves the way for reviving discussions regarding the nature of the transitions (hypersensitivity, ligand-field dependency, etc.) but now with the advantage of a direct link to the molecular orbitals.



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Ligand-to-metal and metal-to-ligand charge transfer in An(IV) molecular compounds

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Separating heavy elements from one another is one of the biggest challenges of nuclear waste management. Because actinide atomic radii get smaller when moving from left to right across the actinide series, metal-ligand bond lengths in actinide complexes usually decrease with increasing atomic number. In addition to the ligand-to-metal charge transfer, there could also be additional interactions, i.e. from the metal back to the ligand (back-donation) that could also affect the An–L strength and impact the actinide contraction trend. In this talk, we will show the various types of the An–L interactions of an actinide center with a varying number of carbon atoms constituting the ligand that lead to unique chemical bonding motifs. We will also demonstrate how certain bonding patterns may be invoked that can promote enhanced An–L covalent interactions in An(IV) compounds, which hold potential implication in nuclear separation chemistry.

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Computationally-guided assignment on the vibrational features of neptunyl engaged in actinyl-actinyl interactions

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Due to its long half-life, neptunium (Np) is a major contributor to the extended radiotoxicity of spent nuclear fuel (SNF). Therefore, the effective removal of Np is necessary in development of new nuclear fuel reprocessing techniques, but its extraction is difficult due to the various oxidation states formed in the SNF environment. In its most common oxidation state (V), Np forms into the distinct neptunyl unit, NpO_2^+. Previous experimental data has shown this molecular unit can engage in unique actinyl-actinyl interactions where the O_{yl} group on one unit can bond with the Np atom along the equatorial plane of another. This type of interaction can lead to dimerization, and even higher oligomerizations of trimers and tetramers at high Np concentrations. Elucidating the structure and specific bonding of these neptunyl oligomers in solution is vital as these interactions may stabilize Np complexes in SNF which presents an added difficultly for Np separations. In this work, we present a systematic Density Functional Theory (DFT) study of neptunyl units engaged in neptunyl-neptunyl interactions to form dimeric, trimeric, and tetrameric species. For each system, a frequency analysis was conducted to reveal the unique vibrational modes developed from the formation of different oligomers. We find the formation of these species can change the overall symmetry forming new vibrational bands composed of combinations of the v_1 and v_3 modes on different neptunyl units. The energetics of these modes are compared directly

to the Raman spectroscopy from a fast evaporation experiment performed on a Np(V)/nitric acid solution and used to interpret the specific oligomers formed during the evaporation process. We go on to investigate the specific bonding in these systems through population analysis. Overall, this work presents the first computational analysis on the vibrational features of neptunyl oligomers which can be used for future IR/Raman spectroscopic studies.

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First Principles Molecular Dynamics Simulations of U(III) and U(IV) in Molten Chlorides

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In this talk, I will discuss how we use first-principles molecular dynamics simulations to investigate the structure of UCl3 and UCl4 in molten NaCl and $MgCl_2$ at various mole fractions and their mixtures. Coordination, structure, and dynamics of the first solvation shell will be analyzed in detail as a function of increasing uranium concentration. In addition, network formation will be examined in detail to compare the difference between UCl_3 and UCl_4 as well as that between NaCl and $MgCl_2$.

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On discrimination of nuclear waste barrels subject to in-drum mixing by muon scattering tomography: A characterization study based on GEANT4 simulations

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Decontamination, decommissioning, and remediation constitute a fundamental part of the nuclear waste management, and among the prevalent methods is the cementation process of the radioactive waste for the purpose of immobilisation as well as storage. Moreover, the cemented nuclear waste forms are routinely obtained by means of two conventional procedures where the first technique commonly referred to the in-drum mixing homogeneously combines the nuclear wastes with the cementitious materials in the final container, whereas the latter method generally called the in-line mixing performs the mixing activities outside the terminal container. By reminding the security fact that the structural characterization of the nuclear waste barrels is considered a challenging legislative duty, the muon scattering tomography, where the target materials are discriminated in accordance with their density, their atomic number, and their thickness at a given muon energy, might find application in the coarse compositional assessment of the nuclear waste drums. Motivated by the feasibility verification of cosmic ray muon tomography in the discrimination of the nuclear waste/cement mixtures, we employ the GEANT4 simulations by using our tomographic setup consisting of plastic scintillators in order to determine the characteristic parameters such as the scattering angle, the muon absorption, and the muon displacement owing to the nuclear waste barrels exposed to the in-drum mixing over a set of radioactive materials consisting of cobalt, strontium, caesium, uranium, and plutonium in the present study. Upon our simulation results based on a cylindrical stainless steel drum with a radius of 29.6 cm as well as a height of 96 cm in which the nuclear materials of volume 8000 cm^3 are homogeneously combined with the regular concrete, we show that the presence of uranium and plutonium in the cementitious forms is qualitatively and quantitatively visible from the characteristic parameters, while the remaining radioactive waste/cement mixtures with the nuclear sources such as cobalt, strontium, and caesium do not exhibit a significant difference in comparison with the ordinary concrete slab since the intrinsic properties of the resulting mixtures that shape the characteristic parameters are predominantly governed by the matrix properties unless the associated additives are drastically denser along with the substantially higher Z-values.

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High Performance Computing in 2022 and Progress in Modeling Rare Earth Elements and Actinides

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High Performance Computing (HPC) has been critical in nuclear- and radio-chemical advances. However, challenges stemming from an imbalanced hardware-software ecosystem present limitations in advancing accurate descriptions of compounds containing rare earth elements (REEs) and actinides. This presentation will provide a historical perspective of the evolution of HPC since the 1990s, and progress and challenges modeling REEs and actinides as HPC moves into the Exascale era.

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Challenges and Progress in Developing High-Throughput Computational Methods For Heavy-Element Materials

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Materials that contain *f*-block containing elements are of critical interest for applications in electronics and in nuclear energy. Computationally searching and predicting materials with targeted properties must balance accuracy with calculation throughput. High-throughput algorithms for main-group materials have been implemented and used for material discovery but have not been adapted to actinide and lanthanide compounds. This talk discusses challenges and possible solutions to creating high-throughput computational methods to aide in experimental discovery of novel heavy-element materials.

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Prediction of stability constants of metal-ligand complexes by machine learning and design of optimal ligands for metal ion selectivity

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The directed message passing neural network (D-MPNN) approach of machine learning (ML) was applied to predict the stability constants of metal-ligand complexes. The ML algorithms were trained on reliable experimental data extracted from a legacy NIST database based on the multi-volume work of R. M. Smith and A. E. Martell "Critical Stability Constants". Molecular properties used in the ML process include multipole moments, Mulliken population analysis, and chemical shield tensors computed by ab-initio methods as well as the number of freely rotating bonds in the ligand that are frozen on metal chelation, MM3 strain energy, and negative Gibb's free energy of hydration obtained by the de Novo molecular design software HostDesigner software. The LOGKPREDICT program was created to interface HostDesigner with the ML program Chemprop. LOGKPREDICT creates a mutually benefical synergy between HostDesginer and Chemprop. On the one hand, HostDesginer improves the machine-learning process by providing molecular properties to Chemprop. On the other hand, Chemprop improves the ligand design by providing logK values to HostDesginer. Examples of utilizing the novel LOGPREDICT interface for the design of new ligands are presented.

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Smart Spectral Matching: A new framework for machine learning structure–property relationships in uranium minerals

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Smart Spectral Matching (SSM) is a new cloud-based, highly flexible software framework designed to integrate the storage and analysis of scientific datasets in a user-friendly way. The SSM framework comprises many services, including extensions to allow custom analysis modules, and experimental metadata to allow more extensive data inference. Not only is this data readily searchable via the SSM user interface, but

pre- and postprocessing tools can also be easily incorporated into the SSM workflow.

To better understand and assign spectroscopic features in solid-state uranium minerals, we leveraged the SSM framework to perform machine learning (ML) analyses of structural and optical vibrational spectral data. Data from our Compendium of Uranium Raman and Infrared Experimental Spectra (CURIES) including raw structural and spectroscopic data is stored along with any additional metadata in SSM. Examples of metadata compiled for samples in CURIES include secondary chemistry, structure type, coordination of uranium sites in the material, data source, and data collection parameters. Using CURIES as training data, an ML tool has been developed to identify new structure–property relationships and apply these results to the identification of unknown mineral species. First, principal component analyses were performed on the data in CURIES to identify regions of the spectra where specific chemical properties contribute the most to variation across the full dataset. From these results, the SSM ML interface can be used to select for the desired properties, spectral features, and targeted spectral regions, and ML models can be trained on the existing data in CURIES. Highly selective models are saved and stored and can be run on unknown samples to assign spectral features to underlying structural properties. A collection of these ML models can then be used to make inferences about the fundamental nature of the underlying mineral structure and coordination characteristics from optical vibrational spectra.

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Applying Artificial Intelligence Methods to Develop Computational Protocols for Lanthanide and Actinide Systems

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Simulating lanthanide and actinide chemistry through accurate computational methodologies is important to better understand binding selectivity of lanthanides and actinides in nuclear and radiochemical applications. This is crucial for nuclear forensics, designing separation agents, and understanding spectra. Theoretical predictions using molecular modeling methods, like ab initio and DFT, have been popular to simulate binding interactions. Using modern data modeling methods, like Artificial Intelligence techniques, such as machine and deep learning, can be insightful to understanding binding selectivity properties. Findings from recent studies with machine and deep learning applications in separations chemistry will be presented.

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Mechanochemical synthesis of uranyl peroxides: Implications for nuclear fuel reprocessing

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As the world is moving away from traditional fossil-fuel-based energy sources, nuclear power emerges as a promising alternative due to recent advancements in small modular reactors (SMRs) that afford numerous energetic, economic, and environmental benefits. The increase in SMRs technology leads towards a demand for better separations and reprocessing of spent nuclear fuel. Current reprocessing efforts, such as PUREX process, rely on dissolution of solid nuclear fuel in concentrated acids with numerous subsequent solvent extractions, that require sophisticated infrastructure and strict process control. Such approach not only generates large volumes of caustic radioactive liquid waste that is expensive to dispose, but also is not economically viable as we are moving to modular nuclear power. Green alternatives to wet reprocessing could include mechanochemical methods, which have been underexplored within actinide chemistry as a tool to enhance chemical reactivity for reprocessing. Herein, we explore the mechanochemistry of solid uranium dioxide $U(IV)O_2$ and uranium trioxide $U(VI)O_3$ with the range of alkali/alkali-earth metal peroxides to probe the chemistry of uranium in the solid state. We utilized single-crystal X-ray diffraction, powder X-ray diffraction, Raman and IR spectroscopy, as well as, SEM imaging to characterize the resulting product. Mechanochemical grinding of uranium oxides with metal peroxides results in the formation of uranyl triperoxide phases and induces the formation of superoxide anion, which in turn, captures carbon under ambient conditions resulting in alkali metal/uranyl carbonate phases. As a result, mechanochemistry is a solvent-free pathway toward water soluble uranyl peroxide and carbonate phases offering a green alternative to traditional acid digestion of spent nuclear fuels.

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Aggregation, conversion, and degradation: Investigating complex interactions of $U_{24}Pp_{12}$ with tetravalent hafnium

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Uranyl polyoxometalates (UPOMs), a class of large metal oxide clusters, are ideal for investigating f- block bonding and the behavior of actinide-bearing compounds in both engineered and naturally-occurring systems. Envisioned technological applications of their chemistry include alternatives to the energy-intensive and wasteful solvent extraction techniques currently used during the recycling of used nuclear fuel. UPOMs may also be utilized to capture and sequester transuranic elements, which are of particular concern for the management of nuclear waste. This work probes the interaction of $U_{24}Pp_{12}$ ($[(UO_2)_{24}(O_2)_{24}(P_2O_7)_{12}]^{48-}$), a pyrophosphate-functionalized UPOM, with tetravalent hafnium. A heightened understanding of this system is desirable due to hafnium’s neutron-absorbing characteristics and the reliability of the synthesis of

$U_{24}Pp_{12}$. Experiments sought to characterize the role of hafnium(IV) in this system, particularly regarding (i) its potential incorporation into or sequestration within the cluster framework and (ii) its ability to induce aggregation of the UPOMs in solution. Electrospray ionization mass spectrometry, dynamic light scattering, and Raman spectroscopy were used to analyze samples containing $U_{24}Pp_{12}$ as a function of $HfCl_4$ concentration. Crystallization via slow evaporation and X-ray diffraction were also used to evaluate the specific role of hafnium(IV) in crystal formation and its ultimate ability to integrate into the crystal structure. The results reveal a conversion of $U_{24}Pp_{12}$ into U_{24} ($[(UO_2)_{24}(OH)_{24}(O_2)_{24}]^{24-}$) prior to the association of the tetravalent hafnium with the U_{24}. This suggests a cluster degradation mechanism mediated in some manner by hafnium(IV), justifying kinetic modeling and investigation of the conversion of $U_{24}Pp_{12}$ into U_{24} in the presence of hafnium and other tetravalent cations.

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Rapid oxidation of TcO_2 by aqueous Mn(III)-Pyrophosphate under anoxic conditions: A liability for the remediation of Technetium-99

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Technetium-99 is a risk driving radionuclide for several U.S. Department of Energy Nuclear sites across the United States because of its long half-life ($2.13*10^5$ years) and high environmentally mobility. Tc-99 has no natural abundance and is a by-product from fission of U-235 for nuclear power production, and formerly from the production and testing of nuclear weapons. Past poor waste management practices have led to the release of substantial amounts of Tc-99 into the environment at locations such as the Hanford and Savannah River Sites. The oxidation state of Tc-99 is the controlling factor in its environmental mobility. Under most environmental conditions, Tc-99 exists as $Tc(VII)O_4^-$ which is highly soluble and unable to sorb to soil or mineral surfaces, giving it a high environmental mobility. However, TcO_4^- can be reduced to TcO_2, which is insoluble and environmentally immobile. Thus, reductive immobilization has historically been the favored strategy of Tc-99 remediation.

The efficacy of Tc-99 immobilization is contingent on the presence of oxidants in the subsurface. The present study investigates for the first time the role of Mn(III)-pyrophosphate (Mn(III)-PP) aqueous complexes, which are strong oxidants, influencing the stability of reduced technetium forms (TcO_2) under anoxic conditions. on the Oxidative dissolution of TcO_2 by Mn(III)-Pyrophosphate was carried out in batch experiments in an anaerobic glovebox (<0.1 ppm O_2). Mn(III)-PP was able to completely solubilize Tc-99 in a matter of hours, in fact faster than oxygen under oxic conditions. The reaction kinetics are sensitive to pH, Mn(III):PP ratio, and Mn(III) concentration. Our results show that Mn(III)-PP can drastically increase the environmental mobility of Tc-99 and can be a liability for the long-term stability even under anoxic condition where long-term stability would be expected.

NUCL

Adsorption of neptunium and americium on aluminum (hydr)oxide minerals: Surface complexation modeling

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Neptunium and americium are highly radioactive elements that form in irradiated nuclear reactor fuel. Their introduction to the environment due to nuclear weapons testing and improper nuclear waste management practices in the past, as well their future long-term storage in deep underground repositories, warrant more focus on studying their interaction with common minerals like aluminum (hydr)oxides. Surface complexation modeling can help explain the speciation of adsorbed neptunium and americium onto aluminum (hydr)oxide minerals, which can control the fate and transport of these radionuclides in the environment. In this work, we will describe both diffuse layer (DDL) and charge distribution multi-site complexation (CD-MUSIC) models to interpret the extents and trends of neptunium and americium adsorption onto three different aluminum (hydr)oxide minerals—corundum (α-Al_2O_3), gibbsite (γ-$Al(OH)_3$), and γ-alumina (γ-Al_2O_3)—as a function of pH (3 to 10) and ionic strength (0.01 to 0.1 M). Europium adsorption data will be used as an analog for americium adsorption. The speciation of the surface complexes will be based on prior extended X-ray absorption fine structure studies and other relevant literature. Our results show that adsorption of americium onto each of the three aluminum (hydr)oxide minerals by diffuse layer modeling can be explained by the formation of only one surface complex. For americium adsorption on corundum, the sole surface species was found to be $\equiv SOAmOH^+$ (log K = (-4.15 ± 0.15)), whereas for both gibbsite and γ-alumina, the only surface species was $\equiv SOAm^{+2}$ (log $K_{gibbsite}$ = (3.18 ± 0.1) and log $K_{\gamma\text{-alumina}}$ (5.42 ± 0.1)). This modeling study will help explain the surface speciation of both americium and neptunium with various aluminum (hydr)oxide phases and the effect of phase transformation on the stability of the surface species. We will also compare the robustness of the diffuse layer and the CD-MUSIC approaches in modeling adsorption reactions for each metal-sorbent pair of interest.

NUCL

Leveraging nitrogen-linkages in the formation of a porous thorium–organic nanotube suitable for iodine capture

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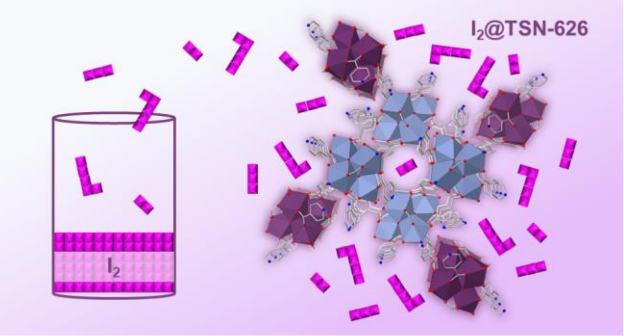
In this work, we report the synthesis, characterization, and application of a novel thorium–organic nanotube, TSN-626. The classification as a metal–organic nanotube (MONT) distinguishes it as a rare subset of metal–organic frameworks (MOFs) and the structure is additionally hallmarked by low node connectivity. TSN-626 is composed of the familiar hexanuclear thorium secondary building units and mixed O/N-donor isonicotinate ligands, which serve as both terminating and bridging moieties. Such Th—N coordination in a MOF had yet to be realized, as hard Lewis acid tetravalent metals have a propensity to bind with electron donors of rival hardness (e.g., carboxylate groups). However, the thorium allowed the formation of key structural Th—N bonds to cap some of the square antiprismatic metal centers, a position usually occupied by terminal water ligands. TSN-626 was characterized by using complimentary analytical and computational techniques: X-ray diffraction, vibrational spectroscopy, N_2 sorption isotherms, and DFT models. The synergy of accessibility through pores, opportunities at the metal-oxo nodes, and pendant N-donor sites allowed an appreciable iodine loading capacity of 955 mg g^{-1} by vapor methods. The crystallization and utilization of TSN-626 justifies further endeavors in the uncharted realm of actinide and N-donor MOFs.



NUCL

Radio-iodine transformations and speciation in the environment as a result of oxidation by manganese minerals: Challenges in iodine fate and transport prediction

***Ilana Szlamkowicz**, iszlamkowicz@knights.ucf.edu, Andrew Fentress, Luke Longen, Vasileios Anagnostopoulos. Chemistry, University of Central Florida, Orlando, Florida, United States*

Radioiodine is a major component of nuclear waste inventory as a by-product of nuclear fission. Specifically, I-129 is a risk driving factor due to its long half-life (16 million years). Past poor waste management has led to accidental releases of radioiodine into the environment, causing adverse effects in the quality of water and the biosphere. In aqueous systems, iodine exists as iodide (I^-), a highly mobile species that interacts minimally with natural substrates, and as iodate (IO_3^-) which is known to sorb and even incorporate into minerals, leading to natural iodine attenuation. Iodate is the prevalent species under oxidizing conditions, with remediation efforts focusing on the oxidation of iodide to iodate as a possible remediation pathway.

Manganese oxides are ubiquitous in nature, with their oxidation potential being disproportionate to their concentration, as small amounts of mineral can significantly affect redox properties of dissolved contaminants. This geochemical control over the fate and transport of redox sensitive risk driving contaminants is attributed to the high reduction potential of the Mn(IV or III)/Mn(II) redox couple and the redox cycling of manganese by microorganisms.

Though manganese oxides are commonplace oxidizing agents, the oxidation of iodide by manganese oxides has not been thoroughly studied. In this work, we investigated the oxidation of iodide by four different manganese oxides under a variety of environmentally relevant conditions, to determine if they provide potential immobilization pathways for iodine in the environment by turning iodide into iodate. It was observed that the reaction kinetics are sensitive to mineral oxidation state, pH, solid:liquid ratio, ionic strength, and initial iodide concentration. Even though the oxidation of iodide to iodate (-1 to +5 oxidation state) is thermodynamically favorable, our results show that redox reaction stops at the molecular iodine intermediate, providing alternative reaction pathways for the fate and transport in the environment.

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Synthesis and evaluation of triarylselenonium salts as precursors for radiofluorination of arenes

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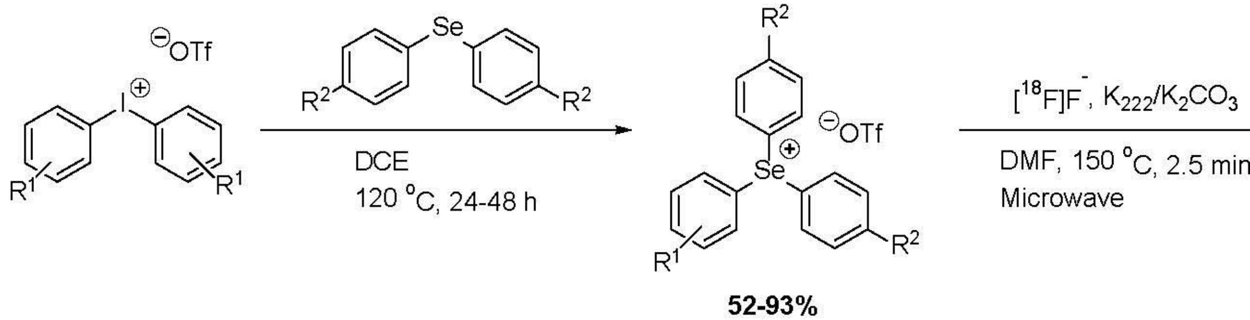
Positron emission tomography is a sensitive imaging tool that can elucidate biochemical processes *in vivo* by using ligands labeled with short-lived positron-emitters, such as fluorine-18 ($t_{1/2}$ = 109.8 min). Several methods for aryl radiofluorination have been developed, but improved and more efficient methods are still sought after. Triarylsulfonium salts are efficient precursors for radiofluorination, but their use is limited to arenes containing electron-withdrawing groups (EWGs). We recently reported that simple diarylselenones may also serve as precursors for aryl radiofluorination. Here we extend this work with regards to the syntheses of more complex salts and the investigation of ring selectivity in radiofluorination. A broad range of functionalized diphenyl-arylselenonium triflates was obtained in moderate to high yields (52-93%) from diaryliodonium salts and commercially available diphenyl selenide. **[^{18}F]1-8**, which bear

EWGs or neutral groups, were produced in moderate to high radiochemical yields (RCYs) by treating the triarylselenonium salts with [^{18}F]fluoride ion in DMF. Electron-rich **[^{18}F]9-12** were produced in low RCYs with an accompanying higher yield of [^{18}F]fluorobenzene as a byproduct from a spectator phenyl group. To improve yields, two salts were made symmetrical (**[^{18}F]13-14**), which led to a three-fold improvement in RCYs (6-34%). Five selenonium salts were then compared to their respective sulfonium analogues, and they showed higher RCYs. These results further indicate the potential value of triarylselenonium salts as precursors for [^{18}F]fluoroarenes.


⊖OTf
R1
R1
Se
R2
R2
DCE
120 °C, 24-48 h
R2
⊖OTf
Se⊕
R1
R2
52-93%
[18F]F-, K222/K2CO3
DMF, 150 °C, 2.5 min
Microwave

Scheme 1. Synthesis and evaluation of triarylselenonium salts as precursors for radiofluorination of arenes

NUCL

Coordination Chemistry of Tetrazolate-derived Ligands with lanthanide and actinide elements

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The lanthanide and actinide elements have been used in diverse practical fields ranging from energy generation to life sciences. However, the separation of lanthanides is challenging due to their similar ion radius and inert redox activity in aqueous media leading to chemical similarities between these elements. The development of simple and cost-effective lanthanide separation methods is highly desirable. A series of tetrazolate-derived ligands build unique periodic trends, due to their rich coordination chemistry, which amplifying differences of lanthanide ions, which allows their application on lanthanide separations. In addition, Intervalence charge transfer (IVCT) is rare in f-element systems since heavily localized f-electrons and weak overlap between the f-orbitals and the ligands. Meanwhile, the research of transuranic complexes exhibiting delocalized f-electrons will help elucidate f-electron interactions and bonding character. Tetrazolate-derived ligands are ideal bridging ligands due to conjugation, their small size, and the easily accessible lone pairs on the nitrogen atoms. The synthesis of binuclear compounds of plutonium and 5-pyrimidyl-tetrazolate lays a solid foundation for future redox and charge transfer studies with plutonium and more transuranium elements.

NUCL

Examining plutonium(III/IV) chemistry, a case when cerium is not representative

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The reduction and oxidation (redox) chemistry of plutonium is well known to be complicated in air and water. Aside from the difficulties of working with radioactive elements, the high level of speciation exhibited by plutonium means that a full understanding of the redox chemistry of plutonium is critical for tracking the element through nuclear and environmental settings. While cerium is often used as a non-

radioactive analog of plutonium to a high degree of success, due to their similar M(III)/M(IV) redox couples. Recent work discussed here examining the structure and bonding in metal-bromide-phosphine oxide complexes displays divergent reactivity between plutonium and cerium. The differences in structural and bonding features will be discussed along with comparisons to similar *f*-element complexes. This work highlights the importance of radiochemical experiments.

NUCL

Iridium Adsorption on Gold-Coated Silicon Detectors Functionalized with Thiolate Self-Assembled Monolayers

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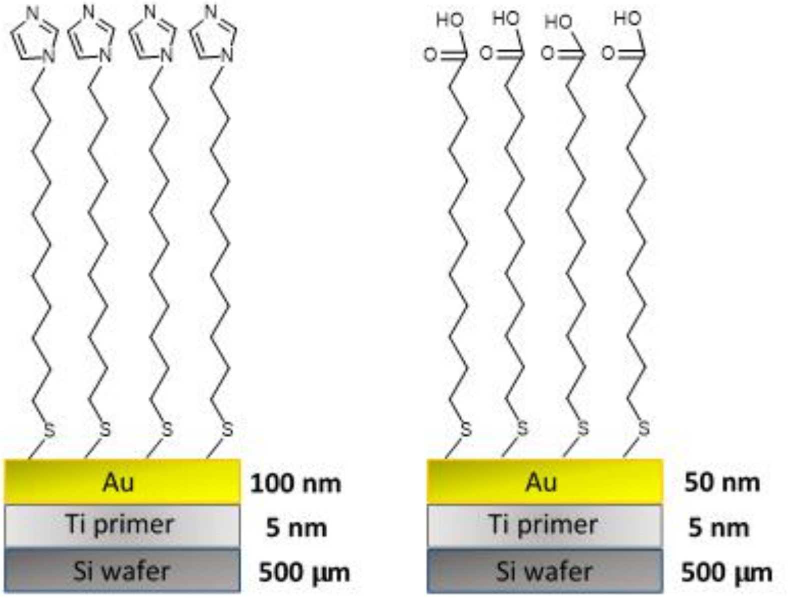
One of the first uses of gold-coated silicon in the field of heavy elements was reported during the chemical characterization of element 112, Cn. The results showed that the chemical sorption of the named element occurred better on the modified surfaces rather than on the non-modified. However, element 113, Nh, showed an enhanced reactivity towards gold, preventing the proper chemical characterization of this element. Therefore, a need for new chemically modified silicon detectors has emerged. Such detectors will selectively bind the atoms of interest but with weaker interactions. Meitnerium is expected to be a member of Group 9 of the periodic table, and new chemical research is needed to confirm this classification. In this project, the self-assembly of two commercially available thiols on gold-coated silicon chips that mimic functionalized gold-coated silicon detectors has been studied. The main goal of the devices of such kind is to compare adsorption properties of meitnerium’s lighter homolog(s) during online cyclotron-based experiments.
The functionalized chips were characterized via atomic force microscopy, cluster secondary-ion mass spectrometry, X-ray photoelectron spectroscopy, ellipsometry, and neutron activation analysis**.**
This talk will include the newest results on the adsorption kinetics of iridium and rhodium (meitnerium’s lighter homologs) on functionalized gold-coated substrates from aqueous solutions, the effect of HCl concentration on the sorption efficiency, and the sorption mechanism. The comparison of iridium (the heaviest homolog) sorption both from the aqueous and the gas phases using thiols with imidazole and carboxylic acid functional groups grafted on either gold-coated substrates or alpha-detectors, respectively, will be discussed.



Schematic diagrams of the substrates investigated in this study.

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Development and Biodistribution Studies of ^{77}As-Labeled Trithiol RM2 Bioconjugates for Prostate Cancer

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Recent progress on the production of ^{72}As (2.49 MeV β^{+}_{avg}, $t_{½}$=26.1 h) and ^{77}As (0.225 MeV β^{-}_{avg}, $t_{½}$=38.8 h) has facilitated their evaluation as a potential “theranostic pair” for PET imaging and radiotherapy. Previously reported ^{77}As-labeled trithiol bioconjugates showed high *in vivo* stability, but cleared through gastrointestinal system due to their high lipophilicity. In this work, a more hydrophilic trithiol chelator with two carboxylic acid groups was synthesized and conjugated to the RM2 peptide - a gastrin-releasing peptide receptor (GRPR) antagonist for targeting of GRPR in prostate cancer.
No carrier added (nca) ^{77}As was produced via neutron irradiation of enriched $^{76}GeO_2$ followed by decay of ^{77}Ge to ^{77}As. Arsenic-77 was separated as $[^{77}As]H_2AsO_4^-$, which was reduced and complexed with a monothiol transfer ligand prior to radiolabeling. The chelator was conjugated to the RM2 peptide via solid phase peptide synthesis through

two different linkers, Ser-Ser and Glu-Ser. The RM2 trithiol bioconjugates were radiolabeled with nca ^{77}As and compared in initial biodistribution studies. Radiolabeling of the RM2 conjugates with ^{77}As resulted in over 85% radiochemical yield for ^{77}As-Ser-Ser-RM2 and 90% for ^{77}As-Glu-Ser-RM2. Both radiotracers demonstrated excellent *in vitro* stability (≥ 90% remaining intact through 24 h in PBS buffer). Both tracers were found to be more hydrophilic (log $D_{7.4}$: -0.2 for ^{77}As-Ser-Ser-RM2 and -1.3 for ^{77}As-Glu-Ser-RM2) than our previous version of ^{77}As-ester-RM2 (log $D_{7.4}$: 0.7). Biodistributions of both radiotracers in healthy CF-1 male mice demonstrated blockable pancreatic uptake (%ID/g at 1 h in pancreas: 11.0 for ^{77}As-Ser-Ser-RM2 and 7.8 for ^{77}As-Glu-Ser-RM2 vs. 1.9 and 1.8 with blocking, respectively) indicating specific GRPR uptake. Both radiotracers demonstrated mainly hepatobiliary clearance. Compared to ^{77}As-Ser-Ser-RM2, ^{77}As-Glu-Ser-RM2 showed slightly higher renal clearance (%ID/organ at 24 h in urine: 24.8 for ^{77}As-Glu-Ser-RM2 vs. 18.3 for ^{77}As-Glu-Ser-RM2) due to the higher hydrophilicity of Glu than Ser. Further studies to increase the hydrophilicity of the tracer for faster renal clearance are underway.

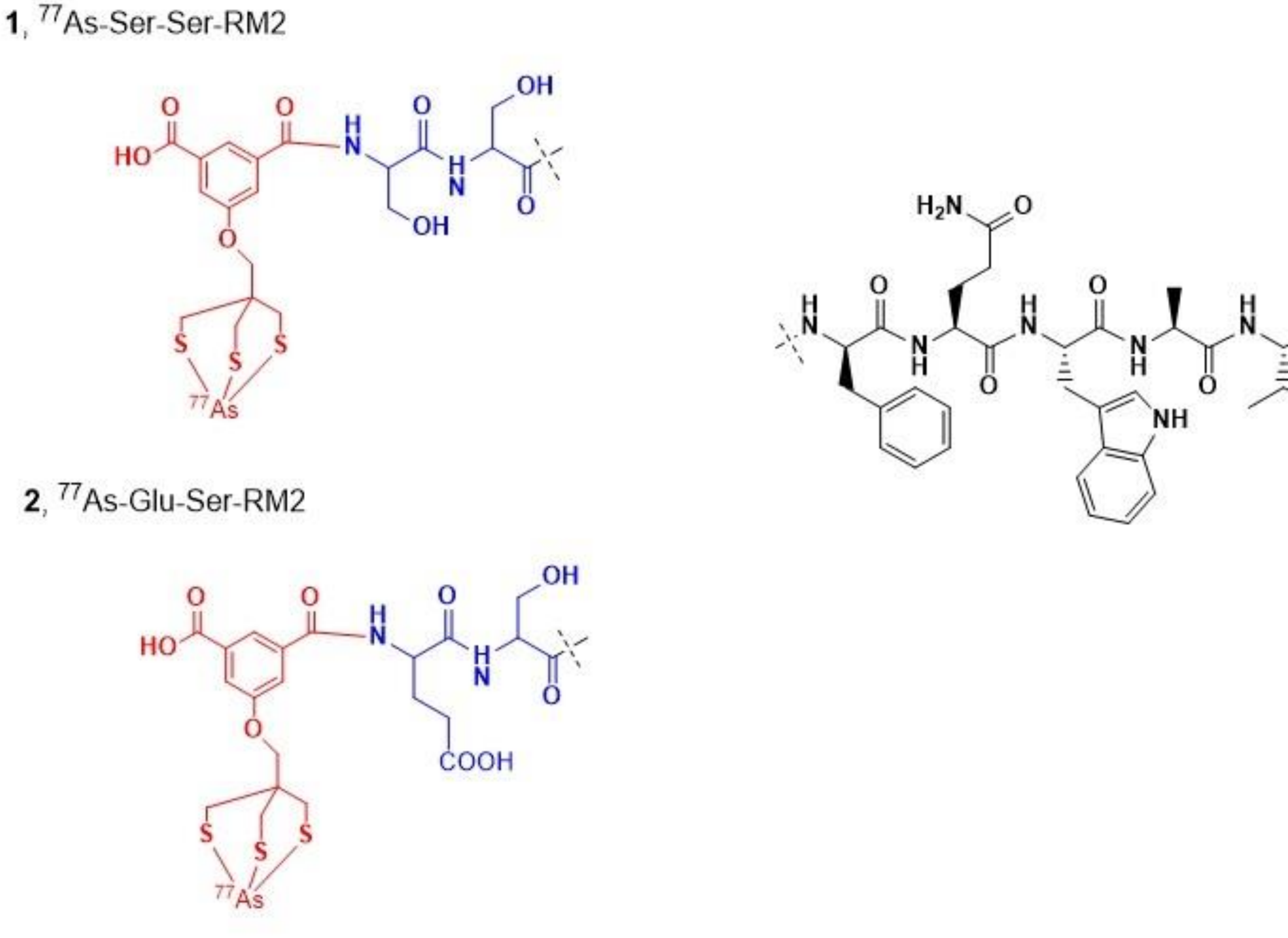

Figure 1. Structure of the bioconjugates, peptide **1** ^{77}As-Ser-Ser-RM2 a

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Solid-phase radiosynthesis accompanied by photocleavage strategy for synthesis of radiopharmaceuticals

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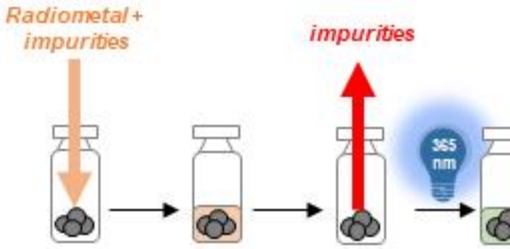
The clinical translation of new radioisotopes is accelerated by ease of synthesis of radiopharmaceuticals, specifically by shake-only kit formulations. To date, the routine use of radioisotopes using room temperature labeling compatible kits is hampered by the lack of corresponding radiochemical labeling approaches. Additionally, emerging

isotopes such as ^{44}Sc and ^{68}Ga require secondary purification of cyclotron or generator eluate, which significantly reduces the ability of radiopharmacies to produce large numbers of patient doses.

We proposed that these shortcomings could be addressed by a radiochemical synthesis approach that combines separation and radiochemical labeling steps efficiently and produces a ready-to-inject radiopharmaceutical using a resin-based, one-pot procedure. We demonstrate, that a solid-phased radiolabeling approach, followed by photochemical cleavage of the ready-made radiopharmaceutical is a convenient and feasible approach to concerted capture and radiolabeling of bifunctional bioconjugates. We successfully achieved the on-resin radiolabeling, subsequent photocleavage and formulation of two clinically translated radiopharmaceutical precursors, NOTA-Aca-BBN (targeting gastrin-releasing peptide receptor) and NOTA-PSMA on resin with ^{67}Ga in under 30 minutes. We will also discuss the feasibility to expand of the scope of this radiolabeling approach to biomolecules and other radioisotopes of interest.



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Development of Aqueous Titanium(IV) Chemistry Towards Applications in Radiomedicine

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The radioisotope titanium-45 has many ideal properties for PET imaging, including a workable 3.09 h half-life, 85% positron branching ratio, minimal production of concurrent gamma rays, and high cross-section reaction from a naturally monoisotopic scandium-45 target. However, this isotope remains nearly unused. Due to its extremely hydrolytic and oxophilic nature, the titanium(IV) ion remains challenging to suitably stabilize in aqueous environments. At pH values less than 4, titanium(IV) chelates must outcompete the strong mono-, di-, and tri-hydroxides. At neutral pH, the low solubility and high stability tetrahydroxide dominates, and at basic pH, the anionic pentahydroxide dominates. Standard donor groups used in radiomedicine such as hydroxamates and 1,2-HOPO derivatives are far too acidic, and therefore only exist at acidic pH. This discrepancy between the extreme hard Lewis acid character of titanium(IV) and the poor match of standard radiometal chelators has made the chelation chemistry of this ion incredibly difficult. In addition, as titanium is derived from a natural scandium target, the resulting titanium isotope must be purified from bulk scandium to create efficient chelation. While high specific activity solutions of titanium-45 can be produced, the process is long, and therefore a significant loss of activity is unavoidable. By evaluating chelators that effectively coordinate titanium, but have low specificity for scandium, the necessity of this lengthy purification can be circumvented, thus creating a much more efficient use of produced titanium-45.
In order to form stable chelate systems with titanium(IV) at a wide range of pH, highly basic ligands must be employed. Herein we describe methods for evaluating the potential of highly basic chelating ligands with titanium for use in the development of bifunctional titanium-45 based radiopharmaceuticals, as well as efficient radioisotope separation.

NUCL

Comparing stabilities of bifunctional N_2O_2 schiff base ligands for Tc(III) and Re(III) radiopharmaceuticals

***Andrew Mitchell**, awmxfp@mail.missouri.edu, Jakob E. Baumeister, Li Ma, Steven P. Kelley, Silvia S. Jurisson. Chemistry, University of Missouri, Columbia, Missouri, United States*

Rhenium ($^{186/188}$Re) and technetium (^{99m}Tc) radioisotopes have shown significant promise for therapeutic and diagnostic applications, respectively. The two metals have very similar chemistries, and as such are considered a theranostic matched pair. Extensive work has gone into designing ligands for use with ^{99m}Tc due to its ideal imaging properties (6-h half-life, 140 keV g) leading to prevalent use in medicine. Slight

differences between Tc and Re reactivity mean that not all the existing ligands used with ^{99m}Tc are suitable for use with Re. However, complexes of the type *trans*-$[Tc(PR_3)_2(\text{Schiff base})]^+$, known as the Tc Q-series have proven useful for myocardial perfusion imaging and multidrug resistant (MDR) tumor imaging, and have potential to work with $^{186/188}$Re as well as ^{99m}Tc.
Salicylaldehyde based N_2O_2 Schiff base ligands have been used to generate a range of Tc(III) and Re(III) compounds for potential use as radiopharmaceuticals. In addition to theranostic potential, these N_2O_2 Schiff base ligands may also serve as bifunctional chelates by appending a targeting vector onto the backbone of the ligand. We have shown that chelates of this type differing only in their backbone makeup have significantly different rates of conversion from the *trans*-M(III) to *cis*-M(V) configuration, which occurs as the metal centers are oxidized. These oxidation rates differ not only between complexes with different backbones, but also between complexes of the same ligand with different metal centers. Characterization using NMR, UV-vis, X-ray crystallography, cyclic voltammetry, and mass spectrometry as well as HPLC separation of radiolabeled complexes have given insight into these stability differences, which will be discussed.

NUCL

Development of radiochemical separation procedures for producing high isotopic purity ^{48}V from a ^{48}Cr/^{48}V generator

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At the Facility for Rare Isotope Beams (FRIB), various potentially useful exotic radionuclides will be regularly produced as byproducts of spallation and fragmentation reactions of unused primary beams in an aqueous beam dump. One such radionuclide is ^{48}V, for which a highly isotopically pure sample could be used as a solid target in direct nuclear reaction studies beneficial for the nuclear data and Stockpile Stewardship programs. Specifically, for high precision cross section measurements of (n, γ) and (n, p) reactions with ^{48}V, the ^{48}V target must have minimal ^{49}V impurity (atoms of ^{48}V/atom of $^{49}V = 10^4$).

One way of obtaining isotopic pure ^{48}V is via a ^{48}Cr/^{48}V generator using ^{48}Cr collected and chemically separated from V in the aqueous beam dump at FRIB. Preliminary results suggest it will be difficult to obtain good initial separation of the Cr and V accumulated on an anion exchange column during harvesting attempts with the FRIB beam dump water due to the loading conditions. As such, much of the proceeding work was directed towards optimizing batch elution processes to extract stable anionic Cr and V species (>90% and >75% for Cr and V respectively) from AG 1-X8 anion exchange resin and developing a subsequent separation methodology to separate those two elements. This talk will cover both the cold and hot experiments performed to demonstrate a working protocol for the production of a ^{48}Cr/^{48}V generator.

NUCL

Radiation Induced Physical Properties of Halogenated Organic Crystals

***Samantha Kruse**, samantha-kruse@uiowa.edu, Len MacGillivray, Tori Forbes. Chemistry, The University of Iowa, Iowa City, Iowa, United States*

Radiation Induced Physical Properties of Halogenated Organic Crystals
Samantha Kruse, Len R. MacGillivray, and Tori Z. Forbes
Department of Chemistry, University of Iowa, Iowa City, IA 52242, United States

High ionizing radiation studies have been largely limited to inorganic and hybrid materials, thus a fundamental understanding of high ionizing radiation effects on purely organic materials is needed. In this study, we report the structural effects of high ionizing radiation on both single- and multi-component organic crystalline materials. The use of multicomponent crystals (i.e., cocrystals) afford chemical and mechanical tunability which have the potential to demonstrate mitigation of radiation induced physical properties. Single- and multi-component crystalline materials were characterized by single-crystal X-ray diffraction (SCXRD), powder X-ray diffraction (PXRD) and NMR both pre- and post-irradiation using Cs-137 monoenergetic gamma radiation source. Our results demonstrate a general decrease in crystallinity revealed by mosaicity and decrease in X-ray peak intensity with respect to the coherent domains of diffraction. Preliminary results suggest the stronger intentional packing within cocrystals mitigates radiation induced physical properties observed in their single component counterparts. CrystalExplorer software was utilized to create Hirsfield fingerprint plots to evaluate bonding energy in the structure. Bonding energy was evaluated using a Density Functional Theory program within CrystalExplorer allowing an understanding of structure/function relationships between the cocrystals and its single component counterparts. Finally, we discuss a mechanistic pathway to explain the radiation induced physical properties observed in one of the single component organic crystals.

NUCL

Investigating Structural Incorporation of Li into Sol-Gel Fabricated Lithium for Breeder Blanket Materials in Fusion Reactors

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Solid-state lithium compounds, such as γ-$LiAlO_2$, are proposed materials to use as tritium breeders in fusion reactors. The purpose of this study was to investigate the

chemical behavior and the structural incorporation of lithium in lithium aluminate samples formed via the internal gelation sol-gel process. Internal gelation is a versatile synthesis method wherein hydrous metal oxide gels are formed through the heating of colloidal precursors. This process can produce large quantities of high-quality metal oxide microspheres and enables the tuning of structural properties. Lithium does not form a gel with this process, but aluminum forms a strong gel that can be used as a carrier for lithium. FTIR, Raman spectroscopy, P-XRD and NMR were used to analyze the samples throughout the gelation process to gain insights about lithium incorporation. The results indicate that lithium does not significantly influence the gelation system until after the gels have been washed and dried, wherein lithium coordination with oxygen is apparent and lithium appears to influence the coordination of aluminum. Upon calcination, the initially amorphous samples appear to undergo a transition through a partially crystalline layered double hydroxide structure before full calcination yields γ-$LiAlO_2$ and $LiAl_5O_8$. The lack of alumina phases indicates a homogenous distribution of lithium. However, the presence of the lithium deficient pentaphase lithium aluminate indicates lithium deficiency in the fully-calcined sample. Future studies will focus on applying the insights about the lithium incorporation gained by our studies to the synthesis of stoichiometric lithium aluminate precursors for breeder blanket applications.

NUCL

Facile formation and in vivo validation of robust Sc-^{18}F ternary complexes for molecular imaging

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As the most widely used clinical isotope, fluorine-18 is an indispensable tool in diagnostic cancer imaging with positron emission tomography (PET). However, incorporation via C-F bond formation often involves low-yielding, multi-step radiochemical syntheses in organic solvents, incompatible with biological targeting vectors. Current alternatives to C-F bond formation are hindered by production of low specific activity radiopharmaceuticals (B-F), incompatibility with aqueous solvents (Si-F) and low in vivo stability (Al-F and Ga-F). Furthermore, fluorine-18 lacks a chemically matched therapeutic isotope. To address this, we hypothesized that our previously developed chelation platform, H_3mpatcn, shown to form robust coordination complexes with scandium radioisotopes, can also form stable Sc-F ternary complexes. To validate this hypothesis, we employed density functional theory calculations to assess the feasibility of forming a $[ScF(mpatcn)]^-$ complex, synthesized and characterized the complex using NMR, and carried out preliminary optimization of radiolabeling conditions to form the corresponding $[^{18}F]$-[ScF] complex. A comparison of a prostate-specific membrane antigen (PSMA) targeted probe radiolabeled with Sc-^{18}F or ^{47}Sc demonstrates no statistically significant differences in biodistribution and tumor uptake in a mouse model of prostate cancer. Sc-^{18}F ternary complexes can be formed in 100% aqueous media between 60-100 in 30 minutes, providing a convenient radiofluorination approach for targeted, ^{18}F-based radiopharmaceuticals, and we propose that Sc-^{18}F complexes can serve as an unusual diagnostic match for the therapeutic ^{47}Sc isotope with excellent potential for clinical translation.

NUCL

Uranium extraction by precipitation with PAMAM dendrimers

***Jacqueline Ferrier**, jferrer1@uci.edu, Lauren Obrien, Kara Thomas, Dmitry A. Fishman, Mikael Nilsson, Sarah Finkeldei. Chemistry, University of California Irvine, Irvine, California, United States*

The use of nuclear power also generates nuclear waste. Since this waste is radioactive for thousands of years, it needs to be safely stored in a deep geological repository. An alternate solution to the open nuclear fuel cycle concept is to close the nuclear fuel cycle. Closing the nuclear fuel cycle not only reduces the amount of nuclear waste that needs to be safely disposed of, but also allows recycling the so-far not utilized fissile uranium 235 of the used nuclear fuel. We have utilized generation 2 (G2) polyamidoamine (PAMAM) dendrimers to separate uranium by precipitation from waste simulant solutions and exploit complementary techniques to gain insights into the separation process, such as laser fluorescence spectroscopy and dynamic light scattering. Future studies will focus on radiation experiments at the UCI nuclear TRIGA reactor to gain insights into the effect of radiation towards the uranium extraction efficiency.

NUCL

Fuel Cycle & Fuel Disposition for Closing the LWR Fuel Cycle with a Fast Chloride-Molten Salt Reactor System.

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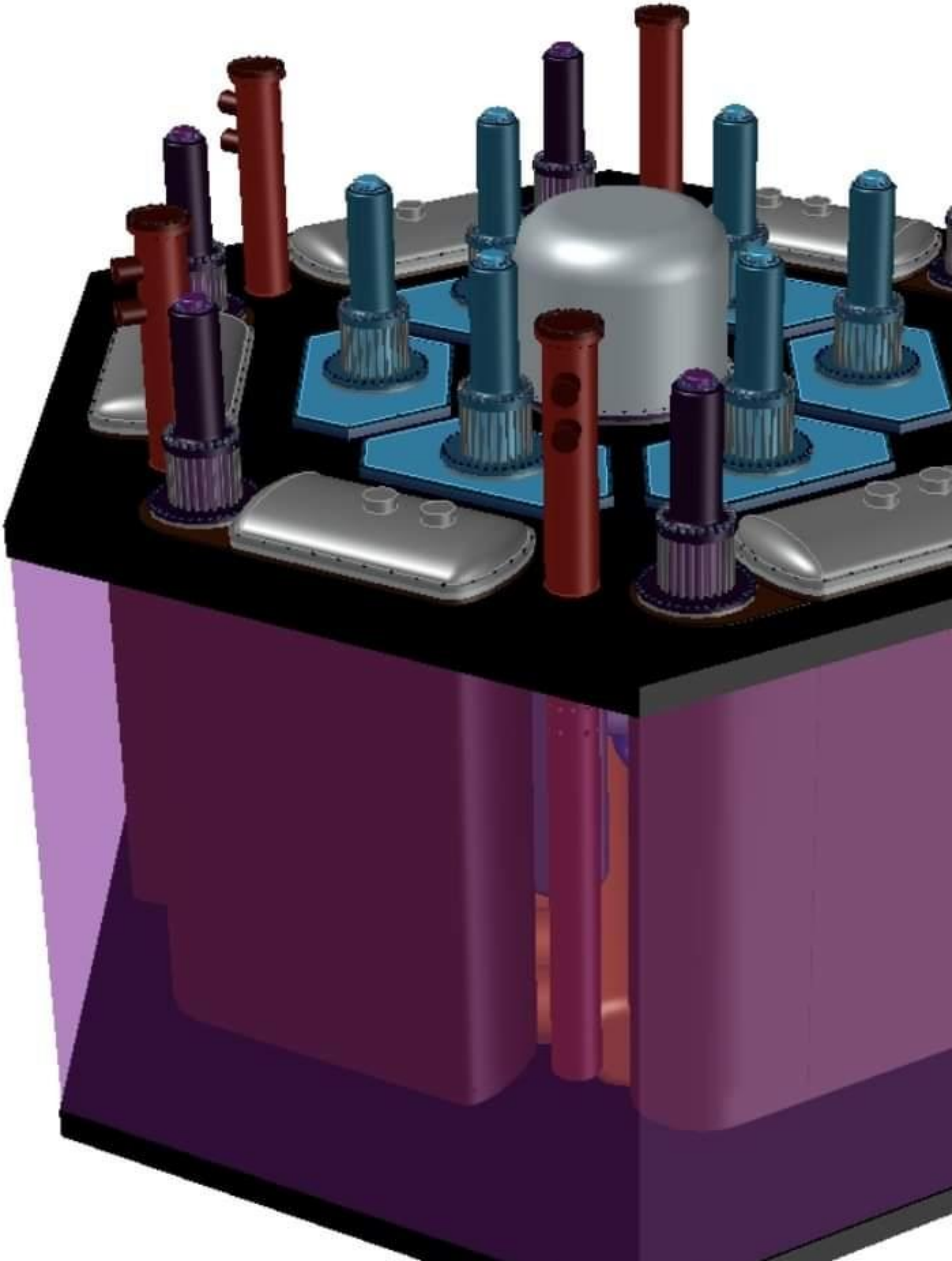
This presentation will discuss the Fast Chloride-Molten Salt Reactor (FC-MSR) at a high level to support fuel cycle discussions. The presentation will discuss different processes for the FC-MSR for:
FC-MSR Front End from LWR Backend of the fuel cycle
A) Converting SNF to Start Up Fuel for a FC-MSE, 1) (prefered) as a method of denaturing weapons grade Plutonium as the primary fissile, 2) as a method of consuming separated reactor grade Plutonium fissile, 3) fissile from SNF without Plutonium separations, 4) SNF Zirconium clad recycling, 5) fissile from HALEU
Main Lifetime Fuel Cycle 3kg/day of SNF
B) Converting SNF to Feed-In Fuel for the all fuel additions following Start Up without added fissile.
C) FC-MSR on-line Purification
Purification & Waste

D) 40-60yr periodic purification to remove excess fission products, actinide & chloride recycling
E) Options for FC-MSR waste product stabiliztion & disposition

Conclusions/Opportunies relative to DGRs



Fast Chloridr-MSR 3000MWth/1200MWe or process heat

NUCL

Machine learning and data mining applications in nuclear waste repository reactive transport modeling and performance assessment

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A fundamental approach to Nuclear Waste Repository research involves the collection of experimental data in a laboratory setting, development of empirical and/or mechanistic numerical models representing those observations, and application of these models (or Reduced Order Models) into reactive transport and performance assessment models as predictive tools for informing society of impacts and risks associated with nuclear waste repository scenarios. Both the assimilation and interpretation of experimental data must take advantage of ML opportunities to improve predictive tools, particularly from the standpoint of uncertainty quantification. However, a number of challenges need to be met in the coming years to successfully integrate these new data science approaches. A recent effort at Lawrence Livermore National Laboratory (LLNL) has led to the developement of a data digitization pipeline to simulate radionuclide sorption that is amenable to both ML as well as traditional surface complexation modeling. With the LLNL Surface Complexation/Ion Exchange (L-SCIE) database that is already available, we have begun developing mechanistic surface complexation and ML models of radionuclide retardation specific to the nuclear waste disposal problem. In this presentation, we will introduce this novel approach to mining community data to develop robust models of radionuclide reactive transport.

NUCL

Monitoring Np Processing with Optical Spectroscopy for the ^{238}Pu Supply Program.

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The domestic capability to annually produce kilogram quantities of ^{238}Pu for space power applications is being restarted at Oak Ridge National Laboratory. Neptunium-containing targets are irradiated at High Flux Isotope Reactor and processed through a series of radiochemical separations at the Radiochemical Engineering Development Center. Methods to enable the ^{238}Pu Supply Program to continue scaling up production are being evaluated, including remote analysis using optical spectroscopy for real-time analytical measurements in hot cell environments. The timely quantification of concentrated Np in nitric acid solutions is needed for Np processing, which is a year-

round, ongoing process at the Radiochemical Engineering Development Center. Several factors render the quantification of Np in aqueous solutions challenging, including simultaneous existence in multiple oxidation states, high extinction coefficients, susceptibility to hydrolysis, and ability to coordinate with a wide range of ligands. The key findings from several studies completed during a recent demonstration campaign, Campaign 5, and promising areas for future development will be discussed.

NUCL

Analytical tools for measuring Nd and Pm for chemical separations

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A high demand currently exists for Pm, namely ^{147}Pm, which is used for ß batteries and thin-film measurements. Promethium-147 can be indirectly produced from the decay of neodymium-147, which is produced via (n,γ) reaction upon irradiation of enriched neodymium-146. Neodymium-147 has a 10.98-day half-life and decays to promethium-147 with a 2.6234-year half-life. Once a significant amount of ^{147}Pm has grown-in, it can be separated from the Nd. However, current radioanalytical methods can make it difficult to determine the presence of ^{147}Pm because ^{147}Nd and ^{147}Pm both exhibit a common γ-ray energy. This work explores alternative methods for confirming separation using spectrophotometry.

NUCL

Sustainability of the nuclear fuel cycle while transitioning from Gen II/III to Gen IV reactor systems

***Patricia Paviet**, patricia.paviet@pnnl.gov. Nuclear Sciences, Pacific Northwest National Laboratory, Richland, Washington, United States*

Currently, the United States operates 94 commercial nuclear power reactors in 29 U.S. states with a combined installed capacity of approximately 100 GWe. These pressurized water reactors (PWRs) and boiling water reactors (BWRs) generated approximately 19.7% of the US electricity demand in 2016. The current and historic U.S. reactor fleet (of which an additional 36 commercial plants were once operated, but are now permanently closed) has, to date, generated more than 84,000 metric tons heavy metal (MTHM) of spent nuclear fuel (SNF) —fuel withdrawn from a nuclear reactor following irradiation, which is referred to as “used” fuel by the nuclear industry because it contains potentially reusable uranium and plutonium—are in temporary storage at 75 reactor sites scattered across 33 states. This inventory may continue to grow at approximately 2,000 MTHM per year for at least two more decades. Although the SNF inventory continues to be stored and managed safely, the nuclear fuel cycle is facing a key challenge, which is the sustainability of the nuclear fuel cycle, which implies closing the

fuel cycle. This presentation will examine how recycling of used nuclear fuel, which is known since the 1950s, can support advanced reactor systems such as sodium fast reactors (SFR) or liquid fueled molten salt reactors (MSRs), which advanced waste-forms are being developed and how Gen IV reactor systems can contribute to the mitigation of climate change and global warming while saving energy resources.

NUCL

Characterisation of materials from the Hunterston A spent nuclear fuel storage pond

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Nuclear power plants can become heavily contaminated with fission and corrosion products during their operational lifetime. These contaminated materials give rise to high doses of radiation and heat, increasing risk to workers and the surrounding environment. Rapid identification of radionuclides and the extent of their penetration into nuclear materials could help reduce the volume of intermediate level waste (ILW) produced during decommissioning and minimise the costs of post operation clean out (POCO) procedures. Characterisation of legacy samples provides key insight into the long-term contamination effects of storing nuclear waste and is vital towards developing an appropriate strategy for future decontamination and decommissioning tasks.

A concrete core was obtained during the decommissioning of the Hunterston A spent fuel storage pond. The core was taken from the middle of the pond wall, where it was exposed to the contaminated pond water. A multi-layered protective coating was applied to the concrete walls during plant operations to prevent uptake of radionuclides. The majority of the activity of the core is due to the presence of ^{90}Sr, ^{137}Cs, ^{241}Pu, and ^{241}Am which has been shown to be associated with the painted surface. Autoradiography results have also indicated that some activity may have penetrated through to the bulk concrete. Sorption experiments were completed using concrete coupons in stable Sr, Cs, or Co doped solutions to determine the effects of contamination within the bulk concrete material. Samples were analysed using Laser-Induced Breakdown Spectroscopy (LIBS) to assess its capability as a rapid, multi-elemental characterisation technique within the nuclear industry.

Furthermore, plastic samples were taken from a pontoon which was floated on the pond water and used by workers during decontamination operations to reach the inside of the pond walls. Jet washing of the pond walls caused the wastewater to splash on top and down the sides of the pontoons, contaminating them in the process. Gamma spectroscopy indicated that the radioactivity within the samples is predominantly caused by ^{137}Cs and ^{241}Am. Autoradiography was performed on these discs to map the location of the radiation and identify areas of increased contamination for further analysis. LIBS analysis was also carried out to further evaluate its ability to identify radionuclide species on materials used throughout the nuclear industry at concentrations found *in-situ*.

NUCL

Nuclear Chemistry Revival by Design – new activities at UC Irvine

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A summary of recent progress in materials chemistry involved in the synthesis and performance of advanced nuclear fuels, as well as their disposal to increase the safety and efficiency of the nuclear energy sector will be presented. Utilization of wet-chemical, innovative synthesis approaches in combination with a wide range of characterization tools, facilitate a better understanding of the structure-property relationships of advanced nuclear fuel and its waste forms. This knowledge is applied to tailor and fine-tune materials with targeted functionality that relies on a well-defined set of physical properties. Such approach enables to fabricate a large variety of feedstock for high-performance nuclear fuels for current and future reactor types (LWRs, SMRs, HTGRs), while suppressing airborne radioactive particles. Several classes of materials will be discussed, including complex oxides as potential nuclear waste forms that have received an increased focus of attention due their unconventional response to radiation damage enabling to study their order/disorder transition which is heterogeneous across different length scales. In addition, examining the extent and mechanism by which structural defects in UO_2 pellets affect thermal conductivity provides a step forward in developing a thorough understanding of heat transfer in nuclear fuel under real reactor conditions. The systematic understanding of the role of defects as well as dopants such as Mn, Cr towards the enhanced performance and safety of high-performance fuel will be discussed. Besides novel fuels, the research aimed to advance the current state of the art for nuclear waste management will be discussed. Ongoing efforts at UCI are supported by the recently established cluster of nuclear chemistry laboratories in combination with the TRIGA reactor and characterization facilities and will be briefly introduced.

NUCL

Determination of Organic Acids & Inorganic Anions in Lithium Borated Nuclear Power Plant Waters using Ion Chromatography

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For nuclear power plants using a pressurized water reactor (PWR), the primary coolant includes boric acid as a water-soluble neutron absorber to control the nuclear reaction.1 Boron concentrations at the beginning of the fuel cycle may be as high as 2500 mg/L (ppm), corresponding to 1.4 percent boric acid. At the high temperature and pressure in the PWR, this boric acid concentration can form crud that deposits metal oxides on the fuel rods. To prevent crud buildup, lithium hydroxide is added to increase the pH300 °C to 6.9 or higher. However, trace anionic impurities at low- or sub-µg/L (ppb) concentrations from the water source (or materials such as ion-exchange polisher resins) can serve as catalysts for corrosion.

A key application for minimizing corrosion in pressurized water reactors in nuclear power plants is the determination of inorganic anions and organic acids. The experimental approach combines a large volume direct injection, and tetraborate eluent produced with assistance of electrolytic eluent generation to analyze lithium borated water for fluoride, formate, chloride, and sulfate with the addition of a continuous regenerating cation trap column (CR-CTC III) to remove lithium and other cations from the sample. The presence of lithium can interfere the determination of fluoride.

NUCL

Quantitative Laser-Induced Breakdown Spectroscopy in the field: the next step in field nuclear analysis

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The quantative analysis of radionuclides and their products has always been a challenge from a non-proliferation point of view to the environmental impact of these compounds. While traditional radiation-based spectroscopy has established a strong presence in the area, elemental analysis using mass spectrometry or optical emission spectroscopy has always showed a record of high sensitivity and low limits of detection. One of the techniques of interest since the 1970's has been Laser-Induced Breakdown Spectroscopy (LIBS).
LIBS uses a laser pulse for the sampling and excitation of any substrate in order to detect analytes of interest via elemental optical emission. While LIBS has become a strong analytical technique in the laboratory, recent developments in field instrumentation fulfill the dreams of early groups for elemental optical analysis in the field: good portability combined with high resolution spectroscopy and long-lasting battery life. Nonetheless, LIBS stays very sensitive to matrix effects. One approach to counter them and provide a global quantitative elemental analysis is to establish calibration-free protocols for handheld LIBS instruments.
This presentation will quickly review the use of LIBS for nuclear analysis (with a focus on field instrumentation) and show the results from our group on using LIBS for Tc

detection and analysis, and the development of protocols for quantitative portable LIBS based on calibration-free approaches.

NUCL

Electrochemical Recovery of UO_2 from the Direct Dissolution of U_3O_8, UO_2, and UO_3 in Ionic Liquid

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This work explores the dissolution, speciation, and recovery of UO_2 from U_3O_8, UO_2, and UO_3 dissolved in ionic liquids and applying the results to existing nuclear forensics data. Ionic liquids are designed solvents made up of a paired cation and anion, usually large organic compounds. By using ionic liquids as the solvent, the uranium compounds can be analyzed using a variety of spectroscopic techniques that will provide information on the mechanism of dissolution. Ionic liquids are also uniquely suited (because of the inherent charge pairs) for electrochemical study, which will provide information on the speciation in solution in addition to the recovery of uranium through deposition. The uranium oxide solids in ionic liquid are dissolved using ozone gas. Once dissolved, the solution is electrochemically reduced for the collection of uranium deposits. These deposits are analyzed by SEM/EDS, showing the presence of recovered uranium oxide. Although some work has been performed on actinide speciation and deposition in ionic liquids, dissolution using ozone is novel and the subsequent electrodeposition is not comprehensive. The methods derived in these studies may provide advances in separation, recovery, and utilization of uranium.

NUCL

Hyper-stoichiometric uranium dioxides: Rapid synthesis and irradiation-induced structural changes

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This work reports the preparation of $UO_{2.12}$ nanomaterials and thin films through a rapid and simple combustion process in *uranyl nitrate – glycine – water* reactive solutions. Thin films of $UO_{2.12}$ up to 300 nm thicknesses were deposited by spin coating of reactive solutions on Al substrate followed by brief (20 min) annealing at 400°C. Irradiation of

films with Ar^{2+} ions (1.7 MeV energy, fluence up to 1 x 10^{17} ions/cm^2) shows unusual defect-simulated grain growth and chemical mixing of $UO_{2.12}$ with the substrate. We also report the in-depth mechanism and kinetics of combustion synthesis reactions. The extracted activation energies from a set of thermal analysis measurements identified the rate-limiting step of the process as the partial oxidation of glycine by nitrogen dioxide released from the decomposition of $UO_2(NO_3)_2$. However, the exothermic decomposition of a coordinate compound containing the uranyl moiety, glycine, H_2O, and NO_3^- groups determines the maximum combustion temperatures. *In situ* transmission electron microscopy (TEM) and electron diffraction analysis show that the decomposition of the coordinate compound produces UO_2, which incorporates oxygen at the cooling stage of the combustion process to form $UO_{2.12}$.

NUCL

Optimizing Synthetic Conditions for the Stabilization of Divalent Actinides in the Solid-State with Organic Macrocycles

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Synthesis with the lanthanide and actinide elements is commonly constrained to the trivalent states of these elements except for some of the early actinides (Th, U, Np, Pu) that can access high valent states owing to influences such as spin-orbit coupling and relativistic effects. To this point, isolation of the each of the lanthanide elements (aside from Pm) in their divalent states has been achieved as well as some of the early actinides in the solid-state in the form of single-crystal structures. As the limits of synthetic chemistry at the end of the periodic table are pressed, the behavior of the divalent actinides becomes increasingly relevant. Exploration of divalent lanthanide analogues (Sm, Eu, and Yb) and their interactions with macrocycles in the solid-state has yielded insight into potential strategies for obtaining crystal structures containing divalent actinides. Furthermore, these studies have elucidated some interesting behavior in the divalent lanthanides as a result of not only the local coordination environment surrounding the lanthanide ion, but also the influence of non-coordinating ions within the crystal lattice.

NUCL

Nanoscale interactions of uranyl peroxide nanoclusters with neptunium and plutonium

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Polyoxometalates (POMs) are metal oxide clusters truncated by doubly- or triply-bonded O atoms. Whereas transition-metal POMs have been extensively studied, uranyl-based POMs, also known as uranyl peroxide nanoclusters, have been known for

approximately a decade. In contrast to most transition-metal POMs, the uranyl peroxide nanoclusters can form cages that encapsulate cations. They are stable in aqueous solution and their very large surface-to-volume ratios ensure that liquid-“solid” interfaces can be probed at the nanoscale. This work describes the nanoscale interactions of the uranyl peroxide nanoclusters U_{60} ($Li_{48}K_{12}(OH)_x[(UO_2)(O_2)(OH)]_{60}(H_2O)_y$) and $U_{60}Ox_{30}$ $[\{(UO_2)(O_2)\}_{60}(C_2O_4)_{30}]$ with plutonium(VI) and neptunium(V). Ultra-small angle X-ray scattering (USAXS), small angle X-ray scattering (SAXS), and dynamic light scattering (DLS) were used to describe the aggregation of individual nanoclusters into secondary and tertiary structures in solution, whereas UV-vis-NIR spectroscopy was used to monitor for redox changes. The latter indicated a reduction of Pu(VI) to Pu(V) in the presence of $U_{60}Ox_{30}$, whereas no oxidation state changes were observed in the presence of U_{60}. Understanding such redox chemistry and aggregation is essential for the consideration of actinide separation schemes via size filtration, which could potentially lead to new approaches to the reprocessing of used nuclear fuel.

NUCL

Chloride to nitrate conversion for SRPPF aqueous recovery

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The Savannah River Plutonium Processing Facility (SRPPF) is planning to treat spent pyrochemical residues from plutonium metal preparation through the Aqueous Recovery System (ARS), a nitrate-based process line. Pyrochemical residues from salt scrub (SS), electrorefining (ER), and molten salt extraction (MSE) may contain significant amounts of chlorides entrained from the calcium chloride ($CaCl_2$) flux. There is a necessity to remove the chlorides to mitigate corrosion of downstream nitrate-based aqueous processing equipment. Reacting $CaCl_2$ with high concentrations of nitric acid (8-12 M) was demonstrated and is a promising means of chloride removal without the use of NO_2 gas or mercury, as previously explored at the Savannah River Site. The chloride ions reacted with nitric acid to form gaseous Cl_2 and ClNO, which were sparged from the system. A significant amount of chloride from $CaCl_2$ was dissolved and off gassed within six hours at elevated temperatures of 50, 75, and 100°C in high concentrations of nitric acid. Kinetics of chloride removal were dependent on nitric acid concentration, initial chloride content, sparge rates, and temperature, but the trend of chloride removal was predictable. The largest amount of chloride removal occurred within the first hour of the process at the conditions tested and was generally second order with respect to chloride. The reaction mechanism changed over the next few hours to a slower first order rate (i.e., exponential decay) of the chloride. The first order region was influenced by sparge rate, enhanced chrloide removal was observed at higher spage rates. Optimizing sparge rate would enable lower temperature operations while maintaining high efficiency and reducing corrosion rates. The capacity to process high concentrations of chloride salts demonstrates the potential feasibility in processing the salt directly in ARS, completely replacing the salt scrub process.

NUCL

High temperature calcination products of UO_2F_2

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Uranyl fluoride (UO_2F_2) is the hydration product of UF_6, an important intermediate in the nuclear fuel cycle. To examine the thermal stability of UO_2F_2, samples were calcined for 1 hour at a range of temperatures and monitored for chemical and structural transformations using a variety of analytical techniques. After cooling to room temperature, powder X-ray diffraction and Raman spectroscopy were implemented to examine bulk structural and vibrational spectroscopic changes in UO_2F_2 calcination products, respectively. Bulk and point elemental analyses were conducted using energy dispersive X-ray spectroscopy coupled to a scanning electron microscope (SEM-EDS) which was also employed to examine differences in sample morphology as a function of firing temperature. Lastly, high-sensitivity ion ratios were determined via nanoscale secondary ion mass spectrometry (nanoSIMS). Preliminary results suggest that samples prepared at lower temperatures do not undergo complete fluorine loss as evidenced in chemical analyses from SEM-EDS and NanoSIMS. This observation is confirmed by the presence of characteristic Raman shifts that are consistent with UO_2F_2 environments.

NUCL

Corrosion resistance of boron-doped diamond in chloride and fluoride molten salts

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Nuclear power is a clean, reliable source of energy that can help mitigate the effects of global climate change, but safety and waste management concerns often overshadow its potential. Generation IV Molten Salt Reactors (MSRs) use liquid salt fuel systems to eliminate a primary safety concern: core meltdowns. MSRs also consume used nuclear fuel waste as a form of fast reactor technology. Electrochemical methods can probe several fundamental aspects of molten salt chemistry so long as the electrodes can withstand the molten salt environment for prolonged periods of time. Boron-doped diamond (BDD) is expected to be resilient against harsh molten salt environments, given its sp^3-carbon structure. As such, BDD could potentially be used for *in situ* corrosion control and monitoring in molten salt containment vessels. However, the corrosion of BDD in molten salt needs to be understood first and this has yet to be fully

investigated in literature. In this study, we investigated the corrosion resistance of BDD by soaking the material in chloride and fluoride molten salts (LiCl-KCl, NaCl-KCl, LiF-KF, and FLiNaK) at 600 ºC over 250 hours. Scanning electron microscopy (SEM) and Raman spectroscopy were used to identify topographical changes in diamond crystal structures. Electrochemical techniques like cyclic voltammetry (CV), differential pulse voltammetry (DPV), and chronoamperometry (CA) with several 1-electron transfer redox couples were used before and after salt soaking to determine the following redox and thermodynamic properties: formal reduction potential ($E°'$), electron transfer stoichiometry, diffusion coefficients (D), and electroactive surface area of the BDD. In general, little corrosion or change to the BDD was observed. This work advances the understanding of MSR chemistry, while simultaneously proving the applicability of BDD as electrode material for harsh environments.

NUCL

Microliter source preparation for absolute assays of massic activity by decay energy spectrometry

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If a radioactive source can be embedded within an absorber and coupled to a low-temperature detector, a type of single decay event microcalorimetry can be achieved. In such a configuration, it is possible to measure all of the energy from the decay event, rather than just the energy of one or another decay products (alpha particles, electrons, x-rays, or gamma-rays) and so this method has been referred to as “Q Spectrometry” or “Decay Energy Spectrometry” (DES). In cases where the radioactive source is entirely contained within the volume of the absorber, very high efficiencies can be achieved, with only neutrinos and high-energy gamma rays escaping, and even then inducing clear and interpretable events that can be counted. In contrast to other spectroscopic approaches to quantifying radioactivity, DES provides simple energy spectra (one peak per radionuclide for ideal alpha decay) and truly remarkable resolution (e.g., < 1 keV FWHM on a 5 MeV alpha peak). The impact of this powerful technique will be magnified if the radioactive sources embedded in DES detectors can be gravimetrically linked to bulk samples such that the measurand becomes massic activity. We describe advances with a microliter gravimetric dispensing technique to prepare deposits of aqueous radioactive solutions on gold foils for DES measurements. We start with a well-characterized Am-241 standard reference material and perform liquid scintillation-based primary activity assays in parallel as a radiometric check of the gravimetric dispensing and as a rigorous check of the massic activity of the bulk solution.

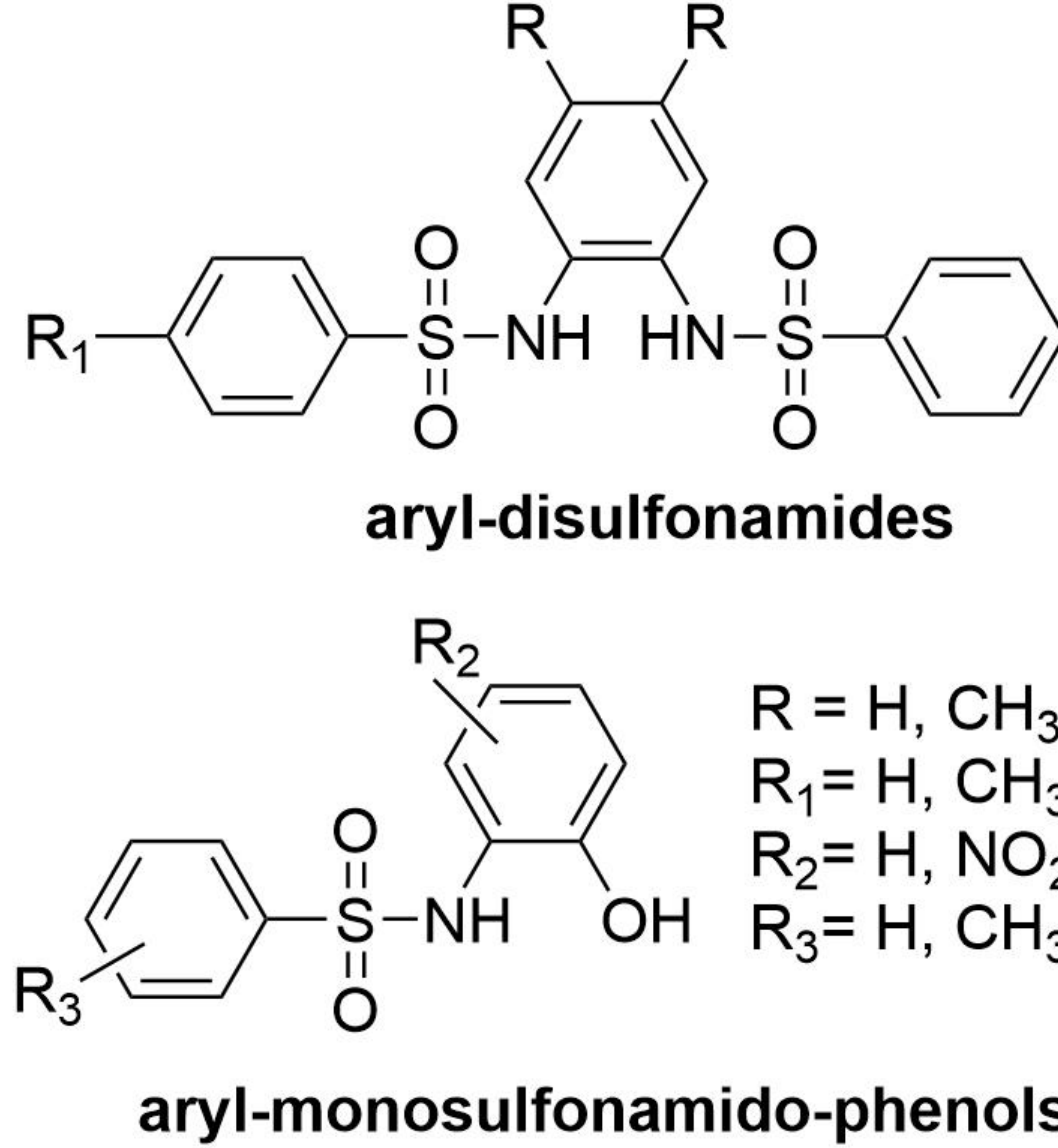
NUCL

Highly-lipophilic sulfonamide chelators and analogs for actinide separation from caustic high-level waste

***René Panzer**, rpanzer@fiu.edu, Oluwaseun W. Adedoyin, Xinrui Zhang, Indranil Chakraborty, Alexander N. Morozov, Alexander M. Mebel, Konstantinos Kavallieratos. Department of Chemistry & Biochemistry, Florida International University, Miami, Florida, United States*

The cold war era reprocessing of nuclear fuel via the PUREX process for plutonium production has led to the generation of large volumes of caustic high-level waste (HLW) stored in underground tanks at the Savannah River Site (SRS) and the Hanford Site (HS) in the US. Current reprocessing at SRS is based on a two-step process, consisting of the Actinide Removal Process (ARP) for ^{90}Sr and actinides (An) by sorption on monosodium titanate followed by the Next-Generation Caustic-Side Solvent Extraction process (NG-CSSX) for ^{137}Cs separation. Actinide chelators compatible with the NG-CSSX process could potentially achieve simultaneous separation of Cs, Sr, and An, by a one-step solvent extraction process, reducing the contact times and amounts of titanate sorbent during the slower ARP process and thus significantly improving the efficiency of overall HLW processing. Recently, we reported effective extraction of Sm(III), used as a surrogate for Am(III), from alkaline aqueous media by *o*-phenylenediamine-derived aryldisulfonamides. Sm(III) recovery up to 81% at pH 13.0 in chlorinated solvents after just one loading-stripping cycle was demonstrated. Encouraged by these results we extended our work to *o*-(monosulfonamido)-phenol type ligands and achieved Sm(III) extraction efficiencies of > 90% at pH = 14 in dichloromethane.

The use of chlorinated solvents however, represents a major drawback for industrial application. Hence, to facilitate application of these high- performing ligands, we have now developed and present new highly-lipophilic aryl- and alkyl-substituted disulfonamide and *o*-(monosulfonamido)-phenol derivatives, that can extract Sm(III) efficiently in process solvents, such as *n*-dodecane, *n*-dodecane/octanol from up to 2M NaOH. Preliminary experiments with some of these ligands in the actual CSSX solvent and process compatibility issues will also be discussed.



Aryl (left) and alkyl (right) sulfonamide chelators: Highly lipophilic derivatives (R_4 = dodecyl or

2-ethylhexyl) are soluble in dodecane and dodecane/octanol mixtures and can extract Sm(III) from 2M NaOH.

NUCL

Ionic M−N Bonding in Multinuclear Organometallic Transuranic Complexes

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Recent advances in the growing field of organometallic transuranic chemistry has lead to a further understanding of bonding and electronic properties in the actinides. A reaction between Cp'_3M (Cp′ = trimethylsilylcyclopentadienide) and 4,4′−bpy (4,4′−bipyridine) has yielded a series of organometallic multinuclear transuranic complexes, $(Cp'_3M)_2(\mu{-}4,4'{-}bpy)$, displaying surprisingly ionic M−N bonding. These systems provide some of the first structural characterization M−C bonds in transplutonium elements, as well as spectroscopic properties distinctive to organometallic *f*-block molecules. Structural and spectroscopic characterization of an organometallic multinuclear transuranic system, $(Cp'_3M)_2(\mu{-}4,4'{-}bpy)$, as well as the challenges of characterizing air sensitive, radioactive compounds is discussed.

NUCL

Development of a methodology for the radiochronometric analysis of 226Ra containing radiological samples for nuclear forensics

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Radium pigments and paints were used in the early 1900s for the watch dial industry, military instrumentation, and household applications due to their attractive, self-luminescent properties. These pigments and paints are no longer used modern day as they pose many health hazards. In addition, the International Atomic Energy Agency (IAEA) has identified ^{226}Ra, the main radioactive component within the sample, as a potential threat in the use of radiological dispersive devices (RDDs). To combat nuclear terrorism events, nuclear forensic analytical techniques are used for origin attribution in interdicted samples. Many techniques used to analyze nuclear materials are well documented in the literature; however, the analysis of ^{226}Ra radiological samples under the lens of nuclear forensics is sparse to nonexistent within the literature. This work focuses on developing a methodology for the radiochronometric analysis, a common forensic analysis technique to determine the sample “age,” of ^{226}Ra containing radiological samples. Complete sample dissolution has proven to be challenging due to chemical dissimilarity of the pigment components (ZnS (~99%), $RaBr_2$ (~1%), and $PbBr_2$ (>>1%)). Effective dissolution of small quantities of a mock, radium pigment sample was performed using a solution of bis-tetrakis(hydroxymethyl)phosphonium sulfate, ammonium chloride, concentrated HCl, and water under conditions of stirring and high temperature. In preparation for radiochronometric analysis, retention factors for Ba, Pb, Po, Bi and Zn will be measured using this novel solution and extraction resins with low selectivity towards alkaline earth metals (such as DGA, LN, CL, etc.). The most efficient and timely separation path for radiochronometric analysis is to be determined. These results will establish a nuclear forensic database for ^{226}Ra radiological samples, ultimately to be used to combat events of nuclear terrorism.

NUCL

Lanthanide and actinide complexes with a redox-active 1,2-dithiolate ligand

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Non-innocent 1,2-dithiolate ligands have a rich and well explored chemistry with the transition metals, but complexes of the *f*-block elements with them remains sparse. These ligands are of interest due to their ability to form complexes with a high degree of electron delocalization and covalency in the metal-ligand bonds and unusual magnetic and redox behavior. Homoleptic dithiolate complexes have been synthesized with the lanthanides and some trans-uranic elements and have been characterized by UV-Vis-NIR spectroscopy and single-crystal X-ray diffraction. The effect of high pressure on the metal-ligand bonding is also discussed.

NUCL

Critical Phenomena and Organic Phase Mesostructure in Liquid-Liquid Extraction

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Liquid-liquid extraction is a chemical separations technique commonly utilized in radiochemical applications. A fundamental limitation to this technology is third phase formation, where sufficient loading of metal ions into the organic phase induces a liquid-liquid phase transition. The molecular-scale origins of this phase transition are challenging to understand in complex, hierarchically structured organic phases. We propose that organic phase structure and phase behavior are fundamentally connected in a way that can be understood by applying critical phenomena theory. By combining small angle X-ray scattering with molecular dynamics simulations, we demonstrate that organic phase mesostructure over a wide composition space is dominated by critical fluctuations. These fluctuations originate from the critical point associate with the third phase formation phase transition. For a range of liquid-liquid extraction systems with varying complexity, we find these fluctuations are consistent with the 3D Ising model. Scaling relations provided by critical phenomena theory provide a robust physical connection between aggregation in the organic phase and its phase behavior, deepening our understanding of both. These results will inform the design of more efficient third phase formation-resistant separations processes.

NUCL

Structural and Spectroscopic Trends of the Lanthanides and Actinides with Mellitic Acid

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Mellitic acid resembles humic and fluvic acids found in fertile soils and is found in organic minerals. Mellitic acid formation from the digestion of uranium carbides have also been observed in the literature. Multidimensional structures have been characterized with the lanthanides as well as higher valent uranium (U^{4+}, $U^{VI}O_2^{2+}$) and neptunium ($Np^{V}O_2^{+}$). However, the trivalent actinide mellitates were under investigated with respect to the rest of the *f* element series. We sought to synthesize and characterize mellitate compounds with several of the transuranium elements. We compare these compounds to relevant lanthanide analogs with varying ionic size and spectroscopic properties. We also introduce these compounds to immense pressure to investigate the pressure response of the Laporte forbidden $nf \rightarrow nf$ transitions within these compounds.

NUCL

Manganese oxides and Mn(III) aqueous complexes play a key role to the proliferation of technetium-99 in the environment

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Manganese oxides and Mn(III)-ligand aqueous complexes are ubiquitous oxidizing agents in the environment and are capable of oxidizing many reduced metal species. They play a key role in contaminant mobility due to two reasons: the high reduction potential of the Mn(IV or III)/Mn(II) redox couple and the redox cycling of manganese by microorganisms. The later factor ensures that high valent manganese concentrations remain relatively stable during redox interactions even under anoxic conditions. Technetium-99 is a risk driving radionuclide for many Department of Energy Nuclear (DOE) sites including the Hanford site, Savannah River site and Oak Ridge site. Past improper handling of legacy waste has led to accidental or intentional the release of Tc-99 into the environment at these sites. Tc-99's environmental mobility is governed by its oxidation state: $Tc(IV)O_4^-$ predominates under oxidizing conditions and is highly mobile, while $Tc(IV)O_2$ predominates under reducing conditions and is relatively immobile environmentally. Because of this remediation efforts have historically relied on the reductive immobilization of TcO_4^- to TcO_2.

In this talk, an overview of solid-solid redox interactions between TcO_2 and manganese oxides under anoxic conditions (<0.1 ppm O_2) will be presented, as well as Mn(III)-

pyrophosphate interactions with TcO_2 under identical conditions. Our results indicated rapid oxidative dissolution of TcO_2 and release of TcO_4^- in the aqueous phase even in the absence of oxygen, which is highly dependent on physico-chemical parameters such as pH, manganese mineral mass and Mn(III)-pyrophosphate concentrations, the presence of divalent cations and ionic strength. This study is the first one that investigates the stability of technetium oxides (TcO_2) in the environment affected by manganese compounds.
Overall manganese minerals, as well as aqueous complexes, pose a substantial liability for Tc-99 remediation methods and will contribute to the proliferation of Tc-99 in the environment even under anoxic conditions.

NUCL

Recent advancements in using metal oxide matrices to investigate non-pertechnetate Tc species

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Technetium-99 (Tc-99) is a long-lived ($2.13x10^5$ years) radionuclide and exists in large quantities in waste tanks at national labs. Its nine accessible oxidation states make it highly reactive and complicate its redox chemistry. The development of long-term storage solutions for Tc require a fundamental understanding of its stability and redox chemistry in the relevant matrices. The $[Tc^I(CO)_3(H_2O)_3^+]$ species may also be present; the chemistry of Tc(I) in environment and waste tank matrices has been sparsely studied. We propose studying the chemistry of Tc^I species using highly controlled metal oxides as models for minerals and solid-state materials. Keggin polyoxometalates (POMs) ($[PW_{12}O_{40}]^{3-}$) are air stable metal oxide clusters, which can be tuned for size, charge, acidity, and redox potential. Experimental and theoretical research has shown that W substitution with one, two or three lower valent transition metals such as Vanadium(+5) or Niobium(+5) increases the surface Lewis basicity of the POM, thus rendering the surface more reactive to low valent metals and offering favorable tripodal coordination. Specifically, Nb and V substituted Keggin POMs, $[PM_xW_{12-x}O_{40}]^{(3+x)-}$, where M = V, Nb and x=1,2, or 3 will provide surfaces that vary in basicity, electronic environment and lability to probe the speciation and stability of Tc(I). An understanding of the speciation of Tc(I) upon binding to these surfaces and then POM features that stabilize the Tc(I) species will allow for the intelligent design of both extractants and complexing agents for the long-term storage of Tc currently present in waste streams. Herein, we present an alternative approach to low pressure CO synthesis of the $[Tc^I(CO)_3^+]$ core and provide an update on the surface stabilization of $[Tc^I(CO)_3^+]$ on electron-rich metal oxide surfaces.

NUCL

Radiolysis in a flowing-water target during high intensity proton irradiation

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At the Facility for Rare Isotope Beams (FRIB), the interactions between heavy-ion beams and the beam-dump water will create a plethora of valuable radionuclides that can be accessed by a technique known as 'isotope harvesting'. With the dissipation of such large amounts of energy, not only nuclear, but also radiolysis reactions are induced. From the generated radiolysis products, hydrogen, hydrogen peroxide, and oxygen, exhibit sufficiently long lifetimes to accumulate in the irradiated water and possibly affect the harvesting chemistry.

Here we examined the formation of radiolytic H_2, H_2O_2, and O_2 during a high intensity proton beam irradiation of a flowing-water isotope harvesting target and the experimental results were compared to a simulation. The simulation was developed in Python, and it kinetically models the chemical reactions occurring in the homogeneous radiolysis phase during proton irradiation of the flowing-water target. Both, the experiment as well as the simulation demonstrate significantly lower H_2, H_2O_2, and O_2 quantities than predicted by the primary radiolytic yields. This undermines the considerable impact of homogeneous phase reactions on the chemical composition of the water within the high-beam intensity regime. Additionally, the simulations suggest that the bulk outcome could be represented by a simplified steady state model. Comparable conditions at the upcoming FRIB allow a translation of the steady state model to predict the hydrogen, hydrogen peroxide, and oxygen content within the entire isotope harvesting system.

NUCL

Quantitative Determination of Total Cesium by Inductively Coupled Plasma Emission Spectroscopy (ICP-ES) in Savannah River Site (SRS) Radioactive Tank Waste and Simulants.

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The analysis of cesium (Cs) is fundamental for waste characterization and source identification of fission products in nuclear waste remediation and in non-radioactive simulant tests to support tank closure programs. Inductively Coupled Plasma Emission Spectroscopy (ICP-ES) has not been utilized for total Cs determinations in the past due to the inability for quantitative determination below sub-parts per million (ppm) levels and spectroscopic interferences. Currently, Cs radioisotopes analysis for tank waste at SRS is performed by Inductively Coupled Plasma Mass Spectrometry (ICP- MS). However, total Cs by ICPMS faces the problem of isobaric interferences of some Cs isotopes by natural barium (Ba) when present in samples which is routinely present in

SRS tank waste. Utilization of the expanded wavelength detection range of the Leeman Prodigy ICP- ES in combination with an ionization buffer (IB) results in a significant increase in spectral intensity without the impact of potential Ba interference when present in sample. This technique increases the sensitivity of the analysis of Cs by ICP-ES from low ppm concentrations to low parts per billion (ppb) concentration detections.

NUCL

Synthesis of nanoscale UO_2 through thermally induced reduction of uranyl-based materials

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Nanoscale materials present as an area of increasing interest due to unique properties that can enhance use in a variety of applications. As nuclear fuel pellets are typically comprised of UO_2 with micron-scale sized grains, synthesis of nanoscale UO_2 could provide heightened performance. This work presents a method of UO_2 synthesis that produces spherical particles of roughly 250nm in diameter. Through liquid spray through a furnace at various temperatures, the degree of reduction can be controlled to produce a variety of uranium oxide materials from UO_3 to stoichiometrically pure uranium dioxide. This process is novel in that its starting material is a class of uranyl-based polyoxometalates (POMs) known as uranyl peroxide cage clusters (UPCs). Several methods of material characterization were conducted including X-ray diffraction, dynamic light scattering, scanning electron microscopy, and a variety of spectroscopic techniques.

NUCL

Complexation of Lanthanide and Actinide Ions with Polyoxometalates

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Improving nuclear waste reprocessing to reduce the volume of material converted for long term storage remains a challenge. The use of polyoxometalate complexes for separation of actinide species from nuclear waste is a viable alternative. Polyoxometalates (POMs) are ligands composed of metal-oxygen anionic clusters composing of transition metals such as vanadium and tungsten in high oxidation states. POMs are immensely redox-active and have been shown to greatly affect the redox potential windows of lanthanides in solution. Herein, we report the synthesis and structural investigation of lanthanide and actinide complexes with various polyoxometalates.

NUCL

The effect of siderophores on actinide mobility in the environment: Eu interaction with iron oxides in the presence of Desferrioxamine B (DFOB)

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Trivalent actinides such as Americium are among the many risk driving contaminants in nuclear waste. Due to past accidental releases and for reasons related to performance assessment, the environmental fate of actinides is a crucial field of study. In the present study, the effect of siderophores in the mobility of trivalent actinides in the environment was investigated. Europium was used as a non-radioactive surrogate of Americium and its sorption on abundant natural substrates in the presence and absence of the siderophore DFOB was studied. Siderophores are biologically produced organic ligands that strongly complex with Fe (III) but can also form strong complexes with other metals such as Mo, Mn, Co, and Ni. Batch experiments were conducted where Eu was brought into contact with magnetite or goethite in the presence and absence of DFOB in a 4-8 pH range. The[VA1] concentration of Eu in the aqueous phase was monitored by ICP-MS, whereas the concentration of DFOB was monitored using Uv-Vis. Results show that at pH 4 the presence of DFOB does not play a significant role on Eu sorption while at pH 6, DFOB hinders Eu sorption, thus contributing in the proliferation of the contaminant in the aqueous phase. At pH 8, free soluble europium does not exist, but in the presence of DFOB, a stable Eu-DFOB complex persists in the aqueous phase. Overall, the presence of siderophores seems to enhance the mobility of trivalent actinides under environmentally relevant conditions. Future studies include sorption of Eu-DFOB complex on manganese oxides, which exhibit high sportive capacity, with the objective of gaining enough knowledge to propose relevant remediation schemes.

[VA1]Here you need a sentence describing your experiment: for example “batch experiments were performed bringing in contact x and y iron oxides with europium in the presence and absence of dfob at a range of pH, concentrations and la la la la” [VA1]

NUCL

SEM, EDS, and XRD analysis of synthetic trinitite as compared to authenitic and remelted trinitite samples

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In the event of a nuclear attack, the analysis of fallout debris will be crucial to the timely attribution of the nuclear materials used. As such, the synthesis and analysis of realistic, urban, melt glass has been the focus of many projects in recent years. Traditionally, these synthetic materials have been prepared using furnaces to heat the glass over several hours. A novel preparation method which uses a vacuum arc welder to simulate

a nuclear fireball plasma allows for the instantaneous heating of materials to temperatures over 3000C, while in a reducing environment. In this study, the vacuum arc welder was used to prepare synthetic trinitite, as well as remelt a sample of authentic trinitite. Additionally, a sample of authentic trinitite was remelted using the more traditional MTI furnace. An authentic sample of trinitite along with the prepared samples of trinitite were then compared via SEM, EDS, and XRD analysis.

NUCL

Solid-State Analysis of Lanthanide and Actinide Diglycolamide Complexes

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Nuclear Power has some of the lowest emissions coupled with the highest energy density making it one of the most ideal options for clean energy. However, the advantages of nuclear power are hindered by the challenges of safely storing nuclear waste. Diglycolamide (DGA) ligands have shown to have a strong affinity towards Ln^{3+} and transuranic An^{3+} and are used in the separations of minor actinides from nuclear waste. Further understanding of the bonding behavior between lanthanides and actinides with variations of the DGA molecules will help to better understand the role of these ligands in nuclear waste separations. Radiolysis induced degradation of DGA ligands will compromise their separation efficiency. Studying the components found in degradation products of DGA molecules as well as complexes with *f*-elements will improve our understanding of these separation strategies. Furthermore, structural knowledge of these complexes, especially with actinides, are lacking. Here, we present crystallographic and spectroscopic data of lanthanide and actinide DGA complexes in the solid-state along with supplementary quantum mechanical calculations. Preliminary radiolysis experimental results will also be discussed.

NUCL

Mixed N,S donor ligands for selective complexation of americium

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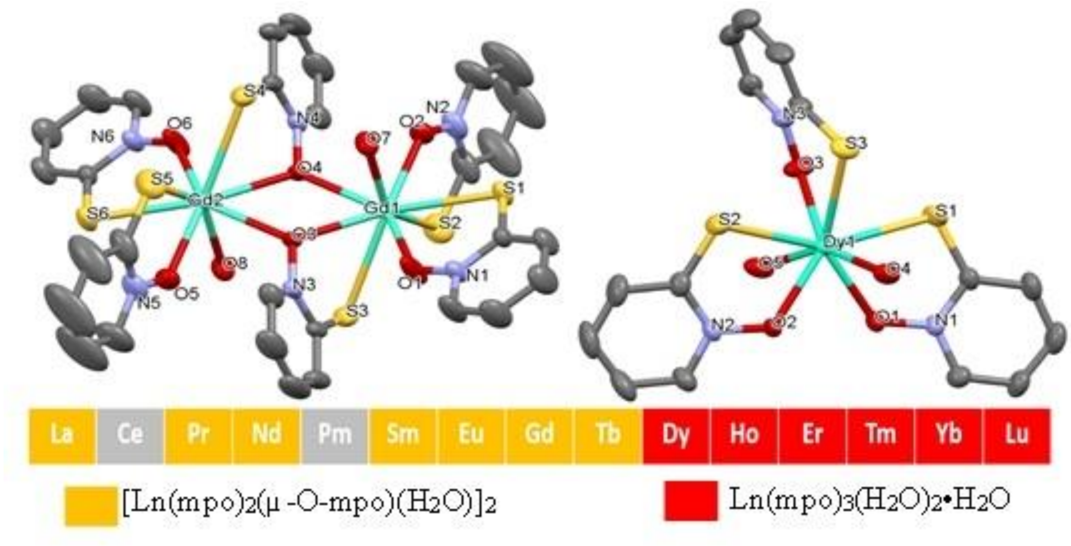
Pyridine N-oxides have long been investigated as efficacious chelating moieties of *f*-element ions and have found appreciable use in magnetic resonance imaging, luminescent labeling of biomolecules, and fluoroimmunoassays. With the goal of selectively complexing americium and curium over the lanthanides, a series of mixed S,N donor pyridine thiol complexes with lanthanides and americium have been prepared and fully characterized. The crystal chemistry, spectroscopy, and quantum mechanical analysis of bonding of this family of compounds is presented. In particular, the basis of a structural change from mononuclear to binuclear complexes across the *f*-block is

explained. The presence of stronger bonding interactions in the binuclear americium compound are rationalized and compared to its isostructural Nd analogue.



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Copper-Catalyzed ^{11}C radiolabeling of Arenes via C-H Activation Route

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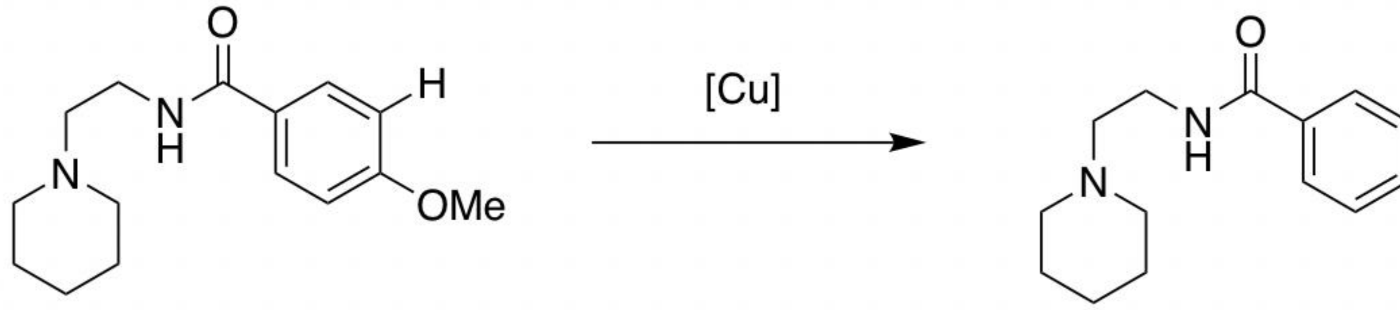
Introducing ^{11}CN and ^{11}CO into arenes at a late stage has gained significant recent attention as a powerful tool for radiotracer development for Positron Emission Tomography (PET). The use of first-row transition metal mediators, such as Cu, is of particular interest because of their low toxicity. This study uses Cu mediators to introduce ^{11}C into complex molecules via a one-pot C–H halogenation/radiolabeling protocol. This sequence proceeds with high radiochemical yield and excellent functional group tolerance and is applied to the preparation of several PET radiotracers.



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Oxidative dehalogenation of aryl halides

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Alpha-particle emitters are promising radionuclides for the treatment of small tumors. When such a radionuclide is attached to a suitable targeting agent, the short path length of the a-particles (25-100 mm), along with their high LET (4-8.5 MeV), make them very effective therapeutics against cancerous cells with a minimum damage to the surrounding healthy tissues. Astatine-211 has advantages over other a-emitters such as a moderate half-life (7.21 h) that allows local and regional shipping of ^{211}At-a-RPTs and is considered to be one of the most promising radionuclides for alpha-emitting radiopharmaceutical therapy. However, the *in vivo* release of ^{211}At from pharmacological targeting constructs diminishes therapeutic efficacy while increasing the potential toxicity of a-radiation on nontargeted tissues. In most cases the unacceptable stability *in vivo* is due to the weakness of the astatine–biomolecule bond and to avoid release of free astatine and toxicity issues, a highly stable ^{211}At-a-RPTs is required.

In this study, we screened the stability of a series of aryl halides with different substituent groups on the aromatic ring at *para* position and explored the effect of electron donating/withdrawing groups on the strength of At-C and I-C bonds. First, we computationally assesed the stability of halo compounds by calculating first ionization potential (IP_1), energy of HOMO and bond dissociation energy (BDE) of C-Halogen for each construct. Higher IP1 and relative BDEs and HOMOs with lower energy were interperted as higher stability. Next, we empirically tested the chemical stability of compounds toward oxidation in the presence of sodium permanganate.

Our empirical results show that astato compounds are more prone to oxidation than their iodo counterparts which ultimately leads to a faster cleavage of C-At bond. Our calculations show that for a given halogen, the bond dissociation energies of all constructs with different functional groups are almost the same. However, our empirical data illustrate that they undergo oxidation with different rates which suggests that BDE necessarily cannot be an indicator of stability of halo compounds while the halogen is the same. In contrast, IP_1 and HOMO energies successfully predicted the chemical stability of studied compounds.

NUCL

Fluorescence sensing and extraction of Ln(III) from alkaline solutions by a lipophilic dansylamide ligand based on the *o*-sulfonamidophenol framework

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The Hanford and Savannah River US DOE sites contain the majority of high-level waste (HLW) in the US, with about 100 MGal in volume and combined activity of over 400 MCi. Several approaches have been adopted to separate the waste into high activity and low activity waste forms, in order to reduce the overall volume and reduce contamination risks by disposing low level waste in cementitious form (grout) and immobilizing remaining low volumes of HLW components in solid form within glass (vitrification).

At Savannah River Site (SRS), the two sequential approaches used are the Actinide Removal Process (ARP) followed by the Caustic Side Solvent Extraction (CSSX). The ARP is a sorption process using monosodium titanate (MST) to remove Sr(II) and actinides. The CSSX process selectively extracts Cs(I) by using a calixarene extractant. Our group is focusing its efforts to CSSX-compatible additives (ligands) for combined extraction of f-elements, together with Cs(I) and Sr(II), thus reducing the amount of MST and contact time needed during the slower ARP process, and thus simplifying overall HLW processing.

We now present N-(5-(tert-butyl)-2-hydroxyphenyl)-5-(dimethylamino)naphthalene-1-sulfonamide ($\mathbf{L_D}$), which is a *o*-sulfonamidophenol ligand bearing the signaling fluorescent dansyl moiety for the sequestration and *in-situ* sensing of f-elements in HLW. We observed 92% extraction of Sm(III) (used as an experimental surrogate for actinides) from pH 13.0 into dichloromethane after one extraction/strip cycle. Addition of several Ln(III) to acetonitrile solutions of ($\mathbf{L_D}$) in the presence of organic bases showed notable fluorescence enhancements, while UV-Vis titrations in acetonitrile suggested 1:1 binding stoichiometry, with binding constant of $\log K = 5.31 \pm 0.33$ obtained using the Hypspec program. Though we have established the stability of ($\mathbf{L_D}$) under alkaline conditions, compatibility studies of the ligand in the CSSX solvent are currently underway.

NUCL

Production of Isotopes at Brookhaven National Laboratory

***Cathy S. Cutler**, ccutler@bnl.gov, Dmitri G. Medvedev, Vanessa A. Sanders, Jasmine Hatcher Lamarre, Dohyun Kim. Brookhaven National Laboratory, Upton, New York, United States*

In the 1970's the Brookhaven Linac Isotope Producer (BLIP) came online to accept protons from the 200 MeV Linac that synergistically supports multiple programs including the isotope production program, the Nasa Space Radiation Laboratory (RHIC) as well as the Relativistic Hadron Ion Collider (RHIC). In addition to the BLIP the isotope program operates the Radionuclide Research and Production Laboratory (RRPL) which contains laboratories and hot cells for processing targets irradiated at the BLIP for external customers as well as internal research. New hot cells have are being brought online to aid in the processing of Ac-225. The BLIP allows the production of isotopes from 200 MeV and down in energies using stacked target arrays that allows for multiple isotope production. High energy accelerators play a critical role in supplying radionuclides such as Sr-82 used in Sr-82/Rb-82 generators for cardiac imaging. They continue to be upgraded to further production yields by installing beam rastering systems that have allowed higher intensities and thus higher production yields. Demand for isotopes that can be produced by these systems have also increased. Linear accelerators such as the one at Brookhaven National Laboratory when operating at maximum proton energy of 200 MeV can have simultaneous production of several medically relevant isotopes. Among those are Ac-225 ($T_{1/2}$=10.0 d), Cu-67 ($T_{1/2}$=64.83 h), Se-72/As-72 ($T_{1/2}$=26 h), Sr-82/Rb-82 ($T_{1/2}$=1.26 min) and Ti-44/Sc-44 ($T_{1/2}$=3.97 h). Discussion of recent facility enhancement and production of these novel radionuclides and recent enhancements will be presented.

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Production of Radioisotopes using Secondary Neutrons at the Brookhaven Linac Isotope Producer

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The Brookhaven Linac Isotope Producer (BLIP) facility at Brookhaven National Laboratory routinely irradiates targets, using a proton beam of incrementally tunable energy (66-200 MeV) and intensity (up to 170 uA), for the creation of a host of radioisotopes for use in medical applications. During irradiation of these targets, secondary neutrons are generated by proton-induced reactions and have thus far largely been an untapped resource. These neutrons have the potential to produce additional isotopes of interest by placing targets downstream of the proton target stack after the protons have been stopped. Prior to their use for isotope production planning, the emitted neutron spectrum first needs to be characterized. To achieve this, three foils (Ti, Co, and Bi) were placed downstream of a BLIP target stack. In this experiment, Co and Bi foils served as the monitor foils, and the Ti foil served to generate the radiotherapeutic isotope ^{47}Sc. After a 24-hour irradiation of the target stack at a proton

energy of 117 MeV and beam current of 116 µA, the foils were measured using gamma spectroscopy for the identification and quantification of the isotopes produced during the experiment with secondary neutrons. Following gamma spectra analysis, the deduced activities (most being between 0.1 and 1.0 mCi at end of bombardment) of several isotopes that serve as flux monitor reaction products were used along with TENDL cross sections to calculate the neutron spectrum. The results of this calculation, next steps for foil irradiations using secondary neutrons, and the yield of several radionuclides of interest (including ^{47}Sc at the mCi level), will be discussed.

NUCL

Towards the development of high-affinity chelators for Ra-223 targeted alpha therapy: A stability constant roadmap

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Radium-223 (Ra-223) is the first and only alpha particle-emitting radioisotope approved for therapeutic use. It is indicated for the treatment of bone metastases in men with prostate cancer. Administered as a simple chloride salt, the radioactive radium ion preferentially accumulates in bone, where its lethal cascade of alpha emissions destroys osteoblastic lesions. To expand the use of Ra-223 to soft-tissue cancers, this radiometal must be stably bound to a tumor-targeting vector via a bifunctional chelating agent. Although recent milestones in the aqueous chelation of the radium ion have been achieved, the successful delivery of Ra-223 to tumors remains elusive. This shortcoming reflects the inadequate stability of radium-ligand complexes in vivo. With the overarching goal of developing new chelators that can effectively stabilize Ra-223 in vivo, we have initiated a research program directed towards more thoroughly understanding the fundamental coordination chemistry of the radium ion, which remains underexplored in comparison to its non-radioactive alkaline earth congeners. In this presentation, we report our efforts to experimentally determine the aqueous stability constants, or log K values, of Ra-223 with a series of macrocyclic ligands of relevance to targeted alpha therapy. These values, which reflect the thermodynamic affinity of a chelator for a metal ion, reveal important structure-stability trends that will be leveraged to guide future ligand design efforts. Moreover, this research has led to the identification of the highest affinity chelator reported to date for the radium ion. Collectively, the stability constant data obtained from this work will provide a roadmap for the generation of novel radium-223-based targeted therapeutics to significantly expand the medicinal scope of this promising radionuclide.

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Zirconium Phosphate Nano-Platelets: A Potential Drug Delivery Vehicle for Ac-225

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Targeted alpha therapy (TAT) for treatment of various kinds of cancer relies on the idea of linking α-particle-emitting radionuclides to carrier molecules, which are tumor selective. Alpha-zirconium phosphate (α-ZrP) is a non-cytotoxic inorganic ion exchange material with a composition of $Zr(HPO_4)_2 \bullet H_2O$ that is stable under biological conditions. The particle shape of α-ZrP is platelet-like, which, compared to spherically shaped particles, should show better adhesion, margination, and binding properties. Combined, the particle size, shape, and ion-exchange intercalation chemistry make α-ZrP very attractive for radionuclide delivery for TAT. The loading and kinetics of uptake for α-ZrP have been investigated with ions relevant to TAT, specifically those in the ^{225}Ac decay-chain, natural Cs^+ (as a surrogate for ^{221}Fr), natural Bi^{3+} (as a surrogate for ^{213}Bi), and natural La^{3+} (as a surrogate for ^{225}Ac). Results of these studies, including ion exchange kinetics, loading capacity, and leaching of the loaded material will be discussed.

NUCL

Process Improvements and Scale-Up of Accelerator-Produced ^{225}Ac at Oak Ridge National Laboratory

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The Tri-Lab Project is a collaborative project between Oak Ridge National Laboratory (ORNL), Brookhaven National Laboratory (BNL), and Los Alamos National Laboratory (LANL) to produce ^{225}Ac on demand without the use of a Th cow. Natural Th is irradiated in a proton accelerator at either BNL or LANL and then shipped to ORNL for chemical processing and distribution. This talk will delve into the chemical purification of ^{225}Ac. The Th target post irradiation is contaminated with many fission products, some of which are volatile and may escape hot cell containment. The processing was improved with an in-cell gas trapping setup designed to capture a wide variety of gaseous isotopes. When implemented in a processing campaign, the gaseous radioactive emissions from the facility were reduced 10-fold. As a part of further process development, we needed to determine how to scale the process up to large quantities of Th starting material. The dissolution and debulking of the Th material was successfully completed with five times the amount of target material present in a typical processing campaign. These process improvements will be implemented in further accelerator-produced ^{225}Ac processing campaigns and will be implemented when chemical

processing moves from ORNL to LANL and BNL.

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Measurement of the ^{230}Th(p,2n)^{229}Pa and ^{230}Th(p,3n) ^{228}Pa reaction cross sections from 14.1 to 16.9 MeV

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Actinium-225 is of interest as an agent for targeted alpha therapy and there is on-going research into methods of producing this isotope, either directly or via the decay of its parent isotopes (^{229}Th, ^{229}Pa, and ^{225}Ra). One method that has been suggested is the ^{230}Th(p,2n)^{229}Pa reaction, however, there is no available cross section data for this reaction in the literature.

This talk will discuss measurements of the ^{230}Th(p,2n)^{229}Pa and ^{230}Th(p,3n)^{228}Pa reaction cross sections, including the target fabrication and post-irradiation chemical processing, and present the results in the energy range where the ^{230}Th(p,2n)^{229}Pa reaction cross section has been calculated to peak. For these experiments, targets naturally enriched in ^{230}Th were fabricated and irradiated at Lawrence Livermore National Laboratory with proton energies ranging from 14.1 to 16.9 MeV. Chemistry development studies were performed to determine a procedure for processing the targets post-irradiation to separate the protactinium activation products. Chemical processing was followed by γ-ray spectroscopy to measure the activities of ^{228,229,230,232}Pa produced in the irradiation. Excitation functions are reported for the ^{230}Th(p,2n)^{229}Pa and ^{230}Th(p,3n)^{228}Pa reactions as well as the ^{232}Th(p,n)^{232}Pa reaction, which was used to verify the experimental conditions.

NUCL

Nickel-63 Production at Oak Ridge National Laboratory

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Nickel-63 is an important isotope that is used to make betavoltaic batteries and electron capture detectors. At Oak Ridge National Laboratory (ORNL), ^{63}Ni is produced using enriched ^{62}Ni targets via the (*n*,γ) reaction. The enriched material is pressed into small pellets and placed into housings called *rabbits*. The rabbits go into the High Flux Isotope Reactor at ORNL for up to fifteen 25-day cycles to produce the maximum amount of ^{63}Ni. For each campaign, the aim is to produce 600 Ci of ^{63}Ni, from approximately 40 g of highly enriched ^{62}Ni. The irradiated ^{62}Ni is transferred from the reactor to the Radiochemical Engineering Development Center for bulk processing. The bulk of ^{60}Co

is removed from ^{63}Ni product before undergoing a fine process to remove the remaining ^{60}Co and Sc from the ^{63}Ni product. This research is supported by the US Department of Energy Isotope Program, managed by the Office of Science.

NUCL

Thorium-229 Production through Proton Irradiation of Thorium-230 Nanoparticle-based Thin Film Targets Co-deposited with Nickel

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The decay products of ^{229}Th ($t_{1/2}$ = 7932 y), specifically ^{225}Ac ($t_{1/2}$ = 9.92 d) and ^{213}Bi ($t_{1/2}$ = 45.61 min), are important alpha-emitting radioisotopes for treating cancer. These radionuclides are in high demand but have a limited supply that includes existing ^{229}Th sources and accelerator-produced ^{225}Ac. To address this shortage, we evaluated a novel method to produce ^{229}Th through the proton irradiation of ^{230}Th ($t_{1/2}$ = 75,400 y). We first developed a uniformly distributed ^{230}Th target that is optimal for charged particle cross section measurements. The electrophoretic deposition of preformed Th nanoparticles with Ni as the electroactive species was used. Direct electrodeposition of Th is problematic because of the difficulty of reducing Th^{4+} ions and has led to many researchers attempting the use of aprotic solvents, molten salts, and ionic liquid electrolytes. The codeposited Ni serves a second important function: it will act as an in situ beam monitor through the measurement of the prompt gamma activity of ^{61}Cu ($t_{1/2}$ = 3.339 h) postirradiation. Using Ce as a cold surrogate for Th, we investigated three Ce-based compositions (e.g., CeO_2, $CePO_4$, and $CeVO_4$) to assess which nanoparticle suspension provides the most uniform co-deposition with Ni metal ions. After establishing the electrophoretic deposition of Ce-based nanoparticles, the uniformly deposited ^{230}Th target(s) will be fabricated and irradiated at the 88-Inch Cyclotron at Lawrence Berkeley National Laboratory. Postirradiation, the target(s) will be processed at Oak Ridge National Laboratory to separate the ^{229}Th decay precursor, ^{229}Pa ($t_{1/2}$ = 1.5 d), from impurities using ion exchange chromatography methods. After measuring ^{229}Pa yield via gamma ray spectroscopy, we will report the ^{230}Th(p,2n)^{229}Pa reaction cross section.

NUCL

Production of Radionuclides Using the University of Washington Medical Cyclotron Facility

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Radionuclides are used across a wide range of industries and scientific disciplines including nuclear medicine, gas and oil exploration, nuclear forensics, etc. The Scanditronix MC-50 cyclotron at the University of Washington (UW) is recognized as a valuable resource for radionuclide production and research due to its high (50-MeV) beam energy and capability of accelerating multiple charged particles (i.e., H^+, H2+, $^2H^+$, $^3He^+$, $^3He^{2+}$ and $^4He^{2+}$). UW is a member of the DOE University Isotope Network and has been providing ^{211}At and high specific activity ^{117m}Sn to U.S. investigators through the National Isotope Development Center (NIDC) for preclinical and clinical research. In addition to routine production of ^{211}At and ^{117m}Sn, an active research and development effort has been focused on improving the targetry and purification processes of ^{211}At, ^{117m}Sn and ^{186}Re to achieve higher yields and purity. Last but not least, the unique capability of the cyclotron has enabled a number of DOE Isotope Program funded research projects that compare different productions routes through collaboration with researchers at the University of Missouri and the Brookhaven, Argonne, Los Alamos and Oak Ridge National Laboratories for novel radionuclides of high interest to the nuclear medicine community. Although our ability to safely process high quantities of radionuclides (except for ^{211}At) has been limited due to the lack of remote target retrieval and hot cell infrastructure, we have conducted early-stage research on a small scale to evaluate new target designs and production of high specific activity ^{186}Re, ^{189}Re, ^{72}Se/^{72}As, ^{155}Tb and ^{230}U/^{226}Th at UW through these collaborative research projects. This presentation will provide an overview of our cyclotron and radiochemistry facilities and the ongoing collaborative research projects directed toward providing radionuclides in short supply.

NUCL

Production and Separation of ^{7}Be for Ion-source Preparation for National Superconducting Cyclotron Laboratory

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The use of offline sources is facilitating the stand-alone operation of the ReA (Re-accelerator) at the National Superconducting Cyclotron Laboratory (NSCL) after the coupled-cyclotron facility ceased operation. To supplement this experimental research program, ~5 mCi ^{7}Be ($t_{1/2}$ = 53.22 d, E_γ = 477.60 keV, I_γ = 10.44 %), a cosmogenic radionuclide, was required. This would be placed in the Batch-mode Ion Source (BMIS), which provides beams of stable or long-lived radioactive isotopes, consisting of an oven, coupled to an ion-source system with arrangements for beam transport. Due to the commercial non-availability of this rare isotope in sufficient quantity for ReA experiments, a production route through ^{10}B(p,α)^{7}Be reaction was explored at the University of Alabama Birmingham (UAB) Cyclotron facility and a subsequent separation methodology was developed. A total of 7 irradiations were carried out at the UAB Cyclotron with a 17.5 MeV proton beam with natural and ^{10}B enriched boron powder targets which led to the production of 9.27 mCi ^{7}Be in total. This boron powder was then dissolved in concentrated HNO_3 followed by separation of ^{7}Be from the bulk boron in HNO_3 medium employing the use of cation exchange chromatographic resin AG MP-50. A >90% ^{7}Be separation efficiency was achieved which was tracked with the gamma spectroscopy. The purified ^{7}Be fractions were then evaporated and reconstituted in a small volume of 0.1 M HCl and deposited onto tantalum foils for introduction into the BMIS for ^{7}Be beam delivery experiments.

Through this experiment, we produced and delivered ~5 mCi ^{7}Be to support the ongoing ReA experimental program of NSCL and established a radiochemical methodology for separating ^{7}Be from a boron target.

NUCL

Titanium-45 radiochemistry with THP^{Me} and TREN-CAM for development of PET radiopharmaceuticals

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The production and chemistry development of new radioisotopes are important steps in designing radiopharmaceuticals for nuclear imaging applications. Titanium-45 (^{45}Ti) is a novel radionuclide with desired physical characteristics for use in PET imaging including a moderate half-life (3.08 hour), decay by positron emission (85%) and low mean positron energy of 0.439MeV. Despite these promising characteristics, the radiochemistry for ^{45}Ti including the development of suitable bifunctional chelators is relatively unexplored. Building on our prior work on optimized production techniques for ^{45}Ti, we aimed to explore chelators which bind efficiently under mild conditions and form complexes which are stable *in vivo*.

Radiolabeling studies of ^{45}Ti were carried with two different chelators (THP^{Me} and TREN-CAM). Radiochemistry optimization was conducted by incubating 500uCi ^{45}Ti with chelators at varying mass and pH conditions. Serum stability studies were performed in mouse serum. *In vivo* imaging studies were performed with both THP and

TRENCAM labeled with ^{45}Ti and free ^{45}Ti. Dynamic PET scans were conducted for 1 hour after injection and biodistribution studies were performed immediately after imaging.
Radiolabeling optimization have shown significant binding of THP^{Me} and TRENCAM with ^{45}Ti is possible with high radiolabeling yields (>95%) for both THP^{Me} and TRENCAM achieved within 30 minutes of incubation at 37^{0}C. Excellent serum stability of ^{45}Ti with labeled chelators was observed where >95% labeled complex was intact after 6 hours of incubation. Tissue biodistribution studies demonstrated that the complexes showed rapid clearance and significantly lower ^{45}Ti in heart, lung and other key organs compared to free ^{45}Ti. This study has opened new possibilities of establishing ^{45}Ti as a novel radionuclide which hold promise for future investigations.

NUCL

Automation of astatine recovery from nitric acid media

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Targeted Alpha Therapy considers ^{211}At as one of the most promising radionuclides. However, the short half-life (~7.2 h) and high medically relevant activities require development of an automated system for the astatine isolation and purification. The majority of existing processes start with the metallic target dissolution in nitric acid. Then this dissolution solution undergoes further chemical manipulations, however, these additional steps result in the astatine losses. Our group has developed a chemical system where the nitric acid dissolution solution is utilized for the astatine recovery. This process is based on the bismuth and astatine separation on extraction chromatography columns, where no additional chemical treatment is needed and the final astatine product can be received within 30 min. The concept of the automated system and first results obtained will be discussed.

NUCL

Radiochemistry at the University of Alabama at Birmingham

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The University of Alabama at Birmingham (UAB), before turning 51 in 2020, was ranked as the #1 Top Young University in the US in the Times Higher Education Young University Rankings in both 2018 and 2019. This, in part, is due to the strength of the UAB School of Medicine and the associated O’Neal Comprehensive Cancer Center,

which have strategically established and supported the growth of the Cyclotron Facility within the Department of Radiology. Since its installation nearly ten years ago, the capabilities of the TR 24 cyclotron located in the Cyclotron Facility have grown to routinely produce, purify, and ship isotopes across North America and has recently become a member of the US Department of Energy's National Isotope Development Center. To help bolster the impact of isotope development at UAB, The Department of Chemistry has established a radiochemistry program to bridge the gap between fundamental and applied science. The capability of the Cyclotron Facility, along with the growing radiochemistry program at UAB will be discussed.

NUCL

Radiochemistry Development of ^{52}Mn for Characterization of PET/MR Imaging Agents

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Manganese-52 (^{52}Mn) is a positron emitting radionuclide that can be used as dual modality signal enhancing contrast agent for PET/MRI in combination with natural Mn^{2+}. ^{52}Mn has a 5.6-day half-life and emits a positron with a branching ratio of 29.4% and a low average positron energy of 242 keV. Mn^{2+} has already been investigated for its use as an MRI contrast agent because of its paramagnetic properties, with 5 unpaired electrons, natural Mn has the potential to replace or complement existing gadolinium compounds. Moreover, the use of tracer ^{52}Mn would enable quantification of the total Mn^{2+}.

^{52}Mn was produced via the nuclear reaction ^{52}Cr(p,n)^{52}Mn via natural Cr targets. ^{52}Mn separation is carried out on AG1-X8 anion exchange resin utilizing a semi-automated system using acid washes followed by elution of the final ^{52}Mn product in 0.1 M HCl. ^{52}Mn purified from natural Cr foils using 5 x 0.5 cm, gravity fed columns yielded non-decay corrected recoveries of 70.8 ± 3.3 % with a time of 8.2 ± 0.6 h whereas ^{52}Mn from the pressed powder Cr and electroplated Cr targets purified using pressurized 1 mL columns yielded non-decay corrected recoveries of 94.5 ± 2.4 % with a time of 4.2 ± 0.4 h. As natural Cr has 4 stable isotopes, impurities included Cr-51 ($t_{1/2}$ = 27.7 days) and Mn-54 ($t_{1/2}$ = 312 days). Enriched ^{52}Cr targets are under development.

PET/MR phantoms were prepared with ^{52}Mn radioactivity ranging from 0-20 µCi and Mn^{2+} concentrations ranging from 0-1 mM.. The ^{52}Mn/Mn^{2+} solution was used for PET/MRI scans where PET was acquired for 10-20 min and MRI was collected at various inversion times ranging from 200-2100 ms to create a T1 map. Preliminary animal studies with ^{52}Mn/Mn^{2+} were also conducted where rats were injected using a syringe pump over 1.4 ± 0.1 h with ^{52}Mn radioactivity of 276.3 ± 20.0 µCi and Mn^{2+} concentrations ranging from 10 - 40 mg/kg. After PET/MR imaging, animals were sacrificed and biodistributions primarily showed ^{52}Mn uptake in organs associated with hepatic excretion (small intestine, large intestine, and liver). These experiments demonstrate promising results for ^{52}Mn/Mn^{2+} as a PET/MRI imaging agent.

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NUCL

Production of ^{229}Th via Fast Neutron Bombardment

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Targeted alpha therapy has been demonstrated as an effective method for treating cancer. The supply of ^{225}Ac available for clinical applications is limited, so the demand for its precursor, ^{229}Th, is increasing. Consequently, the investigation for alternative routes for ^{225}Ac production is necessary. In this experiment, a thick beryllium breakup target was irradiated with 40 MeV deuterons (5 µA) at Lawrence Berkeley National Laboratory's 88-Inch Cyclotron to generate a high-flux fast neutron beam. A 7.6 mg ^{230}Th target was irradiated with this fast neutron beam for 4.5 days. After a long cooling period (>1 year), column chromatography techniques were implemented to obtain ^{229}Th, and the ^{230}Th(n,2n)^{229}Th reaction channel was measured for the first time. The yield was quantified using a high-purity germanium detector and inductively coupled plasma mass spectrometry. The measured yield was compared to predictions from the Particle and Heavy Ion Transport code System.

NUCL

Targeted Alpha Therapeutics to Combat Drug Resistant Pathogens

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Prior to the Antibiotic Era, infectious disease was leading cause of human morbidity and mortality throughout human history. However, with the advent of the first antibiotics pathogens evolved resistance mechanisms. Multidrug resistant pathogens are a pressing human health concern as the pace of now antibiotic development has slowed. Alpha-emitting radionuclides coupled with native metabolic targeting offers a new avenue for antimicrobial/antibiotic development. Here, we examine the chemistry of thorium combined with bacteria-specific siderophores as targeting vectors to kill pathogens such as *Pseudomonas aeruginosa*. Siderphore-based targeting is an attractive strategy that has garnered recent interest owing to intrinsic specificity and requisite nature for bacterial survival. We demonstrate efficacy with the alpha therapeutic Th^{IV}-227 chelated by a variety of siderophores as a promising antimicrobial strategy to fight multidrug resistance infections.

NUCL

Three Decades of Research on Radiometals for Radiopharmaceutical Imaging and Therapy

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The Anderson Lab's research throughout the past 31 years laid some of the foundation for the exploding growth of radiometal-based agents for diagnostic imaging and targeted radionuclide therapy of cancer, a field now coined "theranostics". In the 1990's, through mentorship by Dr. Michael Welch and exceptional trainees that include Jason Lewis, her lab did seminal research on the development of copper-64-labeled antibodies and peptides for positron emission tomography (PET) imaging of cancer that led to the first human study of a copper-64-labeled somatostatin analog to image neuroendocrine tumors. The first commercial copper-64-labeled agent in this class is now FDA approved (Cu-64 DOTATATE). In 2001, her lab published pre-clinical toxicity of the ^{177}Lu-labeled version of DOTATATE, and that agent is now FDA-approved and available for treating neuroendocrine tumors. Throughout the 2000's, her expertise in inorganic chemistry and radiochemistry led to the design of chelators for stably complexing radiometals to cancer receptor-targeted agents. A cross-bridged macrocycle developed through a collaboration with Drs. Edward Wong and Gary Weisman at University of New Hampshire is now a component of a PET imaging agent in human studies at two universities. At the University of Pittsburgh in the 2010's, Dr. Anderson's lab turned their focus to radiometal-based agents to image specific cell types in the immune system for early response assessment of immune-based therapies. Through collaborations with JoAnne Flynn (tuberculosis), Enrico Novelli (sickle cell disease), and Walt Storkus (melanoma), VLA-4 expression in tumors and immune cells was imaged with ^{64}Cu-LLP2A in mouse models, non-human primates, and soon, humans with sickle cell disease. During the 2020's at the University of Missouri, the Anderson Lab's research will have an emphasis on theranostics for treating cancer and other diseases, taking full advantage of the radionuclide production capabilities at

MURR, the College of Veterinary Medicine for trials in companion animals, and NextGen Precision Health for first-in-human studies. All of this research would not be possible except for the hard work and dedication of Anderson Lab trainees and staff who will be recognized throughout this presentation.

NUCL

Zr-89 Labeled Anitbodies for the PET Delineation of Cancer

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Molecular imaging (MI) originated from the need to better understand the fundamental molecular pathways inside organisms in a noninvasive manner. Over the past two decades, two factors have acted in concert to fuel the ascent of molecular imaging in both the laboratory and the clinic: First, an increased understanding of the molecular mechanisms of disease and second, the continued development of in vivo imaging technologies, ranging from improved detectors to novel labeling methodologies. The advent of molecular imaging has, in turn, prompted a paradigm shift in medical imaging as a whole, from its foundations in purely anatomical imaging towards techniques aimed at probing tissue phenotype and function. We have for many years exploited aberrant targets associated with cancer in order to better diagnose, stage, monitor and treat this disease.

The use of Positron Emission Tomography (PET) for cancer imaging is a well-established and widely used molecular imaging modality both in clinical and research settings. Over the last 30 years, our ability to non-invasively diagnose, localize, and treat many forms of cancer has advanced tremendously. Due to their exquisite selectivity and specificity for cancer biomarkers, radiolabeled antibodies have played an important and growing role in this trend. Within the last half-decade, antibodies labeled with the positron-emitting radiometal ^{89}Zr have emerged as enticing tools for the PET imaging of cancer. The use of ^{89}Zr-labeled MAbs will be the focus of this presentation.

NUCL

From isotopes to images:
Oncologic imaging with atypical radiometals at UAB

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With the expansion of FDA approved ^{18}F- and ^{68}Ga- based agents for medical imaging using positron emission tomography (PET), research into the production of isotopes with varying half-lives, chemistry and decay characteristics is expanding. Using the UAB TR24 cyclotron, our group has focused on the development of reaction routes, target materials and the separation chemistry of isotopes to expand the toolbox of nuclear imaging agents. These have included transition metals such as ^{52}Mn, ^{55}Co, ^{89}Zr, ^{43,47}Sc and ^{45}Ti. Additional research has developed chemistry to incorporate these isotopes into new imaging radiopharmaceuticals for preclinical or clinical research. In particular, our group has been exploring the use of ^{89}Zr radiolabeled antibodies for imaging of cell surface receptor expression in preclinical models and in clinical trials of metastatic breast cancer patients. Recent work has also resulted in new radiochemistry techniques for the development of new ^{43,47}Sc, ^{55}Co and ^{45}Ti radiopharmaceuticals for oncologic applications.

NUCL

Development of Copper Radiopharmaceuticals

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Various copper radionuclides have been evaluated in the past three decades for medical imaging and therapeutic purposes. Use of copper radionuclides for these purposes require bifunctional chelators that can be conjugated to biological targeting vectors as well as form high complexes with copper that are thermodynamically and kinetically stable. Many bifunctional chelators have been synthesized and evaluated over the years that have different advantages and/or disadvantages when used for complexing radioactive copper. Labeling kinetics, thermodynamic stability, charge, and lipophilicity must all be considered when designing a chelator and how these might affect in vivo biodistribution of the biological vector. Many vectors have been labeled with radioactive copper including peptides, antibodies, and nanoparticles. This presentation will give examples of the preclinical evaluation of vectors radiolabeled with copper in the context of oncology, infectious disease, and alzheimer's disease.

NUCL

Novel theranostic agents for PET imaging and treatment of metastatic melanoma targeting very late antigen 4 (VLA-4) using a versatile chelator for Lu(III), Tb(III), and Zr(IV)

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Melanoma, a malignant tumor derived from epidermal melanocytes, is the most serious form of skin cancer with high mortality, aggressiveness, therapeutic resistance, and predisposition for late metastasis. Novel theranostic agents for imaging and treatment of melanoma that allow identifying melanoma patients with high-risk primary lesions would facilitate further surveillance and possible adjuvant therapy. Very late antigen-4 (VLA-4) is a transmembrane noncovalent heterodimer overexpressed in melanoma tumors that is associated with tumor growth, angiogenesis, and metastasis by promoting adhesion and migration of cancer cells. The current study describes a VLA-4 targeting molecule, LLP2A, conjugated to a versatile, new chelator (Lumi804) that readily complexes radiolanthanides for targeted radiopharmaceutical therapy, along with Zr-89 for PET imaging. Lumi804 is an octadentate, macrocyclic compound based on four 1-hydroxypyridin-2-one (1,2-HOPO) coordinating units. This was conjugated with the high-affinity VLA-4 peptidomimetic ligand, LLP2A, and labeled with the following radiometals: Zr-89, Lu-177, and Tb-161 at room temperature under 30 min. Binding affinity of ^{89}Zr-, ^{177}Lu-, ^{161}Tb-Lumi804-LLP2A for VLA-4 will be determined and compared in VLA-4-positive B16F10 mouse melanoma cells. The biodistribution of the Zr-89 analogue was determined by PET/CT and dissection with gamma counting in B16F10 subcutaneous tumor-bearing mice. Data for Zr-89 show VLA-4 mediated uptake in the B16F10 tumor-bearing mice. Biodistributions of the ^{177}Lu- and ^{161}Tb-Lumi804-LLP2A analogues are planned.

NUCL

Validation of VLA-4-Targeted PET Imaging in a New BRAF^{V600E} Mouse Melanoma Model

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Objective

Although drastic responses to immune checkpoint inhibitors and targeted therapy occur in melanoma, many patients progress and have few effective alternatives. Our previous work has indicated avid and selective uptake of LLP2A, a peptidomimetic labeled with Cu-64 ([^{64}Cu]-LLP2A), for positron emission tomography (PET) imaging in B16F10 murine melanoma. LLP2A binds strongly to very late antigen-4 (VLA-4, integrin $\alpha_4\beta_1$), a transmembrane protein correlated with tumor growth and dissemination when overexpressed in melanoma and other tumor histologies. Yet B16F10 does not faithfully recapitulate clinical melanomas, as it lacks the BRAF mutation found in ≥50% of clinical specimens, among other aberrations. Here, we evaluated the PET tracer [^{64}Cu]-CB-TE1A1P-PEG$_4$-LLP2A ([^{64}Cu]-LLP2A) in novel, translational BRAF^{V600E} mutant melanoma models with distinct levels of VLA-4 expression - BPR (VLA-4$^-$) and BPRα (VLA-4$^+$).

Methods

To overexpress intact VLA-4, BPR cells were transduced with the α_4 subunit (CD49d), generating the BPRα cell line. The binding metrics of [^{64}Cu]-LLP2A to BPR and BPRα cells were determined by saturation binding assays. Plate-based assays were conducted to assess [^{64}Cu]-LLP2A internalization into B16F10, BPR, and BPRα cells. *Ex vivo* biodistribution and PET/CT imaging were performed in mice bearing either subcutaneous BPR or BPRα tumors.

Results

BPRα bound [^{64}Cu]-LLP2A with high affinity (K_d = 1.4 nM) but binding to BPR was undefined. The VLA-4$^+$ lines (BPRα and B16F10) demonstrated similar time-dependent tracer internalization, but internalization by BPR was essentially undetectable. BPRα tumors displayed notably greater [^{64}Cu]-LLP2A uptake vs. BPR tumors *in vivo* by PET/CT, which was corroborated by biodistribution analyses ($p<0.0001$).

Conclusions and Future Work

As expected, [^{64}Cu]-LLP2A differentiates BPRα (VLA-4$^+$) vs. BPR (VLA-4$^-$) melanomas *in vivo*, encouraging prospective imaging and theranostic studies with these cell lines - particularly BPRα. LLP2A may be especially apt to target clinically relevant and targeted therapy-resistant tumor variants towards eventual translation to patient care.

As proof-of-concept towards individualized ^{67}Cu-LLP2A therapy, longitudinal ^{64}Cu-LLP2A PET images were acquired for BPRα tumor-bearing mice in a separate study for ^{67}Cu-LLP2A dosimetry. Analysis of these images via dedicated 3D Monte Carlo software is ongoing.

NUCL

How it started and where is it going - Development of VLA4 and CD38 Targeted Molecular Imaging Agents for Multiple Myeloma

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Background. A debilitating cancer of abnormal plasma cells in the bone marrow, multiple myeloma (MM) remains largely incurable. There is an unmet need to prevent relapse and refractory disease in MM patients. Molecular imaging can help fulfil this gap by providing non-invasive assessment of disease burden at a whole body level. Based on the plasma cell specific unique functions in MM biology, we have been evaluating the receptor very late antigen 4 (VLA4, CD49d/CD29) and cluster of differentiation 38 (CD38, cADPRH) for imaging malignant MM cells in diverse animal models.

Methods. In vitro and ex vivo VLA4 and CD38 expression was evaluated by flow cytometry. Human MM cells, MM.1S-CG and U266-CG (C: Click beetle red luciferase and G: green fluorescent protein), were injected intravenously in NOD-SCID gamma mice. Tumor progression was monitored by bioluminescence imaging (BLI). Treatment group received bortezomib (1 mg/kg, twice/week) intraperitoneally. All cohorts (treated, untreated and no tumor) were longitudinally imaged with [^{18}F]FDG (7.4–8.0 MBq) and the VLA4 targeted agent [^{64}Cu]Cu-LLP2A (2-3 MBq Molar Activity 44.14±1.40 MBq/nmol) PET, respectively. CD38 imaging was performed with near-infrared (NIR) fluorophore IRDye800CW conjugated antibody, daratumumab.
Results. Flow cytometry confirmed high expression of VLA4 in U266 cells (99%) and moderate expression in MM.1S cells (52%), whereas CD38 expression was 98% and 60% in MM.1S and U266, respectively. Compared to [^{64}Cu]Cu-LLP2A, [^{18}F]FDG PET detected treatment-related changes at later time points. This tracer is currently undergoing safety and dosimetry assessment in humans. The CD38 targeted molecular imaging performed with daratumumab conjugates showed that fluorescent labelling did not affect the biologic activity of the native antibody and allowed for evaluation of the antibody conjugates on a whole-body and cellular level.
Conclusions. Our results demonstrate the utility of plasma cell specific tracers for precision imaging and therapy of MM.

NUCL

Aromatic macrocyclic bifunctional chelators for radiopharmaceutical applications

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The utility of biological ligands attached to radionuclides for in vivo applications depends on the ability of a bifunctional chelator (BFC) to retain the metal ion of interest. Chemists increase the stability of metal chelates by selecting appropriate metal coordinating groups and by pre-organizing the metal binding chelator into a conformation that has been optimized for metal binding. Coordinating groups are chosen based on their affinity for the metal cation of interest, the “bite angle” subtended by the individual atoms in the group, and the number of groups needed to form an optimal coordination geometry. Our chelators exploit two factors that confer conformational rigidity: The use of aromatic coordinating groups and the positioning of these upon macrocyclic scaffolds.

Recently, we reported the properties of aromatic macrocyclic BFCs made from 1-hydroxypyridin-2-one (1,2-HOPO) coordinating groups. These groups are useful both as sensitizers of europium(III) luminescence and as remarkably effective ligands for lanthanides and related tetravalent metal ions of radiopharmaceutical interest. These macrocyclic chelators form bright (Φ = 0.37) europium(III) complexes that are up to 1000-fold more kinetically stable with respect to challenge by DTPA compared to acyclic 1,2-HOPO analogs. Crystallographic characterization of the parent europium(III) complex confirms that the inner coordination sphere of europium(III) cation is fully saturated by the 1,2-HOPO binding units (**Fig. 1**). Both the europium(III) and the corresponding calcium(II) BFCs can be coupled to a variety of targeting moieties (e.g. antibodies) using amide-forming NHS coupling chemistry. The calcium(II) form of the BFC has been shown to label with lutetium(III), zirconium(IV), and thorium(IV) quickly at room temperature, which can facilitate the development of temperature sensitive radiopharmaceuticals containing these metal ions.

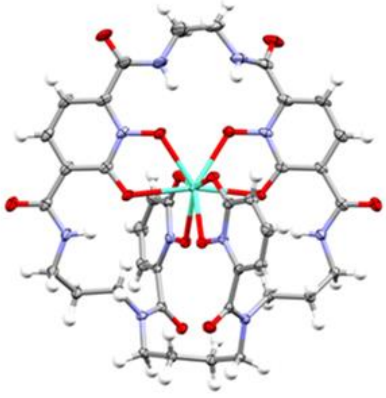

Figure 1.

NUCL

Astatine-211 labeled single domain antibody fragments for targeted alpha-particle therapy of HER2-expressing cancers

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Because of their small size (12-15 kDa), and high affinity, single domain antibody fragments (sdAbs) are attractive vehicles for achieving rapid and selective delivery of the promising α-particle emitter ^{211}At (7.2 h half-life), to tumors. In previous studies, we demonstrated that high and prolonged tumor targeting and rapid normal tissue clearance occurred when anti-HER2 5F7 sdAb was labeled via the residualizing prosthetic agent *N*-succinimidyl 3-[^{211}At]astato-5-guanidinomethyl benzoate (*iso*-[^{211}At]SAGMB). Unexpectedly, tumor targeting, kidney clearance and *in vivo* stability of *iso*-[^{211}At]SAGMB-5F7 were all more favorable than the conjugate prepared with the 3-[^{211}At]astato-4-guanidinomethyl isomer. Herein, we have evaluated the therapeutic potential of *iso*-[^{211}At]SAGMB conjugates of 5F7 and K65R, a structurally similar anti-HER2 sdAb devoid of lysines in its CDR, in HER2-expressing BT474 breast carcinoma cell and xenograft models. In some experiments, an anti-GFP sdAb with no HER2 reactivity served as a control. *Iso*-[^{211}At]SAGMB was synthesized from the corresponding trimethyltin precursor, purified by HPLC, and reacted with the sdAbs. The clonogenic survival of BT474 cells decreased in a dose dependent manner after treatment with *iso*-[^{211}At]SAGMB-5F7 with a D_0=1.313 kBq/ml while no cytotoxicity was observed even at the highest activity concentration of *iso*-[^{211}At]SAGMB-GFP. Three single-dose therapeutic efficacy studies have been performed in mice with subcutaneous BT474 xenografts: 1) *iso*-[^{211}At]SAGMB-5F7 (0, 0.7, 1.9, 3 MBq); 2) *iso*-[^{211}At]SAGMB-K65R (0, 1, 1.9, 3 MBq) and 3) *iso*-[^{211}At]SAGMB-K65R (1.0 MBq) and *iso*-[^{211}At]SAGMB-GFP (1.1 MBq). In all studies, significant dose-dependent tumor growth delay and survival benefit was observed for the *iso*-[^{211}At]SAGMB 5F7 and K65R conjugates compared with PBS. A single 3.0-MBq dose of *iso*-[^{211}At]SAGMB-K65R resulted in complete tumor regression in 8 of 11 animals and increased median survival from 50.5 d to 209 d. The specificity of the therapeutic effect was demonstrated in the third experiment: *Iso*-[^{211}At]SAGMB-GFP at 1.1 MBq (34 d) did not improve median survival compared with PBS (44 d); in contrast, the *iso*-[^{211}At]SAGMB-K65R group had not yet reached median survival at 125 d. No treatment related toxicities were observed. These results suggest that these *iso*-[^{211}At]SAGMB anti-HER2 sdAb conjugates warrant further development as targeted radiotherapeutics for the treatment of HER2-positive malignancies.

NUCL

Radioarsenic chemistry: Toward a diagnostic/therapeutic matched pair

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We have been focused on developing the $^{72/77}$As diagnostic/therapeutic matched pair of radioisotopes for potential radiopharmaceutical applications. Arsenic-72 (^{72}As) is an accelerator produced, 26-h half-life positron emitter, while ^{77}As is a reactor produced, 38.8-h half-life beta emitter. Arsenic is thiophilic and chelate development has involved multidentate thiols (dithiols and trithiols). The production and separation chemistry, chelate and metal chemistry, radiotracer chemistry, specific activity and biological factors that have been addressed or need to be considered will be discussed with the ultimate goal of specific tumor targeting in mind.

NUCL

Update on activities of the isotope program at Brookhaven National Laboratory

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The Department of Energy has developed unique infrastructure that has supported R&D in isotope production leading to major advancements such as the development of the Tc-99m generator. Many isotopes based on national need were first developed at DOE and supported until they could be handed off successfully to the private sector. In the 1970’s the first target end station was built at BNL to accept high energy protons from the 200 MeV Linac to irradiate targets for isotope production. Following this concept was imitated and 100 MeV and greater accelerators were installed in many of the national labs around the world and used for production of radionuclides at energies and currents not available on the small compact machines. These high energy accelerators have played an important role in supplying radionuclides such as Sr-82 used in Sr/Rb generators for cardiac imaging. They continue to be advanced to further production yields by installing beam rastering systems, enhancing target cooling that have allowed for higher beam intensities and thus higher production yields. Demand for isotopes that can be produced by these systems has also increased. Linear accelerators such as the one at Brookhaven National Laboratory when operating at maximum proton energy of 200 MeV can have simultaneous production of several medically relevant isotopes is possible. Among those are Ac-225 ($T_{1/2}$=10.0 d), Cu-67 ($T_{1/2}$=64.83 h), Se-72/As-72 ($T_{1/2}$=26 h), Sr-82/Rb-82 ($T_{1/2}$=1.26 min) and Ti-44/Sc-44 ($T_{1/2}$=3.97 h). Production of these novel radionuclides and recent enhancements to the BNL isotope program will be presented.

NUCL

Preliminary evaluation of alpha-emitting radioembolization in animal models of Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC), the commonest primary liver cancer, is the fifth most frequently diagnosed cancer worldwide. At the time of diagnosis most patients have advanced disease, greatly limiting their options for treatment beyond non-surgical palliative care.Thisalpha-particle emitting radioembolization for the treatment of HCC. A DOTA chelator was modified and radiolabeled with Actinium-225, an α-particle emitting radionuclide. The resulting agent [^{225}Ac]Ac-DOTA-TDA was emulsified with Lipiodol®, an FDA-approved radio-opaque agent, yielding the radioembolic agent [^{225}Ac]Ac-Lipiodol®. Lipiodol® can be targeted to hepatic tumors through the hepatic artery, where it is able to embolize hepatic tumors, accumulating and remaining in the tumors while clearing out of normal liver tissue, making it an excellent vehicle for the selective delivery of therapeutic radionuclides. To confirm retention in HCC tumors of the modified chelator, we initially determined that [^{111}In]In-DOTA-TDA was retained to a greater degree within HEPG2 tumors in a mouse model when emulsified with Lipiodol® (216±145 %ID/g) as compared to [^{111}In]In-DOTA-TDA alone (20.0±15.9 %ID/g) 48 hours post-injection. [^{225}Ac]Ac-Lipiodol® showed significant improvement in the survival of HEPG2 tumor-bearing mice to as compared to controls ($p<0.005$). Selective delivery of [^{225}Ac]Ac-Lipiodol® to hepatic tumors via the hepatic artery was confirmed in the VX2 rabbit model. The rabbit model allowed us to monitor [^{225}Ac]Ac-Lipiodol® with SPECT-imaging of Actinium-225's daughters, Francium-221 and Bismuth-213; distinguishing between [^{225}Ac]Ac-Lipiodol® (Francium-221) and the relocation of the longer lived Bismuth-213. [^{225}Ac]Ac-Lipiodol® demonstrated high retention within the VX2 tumor

(40.6 %ID/g) 6-days post-injection as compared to the normal liver (0.23 %ID/g). Finally, maximum tolerated activity (MTA) studies are currently underway with no evident short-term toxicities (3-month) in healthy rats administered [^{225}Ac]Ac-Lipiodol® via the hepatic artery. Overall these works are supportive of [^{225}Ac]Ac-Lipiodol® as a promising therapeutic agent for HCC.

NUCL

Radiolabeled nanocarriers: Imaging tools for patient-based drug delivery

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Nanomedicines, nanoparticle/ liposomal/ pegylated drug formulations, have been extensively evaluated for the delivery of cancer therapeutics. However, since 2000 there have only been 7 FDA approved nanomedicines, a significantly low number considering all the promising published preclinical successes. These formulations have been shown to significantly alter the pharmacokinetics and toxicological profile of conventional low molecular weight cancer chemotherapeutics (e.g. doxorubicin, paclitaxel, gemcitabine, etc). Encapsulating chemotherapeutics in liposomes or micelles or coupling chemotherapeutics to polymeric/ polyethylene glycol (PEG) molecules reduces their interaction with blood proteins, protects the molecules from metabolic degradation, increases their circulation half-life, reduces potential off target / toxicologic effects and improves target site accumulation. Despite their promising properties, variability in treatment response significantly limits their effectiveness and full clinical translation. Star-PEG polymer-based constructs have been used as vehicles to deliver SN-38, active metabolite of irinotecan, and talazoparib, a PARP inhibitor, to solid tumors. We have developed cognate zirconium-89 labeled star-PEG polymers, with and without the pendant drugs, as imaging agents to assess the pharmacokinetic properties of the nanomedicines in a variety of preclinical solid tumors models. We have shown that the ^{89}Zr-star-PEGs accumulate and are retained in the tumors. Molecular imaging using positron labeled nanomedicines provides a means to non-invasively visualize delivery and quantitate accumulation of therapeutic agents. Thus, this imaging approach may be applicable as a predictive strategy for evaluating drug delivery and concentration in tumors, to overcome the challenge of choosing the right patients in clinical trial and ultimately treatment settings.

NUCL

Improving the kidney toxicity profile of actinium-225 radiopharmaceuticals

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The development of targeted alpha particle therapies (TATs) involving actinum-225 is an active area of research. Despite the therapeutic efficacy that has been observed in numerous studies, several challenges need to be overcome before this strategy can be adopted fully. Minimizing kidney toxicity after radiotherapy administration is one issue that still needs to be resolved. To investigate a potential solution to this problem, we prepared a small library of TATs based upon the parent radiopharmaceutical, ^{225}Ac-DOTA-MC1RL, which is under development for the treatment of metastatic melanoma. This library contained radiopharmaceuticals with a range of lipophilicities (log $D_{7.4}$ values). We conducted biodistribution, pharmacokinetic and radiation dosimetry studies in mice to determine how lipophilicity of the radiopharmaceutical affected these parameters. From these studies, we observed that higher log $D_{7.4}$ values were associated with decreased kidney uptake, decreased absorbed radiation dose, and decreased kidney toxicity of the TAT, and the inverse was observed for lower log $D_{7.4}$ values. These findings suggest that tuning radiopharmaceutical lipophilicity can effectively modulate the level of kidney uptake to reduce morbidity and improve both safety and efficacy.

NUCL

Albumin-binding Lutetium-177-labeled LLP2A derivatives as theranostics for metastatic melanoma

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Very late antigen-4 (VLA-4) is a trans-membrane integrin protein that is highly expressed in aggressive forms of metastatic melanoma. This integrin plays a key role in tumor growth, angiogenesis and metastasis by facilitating cancer cell adhesion and migration. LLP2A, a small-molecule high affinity, peptidomimetic, itself does not inhibit cancer cell proliferation and survival, and therefore is an ideal candidate for imaging and delivery of therapeutic payloads. We previously demonstrated the utility of 177Lu-DOTA-LLP2A as a therapeutic agent against metastatic melanoma in mice in combination with immune checkpoint inhibitors, although tumor growth was marginally inhibited with no cures. We hypothesize that failure to diminish tumor burden after 177Lu-DOTA-LLP2A therapy was due to the rapid renal clearance of the dose from the blood and tumor thereby decreasing efficacy. To improve the pharmacokinetic profile, we designed and synthesized novel analogs of DOTAGA-LLP2A with a 4-(p-iodophenyl)butyric acid (pIBA) albumin binding moiety. We demonstrate the feasibility of

this albumin binding strategy by comparing in vitro cell binding assay, in vivo biodistribution performance, and therapeutic efficacy of 177Lu-DOTAGA-PEG4-LLP2A (**1**) to the albumin binding 177Lu-DOTAGA-pIBA-PEG4-LLP2A (**2**). In vitro cell binding assay results for 1 and 2 showed K_d of 0.4 and 1.75 nM and B_{max} of 200 and 315 fmol/mg respectively. Our in vivo biodistribution data for both tracers exhibited specific uptake in tumor, spleen, thymus and bone due to endogenous organ expression of VLA-4. Tumor uptake for **1** was highest at 1 h (~15 %ID/g) and **2** at 24 h (~27 %ID/g). Clearance from the tumor for **1** occurs at 24 h (<5 %ID/g) while **2** is retained for up to 168 h (~10 %ID/g). Compound **2** also exhibited much longer blood circulation time compared to **1**. Preliminary therapeutic efficacy studies (30 MBq; 800 mCi/mouse for each compound 1 & 2) showed a notable inhibition of tumor growth for compound **2** compared to **1** with tumor volumes of 0.122 and 1.24 cm^3 at 14 and 7 days post dose injection, respectively. Collectively, the in vitro and in vivo data suggest that modifying LLP2A with an albumin binder (pIBA) offers similar VLA-4 receptor binding qualities as the non-albumin binding molecule and provides a remarkable improvement in renal clearance and tumor retention and inhibition. Further efficacy studies are ongoing.

NUCL

Therapeutic Radioisotope Production at MURR

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The University of Missouri is home to the nation’s largest university research reactor. The 10 MW University of Missouri Research Reactor (MURR) is a national resource for research and application of neutron-related science. While the applications are numerous and varied, one of MURR’s key roles is employing nuclear science in the battle against cancer and other chronic human disorders. An overview of MURR’s role as the only domestic producer of four therapeutic radioisotopes will be presented.

NUCL

Targeting of cancer-specific receptors with ^{99m}Tc- and ^{186}Re-labeled NOTA- and NODAGA-functionalized peptides

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The theranostic radioisotopes ^{99m}Tc (diagnostic imaging) and ^{186}Re (therapy) are chemical congeners that allow for the development of structurally analogous complexes with matching chemical and pharmacokinetic behavior. With the goal of developing novel ^{99m}Tc/^{186}Re theranostic cancer agents, several generations of bifunctional chelators were investigated for tridentate facial coordination of the monocationic Tc(I) and Re(I) tricarbonyl cores, *fac*-$[M(CO)_3]^+$, where M = ^{99m}Tc or $^{nat/186}$Re. Early

bifunctional chelators (e.g., with N,S,N and N,S,O donor atom sets) yielded peptide complexes that demonstrated promising in vitro results: high radiochemical yield, matching chemical behavior, high stability and good affinity for the targeted cancer receptor. However, their potential for diagnostic imaging was diminished by slow and predominantly hepatobiliary clearance that was attributed to lipophilic character. Although NOTA and NODAGA chelating ligands are commonly used for Ga and Cu radiometals, they remain largely unexplored for Tc and Re radiometals. Our recent efforts established NOTA and NODAGA as excellent bifunctional chelators for the *fac*-$[M(CO)_3]^+$ core. This labeling approach yielded hydrophilic ^{99m}Tc/^{186}Re complexes of excellent stability that demonstrated improved specific receptor/tumor targeting and renal-urinary clearance in biodistribution and SPECT imaging studies. This retrospective assessment examines the development of receptor-targeting, structurally analogous $M(CO)_3$-labeled complexes with matching behavior utilizing the theranostic ^{99m}Tc and ^{186}Re radioisotopes.

NUCL

Tb-161 and Lu-177 labeling chemistry of DOTAGA-PEG4-LLP2A and Lumi804-PEG4-LLP2A as VLA-4 targeted theranostics

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Very late antigen 4 (VLA-4) is a transmembrane non-covalent heterodimer, which is overexpressed in certain types of cancer cells and is associated with tumor growth and metastasis. Previous studies have shown that ^{177}Lu-DOTA-PEG4-LLP2A provides marginal therapeutic efficacy in B16F10 melanoma tumor-bearing mice. Terbium-161 [6.89 d half-life, β^-:100%, $E_{\beta max}$ = 594 keV, γ emissions: 48.9 keV (17.0%) and 74.6 keV (10.2%)] has physical and chemical properties that are comparable to the clinically established isotope Lu-177 [6.65 d half-life, β^-:100%, $E_{\beta max}$ = 497 keV, γ emission: 208 keV (10.4%)]. In contrast with Lu-177 however, Tb-161 decays with co-emission of ~12 Auger and conversion electrons (≤50 keV, vs. ~1 keV for Lu-177), and along with its low energy β^- particle, results in a higher total electron-to-photon ratio of Tb-161 (5.9) than Lu-177 (4.8). For internalizing radiopharmaceutical therapy agents, higher abundance of low-energy electrons may enhance the killing of tumor cells. Bifunctional derivatives of the macrocyclic chelator DOTA represent the current state-of-the-art for radiolanthanide-based agents. However, fully in-cage chelation of lanthanides by DOTA is slow and sensitive to the presence of transition metal impurities (e.g., Zn^{2+}, Cu^{2+}, Fe^{3+}), which lowers the achievable effective molar activity of radiopharmaceutical therapeutic agents. In contrast, Lumi804 is a recently developed macrocyclic bifunctional chelator that more readily chelates metal ions that prefer 8-coordination, such as Zr^{4+} and Lu^{3+}. A major advantage of Lumi804 over DOTA is its propensity for efficient radiolabeling at lower temperature (25 ^{o}C) and at lower pH (more favorable to aqueous metal ion stability) within 30 minutes. Herein we present our comparative study of molar activities achieved using MU Research Reactor produced Tb-161 (^{160}Gd(n,g)^{161}Gd - ^{161}Tb) and Lu-177 (^{176}Lu(n,g)^{177}Lu) labeled DOTAGA-PEG4-LLP2A (where GA = glutaric acid; **1**) vs. Lumi804-PEG4-LLP2A (**2**). Thus far, only small activity batches of Tb-161 have been produced (< 1 GBq), meaning the effects of trace metal contaminants become more important. Our preliminary labeling results showed quantitative Tb-161 labeling of compound **2** in 5 minutes at room temperature (pH 4-5). In contrast, compound **1** required heating to 95 ^{o}C for 30 minutes (pH 4-5). The highest molar activity reached thus far for **1** and **2**are 40 mCi/nmol and 200 mCi/nmol, respectively. Studies with Lu-177 labeling are ongoing.

NUCL

Imaging Reactive Oxygen Species In Vivo with PET

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Our group has pioneered the development of PET radiotracers for imaging oxidative stress in tissue. The lead compound for radiotracer development for this project was dihydroethidine (DHE), which is oxidized by superoxide to ethidium and trapped in tissues. The most promising radiotracer based on this lead compound is [^{18}F]ROStrace, which is also oxidized by superoxide to form a charged species that is trapped in tissues with high levels of ROS. Since this compound readily crosses the BBB it can measure the proinflammatory form of neuroinflammation, and [^{18}F]ROStrace was validated using a murine model of lipopolysaccharide (LPS)-induced neuroinflammation (ACS Chem Neurosci 2018; 9: 578). Ex vivo staining studies in tissue revealed this radiotracer is localized in activated microglia (Iba-1) and neurons but not astrocytes (BBRC 2019; 516: 397). This presentation will focus on the use of the radiotracer in murine models of Alzheimer's disease (AD), and will present evidence that female mice are more prone to oxidative stress than male mice, and may explain the clinical observations that AD has a more severe phenotype in female versus male subjects.

NUCL

The long and winding road to the development of a new PET myocardial perfusion agent: From ^{64}Cu to ^{18}F and cyclops to rhodamine

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Myocardial perfusion imaging (MPI) is the most commonly performed nuclear medicine procedure in adults. These studies are primarily carried out with ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin. However, ^{99m}Tc radiopharmaceuticals have several limitations in MPI including the challenge of doing attenuation corrections, which makes it difficult to correct for attenuation artifacts, and decreased extraction efficiency at high flow rates,

which makes it difficult to measure cardiac flow reserve. These limitations can be overcome using positron-emitting MPI radiopharmaceuticals, but the existing agents, [^{13}N]NH$_3$ and ^{82}Rb, also have significant limitations including the short half-life of ^{13}N (10 min) and the high cost of the ^{82}Sr/^{82}Rb generator. These limitations can be avoided by using an agent labeled with a radionuclide with a longer half-life, such as ^{64}Cu ($t_{1/2}$ = 12 h) or ^{18}F. Unfortunately, no such agents are currently available.

We initially proposed the development of a ^{64}Cu PET MPI agent based on a lipophilic cationic Cu(II) complex analogous to ^{99m}Tc MIBI and tetrofosmin. We developed a series of such complexes based on the "cyclops" ligand, a monoanionic diimine dioxime, and evaluated their biological properties in rats. These compounds showed significant uptake in the heart, but they also showed high uptake in the liver, presumably because of the high lability of Cu(II); and despite multiple modifications to the ligand, we were unable to develop a compound with low liver uptake.

To circument this obstacle, we turned to ^{18}F ($t_{1/2}$ = 2 h) as an alternative radionuclide and rhodamines as the lipophilic cation. Rhodamines are inherently lipophilic and cationic, and the carboxylate moiety offers a convenient site for radiolabeling. Several ^{18}F-labeled rhodamine derivatives were evaluated *in vivo*, and the ^{18}F-labeled diethylene glycol ester of rhodamine 6G was found to have the highest uptake by the heart and lowest uptake by the liver. This compound also shows high (~85%) first-pass extraction by the heart that doesn't decrease with increased blood flow

Based on these encouraging preclinical results, we proceeded to first-in-human studies. In contrast to the preclinical studies, these images showed high uptake in the RES system and reduced uptake in the heart, suggesting that the compound may be aggregating either prior to or immediately after injection. Current efforts are focused on disrupting/minimizing this aggregation and restoring the high uptake by the heart.

NUCL

Positron Emission Tomography Imaging of Invasive Fungal Infections with D-[5-^{11}C]-Glutamine

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Invasive fungal infections (IFIs), specifically in immunocompromised patients, have become a grave healthcare concern worldwide. Fungi are capable of utilizing external D-amino acids (DAAs) including D-glutamine for their metabolism and growth by rapidly upregulating D-amino acid oxidases. Here we expand the use of positron emission tomography (PET) imaging with D-[5-^{11}C]-Glutamine (D-[5-^{11}C]-Gln) for noninvasive detection of IFIs in mouse models infected with *Candida albicans (C. albicans)*. **METHODS:** Comparative *in vitro* studies of D-[5-^{11}C]-Gln vs. L-[5-^{11}C]-Gln were conducted in fungal (*C. albicans* and *C. tropicalis*) and bacterial strains (*E. coli* and *S. aureus*), where heat-killed cultures were used as negative controls. Dynamic *In vivo* PET imaging was performed from 0 – 60 min post injection of radiotracer in immunocompetent CD-1 mice infected with *C. albicans* subcutaneously (SC) or intramuscularly (IM) in individual hind-limbs, and heat-killed fungi in the shoulder muscle, followed by e*x vivo* histological staining and microbiological culture assessments. **RESULTS:** The dynamic cellular uptake showed significantly higher uptake rates for D-[5-^{11}C]-Gln (~415%) than L-[5-^{11}C]-Gln (~150%) from 30-min to 90-min. No substantial uptake was observed in heat-killed controls. Further, D-[5-^{11}C]-Gln showed significantly ($p < 0.05$) higher uptake in fungi vs. bacterial species. As expected, comparative PET imaging studies demonstrated significantly higher infection-to-background ratios for D-[5-^{11}C]-Gln vs. L-[5-^{11}C]-Gln in both SC (ratio = 1.7, p = 0.016) and IM (ratio = 1.8, p = 0.004) infections with no significant difference observed between localized inflammation sites and untreated muscle background (heat-killed site/muscle: ~1.25). **CONCLUSION**: Our results demonstrated the translational potential of PET imaging with D-[5-^{11}C]-Gln for noninvasive detection of IFIs.

NUCL

Homogeneous precipitation of radioactive metals: Applications in cancer and arthritis

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Precipitation of Sn-117m and Y-90 was performed by slowly increasing the global pH of aqueous solutions of the metal. This was accomplished by the heat degradation of urea included in the solution. Using this method, homogeneous particle sizes were reproducibly prepared. The particles were shown to remain at the site of administration when injected into the synovium of rats or muscle of mice.

Particles of Sn-117m were developed to treat arthritis. After positive results in an arthritis rat model, the product was tested in dogs. The product is commercially available as a medical device for veterinary use in the US. The next step in this technology is human clinical trials.

Particles of Y-90 have been directly administered to tumors. Efficacy in dogs, horses, and one rhino will be discussed. Direct administration of radioactive colloids to tumors could increase the dose to tumors while significantly reducing the dose to normal tissues and organs.

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Preclinical Imaging of Antibodies to Inform Pharmacokinetics and Facilitate Drug Development

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Novel molecular formats have emerged due to advances in protein engineering, providing novel mechanisms of action for antibody therapy and expanding the breadth of structure-activity relationships for biologics. Systemic pharmacokinetics and tissue distribution of antibody therapeutics are dependent upon numerous factors including molecular size, electrostatic charge, and specific receptor interactions, particularly with the neonatal Fc receptor. Diverse radiochemical probes for studying the in vivo disposition of antibodies have been demonstrated as valuable tools for confirming receptor engagement, assessing off-target uptake, and characterizing clearance mechanisms. An overview of the utility of molecular imaging and other radiometric approaches in the preclinical and translational development of biologics will be presented, with an emphasis on the practical advantages of radionuclide probes in the assessment of antibody distribution properties.

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Translation of the M4 PAM specific PET tracer [^{11}C] MK-6884 from non-human primates to Alzheimer's Disease patients

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[^{11}C]MK-6884 is a muscarinic cholinergic receptor subtype 4 positive allosteric modulator (M4 PAM) developed as a PET tracer to facilitate the clinical development of therapeutic candidates for the treatment of neuropsychiatric symptoms in Alzheimer's patients. [^{11}C]MK-6884 was designed to bind to the allosteric site on the M4 receptor (M4R) with high affinity and selectivity. [^{11}C]MK-6884 imaging showed a large, displaceable M4 receptor-specific signal and low test-retest variability. The ability of [^{11}C]MK-6884 to quantify target engagement by therapeutic M4 PAMs was assessed in both rhesus monkeys and humans. These studies successfully determined the receptor occupancy (RO) by M4 PAMs in clinical development, allowing the relationships between drug plasma exposure, RO, and pharmacodynamic activity to be successfully modeled. In addition, the affinity of [^{11}C]MK-6884 for the M4R was increased in the presence of orthosteric agonists *in vitro* and *in vivo*, consistent with its high cooperativity with the orthosteric binding site. Subsequent PET imaging studies were performed in monkeys, healthy volunteers and AD patients in the presence of the acetylcholinesterase inhibitor donepezil to evaluate the effect of changes in synaptic acetylcholine levels on tracer binding. These studies indicated that tracer binding potential was increased by donepezil, which does not directly bind to the M4R, confirming the influence of cholinergic tone on [^{11}C]MK-6884 binding. Consistent with the degeneration of cholinergic pathways in the cortex of AD patients, [^{11}C]MK-6884

PET studies in AD patients showed lower cortical binding potential values compared to healthy controls, with notable cortical heterogeneity and bilateral asymmetry of M4R binding. In summary, the development of the M4 PAM PET tracer [^{11}C]MK-6884 provides a useful tool for determining the target engagement of M4 PAMs in clinical development and may be used as a probe to study the involvement of the M4R in normal and pathological states.

NUCL

Positron emission tomography imaging agents for synaptic vesicle glycoprotein 2A: from benchtop to human brain

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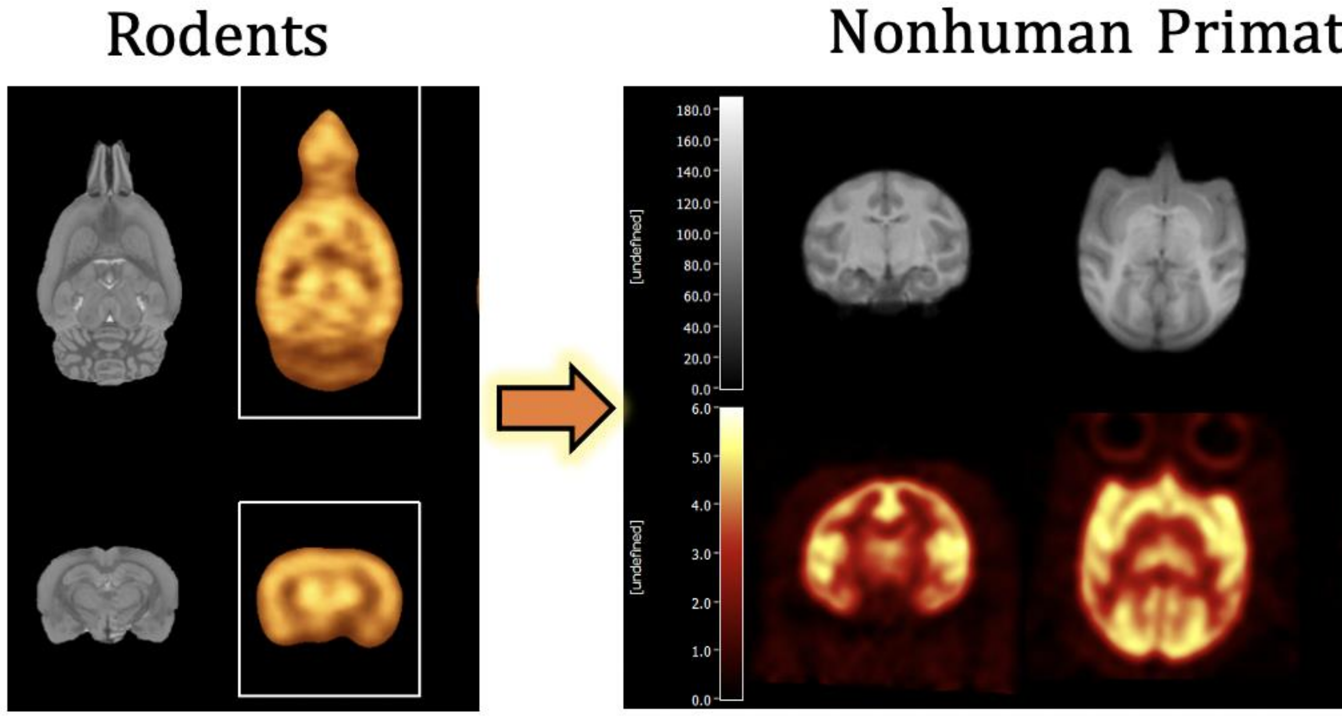
Synaptic vesicle glycoprotein 2A (SV2A) is a member of the synaptic vesicle glycoprotein family and is expressed ubiquitously in the presynaptic vesicles in the central nervous system (CNS). PET imaging agents targeting SV2A allowed for the sensitive *in vivo* measurement of synaptic dynamics in the CNS. Encouraged by the promising results from the proof-of-concept studies using the lead SV2A PET tracer [^{11}C]UCB-J in a broad range of neuropsychiatric disorders, we designed, synthesized, and evaluated several ^{18}F-labeled analogs for multicenter clinical trials and future routine clinical use. This talk will focus on the design, SAR study, *in vitro* and *in vivo* characterizations in animal models, and the clinical translation of the newly developed ^{18}F-labeled SV2A PET imaging agents. The pharmacokinetics, test-retest reproducibility and the extent of specific binding in the brains of different species will also be discussed.



Lyu X. *et al. SNMMI* 2020 Cai Z. et al. *ACS Chem. Neu*

NUCL

Immunomodulation with targeted theranostic pain nanomedicine provides long lasting analgesia in both sexes

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Extremity injuries account for the majority of combat wounds incurred during US armed conflicts. With the advent of combat body armor, there has been a reduction in torso injuries which, when coupled with improved evacuation times, means more casualties are reaching the higher echelons of care with severely injured extremities. Although casualty care advances have resulted in increased survival rates, there has also been an increase in service members with severe, complex traumatic injuries requiring extensive chronic pain management. Continued reliance on opioids as the “gold standard” of pain treatment has resulted in a growing “epidemic” of prescription opioid abuse among veterans returning home from the battlefield. The current non-opioid and local analgesia approaches lack molecular and cellular targeting specificity to effectively engage key cellular players in the neuronal injury milieu. Targeted theranostic pain nanomedicine offers significant safety and efficacy advantages to standard non-opioid treatments by directly engaging these targets and by doing so achieving >1000 fold increase in efficacy. Presented theranostic pain nanomedicine platform is a single-dose, intravenous (IV) injectable, injury-site specific, cell targeted, biocompatible, bi-specific nanomedicine analgesic therapeutic strategy administered at point of injury for acute pain, that can also provide extended pain relief (at least 72h), beyond Role 1-2 echelon care without the adverse effects seen with current treatments. The pain nanomedicine provided distinct pain relief in chronic constriction nerve injury model in rats and inflammatory model in mice in both sexes, while utilizing distinct cellular signatures. Tissue analyses, including immunohistochemistry, immunofluorescence, collagen counting, protein and genetic analyses identified sex differences in neuro-immune response to injury. We also show how theranostic pain nanomedicines can be used to specifically modulate nervous/immune system interactions in both sexes opening doors to sex specific pain treatments which current lack in both civilian and military settings.

NUCL

Oncologic Imaging of Our Furry Friends

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Historically, the development of radiopharmaceuticals for cancer follows a pathway from evaluation in cell models to tumor-bearing laboratory animals to clinical trials in human subjects. This scenario does not include the study of animals with naturally occurring cancers. Animals such as dogs present in the clinic in a way that closely mimics that of human cancer patients. In addition, several canine cancers are very similar to human cancers, both on the clinical and on the molecular levels. The study of molecular imaging agents in animal patients constitutes an important aspect of translational research in the field of nuclear oncology. This evaluation provides an intermediate step from the laboratory toward studies in humans. There are several potential advantages to evaluating tumor-targeting molecular imaging agents in veterinary trials, including the availability of more realistic animal models, patients with minimal treatment history, shorter study endpoints, and reduced regulatory burden. We have performed numerous clinical trials using gamma scintigraphy and PET imaging of dogs with prostate cancer, osteosarcoma, B-cell lymphoma, gastrointestinal stromal tumor, and lung cancer. These studies have utilized antibody pretargeting, antisense targeting, and hypoxia targeting for molecular imaging of these canine cancers.

NUCL

QTAIM, bond order and molecular surface analysis of UF_n (n=1-6)

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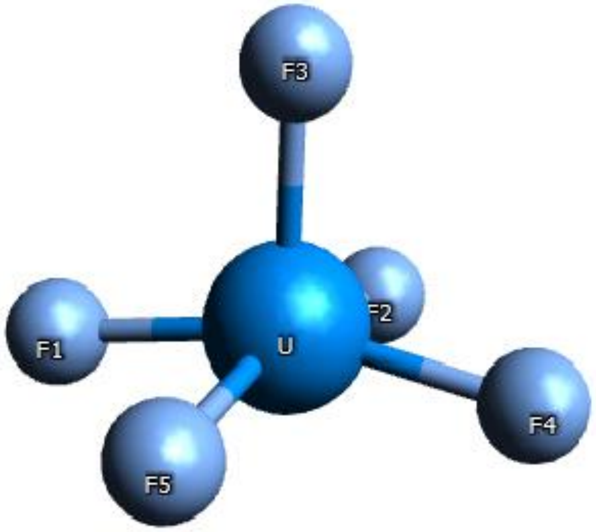
The molecules of UF_n (n = 1 -6) have been optimized by PBE0 in combination with SARC basis set for Uranium. The scalar relativistic Hamiltonian DKH was employed for the calculations. The optimized geometry of UF_5 is shown in Fig.1. For all of these calculations the Orca 5 program package was used. The optimized structures have been analyzed by using Multiwfn 3.8. For n=1 to 3, some systematic variations for the calculated quantities were obtained. The electron densities calculated at the bond critical points within the QTAIM shows increasing tendency as the number of F atom decreases. As a result of bond order analysis, LBO and IBSI values obtained show a consistent trend with BDE values reported earlier. Molecular Surface Analysis was also performed and some related quantities were obtained. Molecular polarity index increases as the number of bonds increases. NBO analysis was done to obtain bonding properties by NBO 6.0 implemented in Jagauar 11.



The optimized geometry of UF_5

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DETERMINATION OF SILICA BY TWO STANDARD AND CONVENTIONAL METHODS IN URANIUM PRECONCENTRATE AND SILICA DISSOLVED IN IMPURE URANYL NITRATE

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This work is a continuity of the realization of the datasheet of the uraniferous preconcentrate and the commercial concentrate. During this work, a set up of standard and conventional analysis methods such as the determination of silica, molybdenum, and dissolved silica was carried out.
The determination of silica is done by taking an aliquot of the preconcentrate and the commercial concentrate, but for the determination of dissolved silica, the test is done in a solution of impure uranyl nitrate (after dissolution), the latter requires the solution of the uraniferous preconcentrate and the commercial concentrate.
The UV-visible spectrophotometry technique was used for the determination of molybdenum and dissolved silica, for the determination of silica, gravimetry was applied.
According to the results of the analysis of the different elements, the contents found for each element do not exceed the tolerated limit according to the ASTM C 799-12 datasheet. (Specification of a preconcentrate and a commercial concentrate), we can conclude that the uranium preconcentrate and the commercial concentrate meet the standard.

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Understanding the Electronic Structure and Spectroscopic Properties of *f*-block Complexes in +2 and +3 Oxidation States: An *ab-initio* Study

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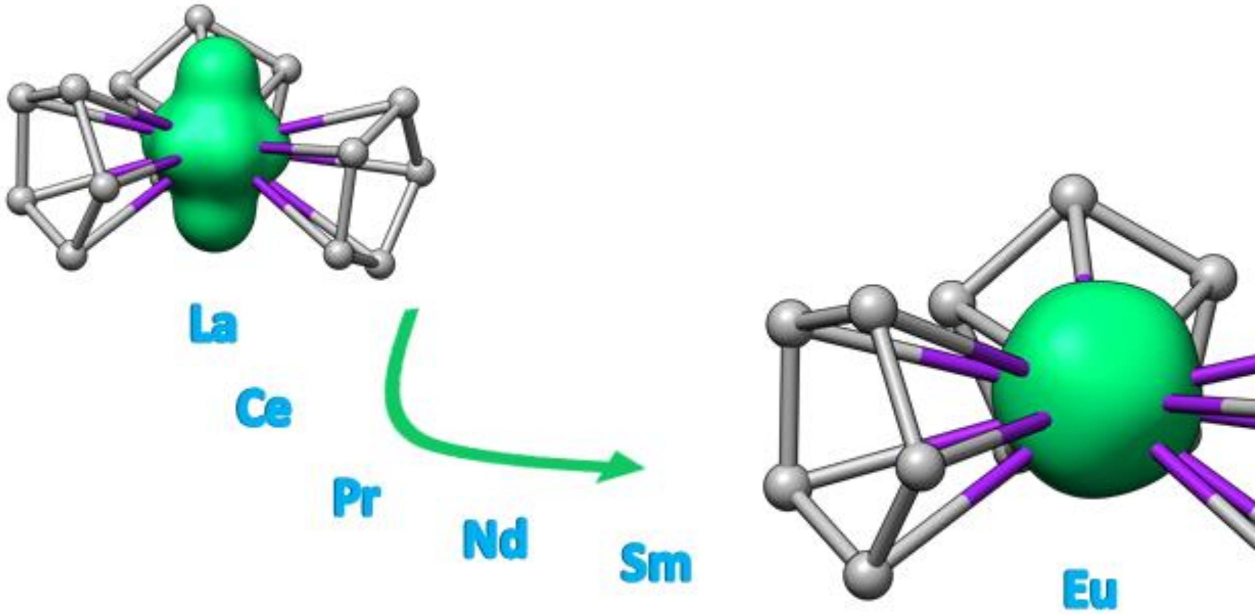
For years, the oxidation state of the *f*-block was considered to be simple and mostly limited to the +3 oxidation state. Until late sixties, Eu^{2+}, Sm^{2+},Yb^{2+}, Tm^{2+}, Dy^{2+} and Nd^{2+} were the only known divalent ions whose existence was explained because of their less negative redox potentials. Recently, research conducted by William Evans and collaborators demonstrated that Ln^{2+} ions are accessible in soluble molecules for all of the lanthanides excepting promethium in a tris(trimethylsilylcyclopentadienyl), $[LnCp'_3]^-$, environment. Further developments led to the synthesis and characterization of some actinides such as U^{2+}, Pu^{2+} and Th^{2+}. Experimental and Density Functional Theory (DFT) studies have shown that Ln^{2+} complexes exhibit variable ground state configurations: $4f^n$ for Sm^{2+}, Eu^{2+}, Tm^{2+}, Yb^{2+}, $4f^n5d^1$ for La^{2+}, Ce^{2+}, Pr^{2+}, Gd^{2+}, Tb^{2+}, Ho^{2+}, Er^{2+}, or both for Dy^{2+} and Nd^{2+} depending on the ligand environment. Structural and spectroscopic properties have also been reported to change going from one configuration to another. Despite these intricacies have been addressed in several works, there is still no clarity about what is the driving force behind the variable nature of the ground states. We have studied the $[LnCp'_3]^-$ series using *ab-initio* multiconfigurational methods which allowed us to obtain the electronic structure, spectroscopic properties and ground state densities of each system. We have overcome several difficulties in the correct prediction of the ground state and explored different avenues in order to provide a more insightful explanation to these experimental observations. In this context, we have proposed that the shape of the ground state

density is related to its nature which is directly linked to the electron-electron repulsion. This offers a predictive and intuitive tool that can be applied in the analysis of new lanthanide(II) systems and its actinides analogues.



NUCL

Lanthanide and actinide spectroscopy: Improving the use of the ligand-field theory

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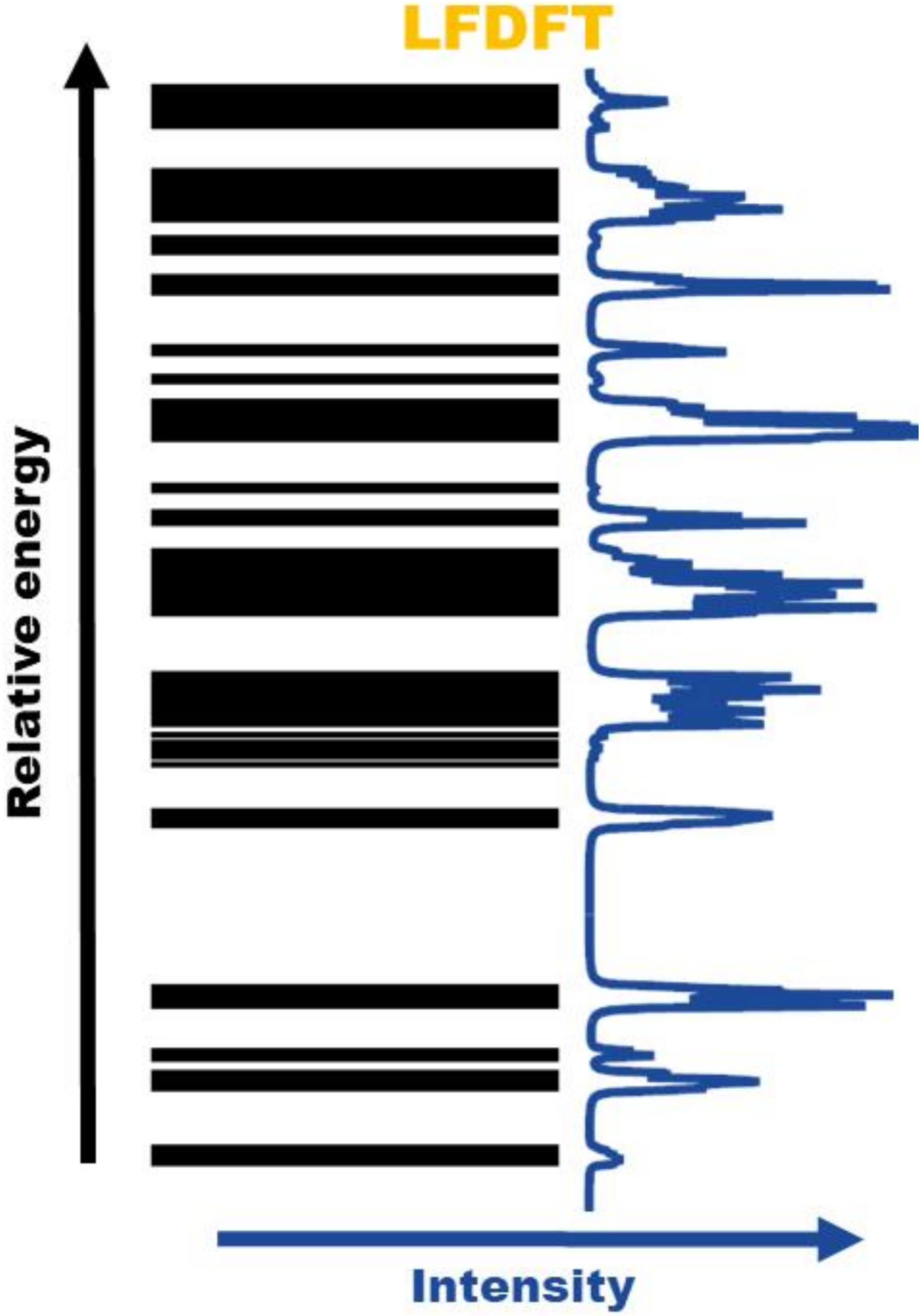
Reproducing and predicting optical spectra of f-block compounds is crucial to understand the nature of the complex transitions involved. However, the intricate interplay between relativistic, ligand field, and electron correlation effects makes this task rather elusive. Semi-empirical ligand field models have been used in the past to interpret f-block absorption and emission spectra, but limited by the lack of experimental data. Non-empirical methods have been proposed based on Density Functional Theory (DFT), the Ligand Field DFT (LFDFT) approach and the wavefunction-based ab-initio

LF theory (AILFT). The accuracy of the predicted multiplet structure strongly depends on the corresponding orbital set used to calculate the interelectronic repulsion (F^k), spin-orbit coupling (ζ_{SO}), and ligand field ($B^k{}_q$)parameters. We have studied the reliability of Kohn-Sham orbitals within the LFDFT approach and explored new avenues to improve its performance. We have implemented a new feature to LFDFT to predict the absorption and emission intensities accounting for electric and magnetic dipole, and electric quadrupole contributions. This paves the way for reviving discussions regarding the nature of the transitions (hypersensitivity, ligand-field dependency, etc.) but now with the advantage of a direct link to the molecular orbitals.



NUCL

Smart Spectral Matching: A new framework for machine learning structure–property relationships in uranium minerals

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Smart Spectral Matching (SSM) is a new cloud-based, highly flexible software framework designed to integrate the storage and analysis of scientific datasets in a user-friendly way. The SSM framework comprises many services, including extensions to allow custom analysis modules, and experimental metadata to allow more extensive data inference. Not only is this data readily searchable via the SSM user interface, but pre- and postprocessing tools can also be easily incorporated into the SSM workflow.

To better understand and assign spectroscopic features in solid-state uranium minerals, we leveraged the SSM framework to perform machine learning (ML) analyses of structural and optical vibrational spectral data. Data from our Compendium of Uranium Raman and Infrared Experimental Spectra (CURIES) including raw structural and spectroscopic data is stored along with any additional metadata in SSM. Examples of metadata compiled for samples in CURIES include secondary chemistry, structure type, coordination of uranium sites in the material, data source, and data collection parameters. Using CURIES as training data, an ML tool has been developed to identify new structure–property relationships and apply these results to the identification of unknown mineral species. First, principal component analyses were performed on the data in CURIES to identify regions of the spectra where specific chemical properties contribute the most to variation across the full dataset. From these results, the SSM ML interface can be used to select for the desired properties, spectral features, and targeted spectral regions, and ML models can be trained on the existing data in CURIES. Highly selective models are saved and stored and can be run on unknown samples to assign spectral features to underlying structural properties. A collection of these ML models can then be used to make inferences about the fundamental nature of the underlying mineral structure and coordination characteristics from optical vibrational spectra.

NUCL

Characterisation of materials from the Hunterston A spent nuclear fuel storage pond

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Nuclear power plants can become heavily contaminated with fission and corrosion products during their operational lifetime. These contaminated materials give rise to

high doses of radiation and heat, increasing risk to workers and the surrounding environment. Rapid identification of radionuclides and the extent of their penetration into nuclear materials could help reduce the volume of intermediate level waste (ILW) produced during decommissioning and minimise the costs of post operation clean out (POCO) procedures. Characterisation of legacy samples provides key insight into the long-term contamination effects of storing nuclear waste and is vital towards developing an appropriate strategy for future decontamination and decommissioning tasks.

A concrete core was obtained during the decommissioning of the Hunterston A spent fuel storage pond. The core was taken from the middle of the pond wall, where it was exposed to the contaminated pond water. A multi-layered protective coating was applied to the concrete walls during plant operations to prevent uptake of radionuclides. The majority of the activity of the core is due to the presence of ^{90}Sr, ^{137}Cs, ^{241}Pu, and ^{241}Am which has been shown to be associated with the painted surface. Autoradiography results have also indicated that some activity may have penetrated through to the bulk concrete. Sorption experiments were completed using concrete coupons in stable Sr, Cs, or Co doped solutions to determine the effects of contamination within the bulk concrete material. Samples were analysed using Laser-Induced Breakdown Spectroscopy (LIBS) to assess its capability as a rapid, multi-elemental characterisation technique within the nuclear industry.

Furthermore, plastic samples were taken from a pontoon which was floated on the pond water and used by workers during decontamination operations to reach the inside of the pond walls. Jet washing of the pond walls caused the wastewater to splash on top and down the sides of the pontoons, contaminating them in the process. Gamma spectroscopy indicated that the radioactivity within the samples is predominantly caused by ^{137}Cs and ^{241}Am. Autoradiography was performed on these discs to map the location of the radiation and identify areas of increased contamination for further analysis. LIBS analysis was also carried out to further evaluate its ability to identify radionuclide species on materials used throughout the nuclear industry at concentrations found *in-situ*.

NUCL

Fuel Cycle & Fuel Disposition for Closing the LWR Fuel Cycle with a Fast Chloride-Molten Salt Reactor System.

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This presentation will discuss the Fast Chloride-Molten Salt Reactor (FC-MSR) at a high level to support fuel cycle discussions. The presentation will discuss different processes for the FC-MSR for:
FC-MSR Front End from LWR Backend of the fuel cycle
A) Converting SNF to Start Up Fuel for a FC-MSE, 1) (prefered) as a method of

denaturing weapons grade Plutonium as the primary fissile, 2) as a method of consuming separated reactor grade Plutonium fissile, 3) fissile from SNF without Plutonium separations, 4) SNF Zirconium clad recycling, 5) fissile from HALEU

Main Lifetime Fuel Cycle 3kg/day of SNF

B) Converting SNF to Feed-In Fuel for the all fuel additions following Start Up without added fissile.

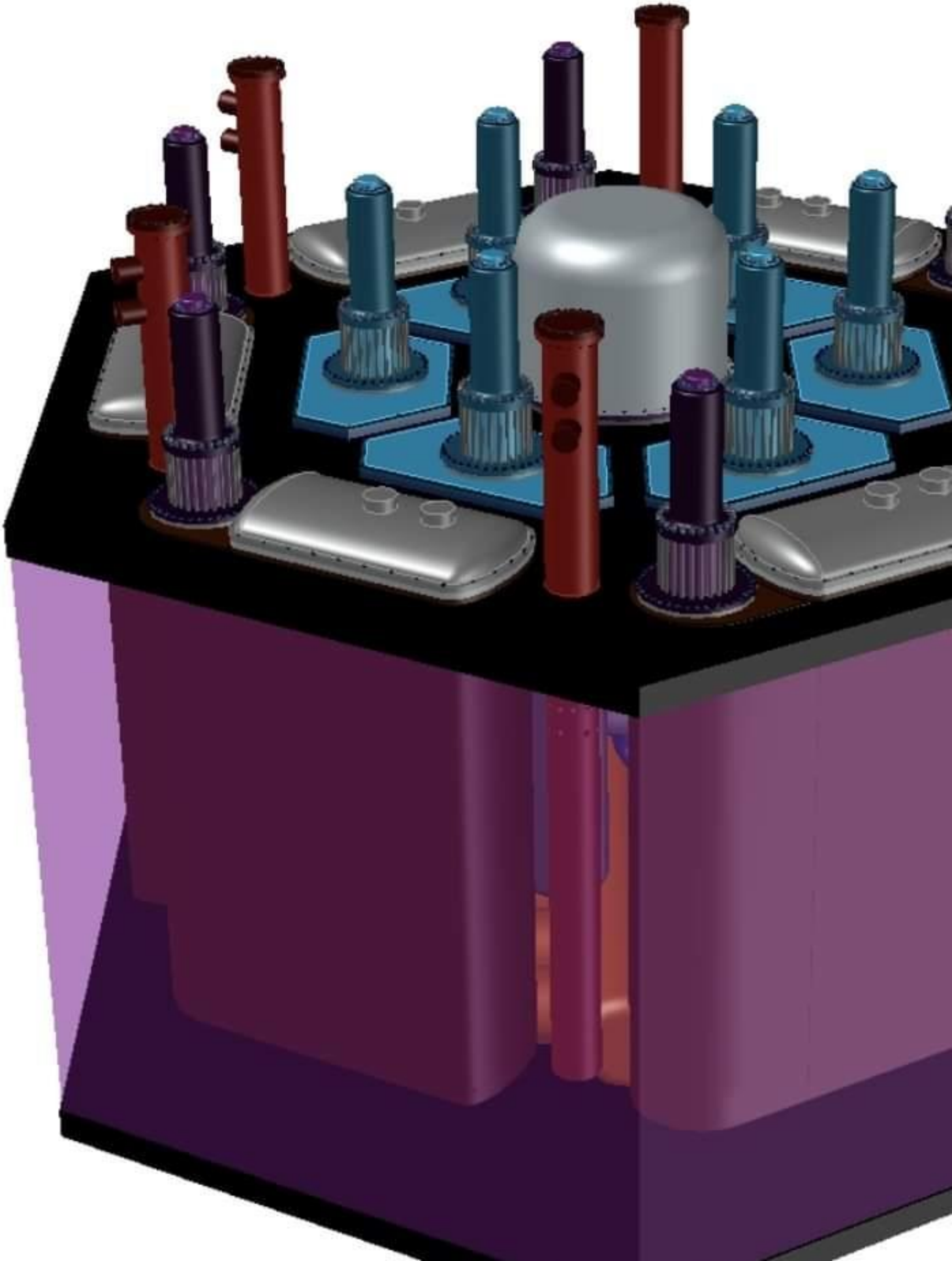
C) FC-MSR on-line Purification

Purification & Waste

D) 40-60yr periodic purification to remove excess fission products, actinide & chloride recycling

E) Options for FC-MSR waste product stabiliztion & disposition

Conclusions/Opportunies relative to DGRs



Fast Chloridr-MSR 3000MWth/1200MWe or process heat

NUCL

Machine learning and data mining applications in nuclear waste repository reactive transport modeling and performance assessment

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A fundamental approach to Nuclear Waste Repository research involves the collection of experimental data in a laboratory setting, development of empirical and/or mechanistic numerical models representing those observations, and application of these models (or Reduced Order Models) into reactive transport and performance assessment models as predictive tools for informing society of impacts and risks associated with nuclear waste repository scenarios. Both the assimilation and interpretation of experimental data must take advantage of ML opportunities to improve predictive tools, particularly from the standpoint of uncertainty quantification. However, a number of challenges need to be met in the coming years to successfully integrate these new data science approaches. A recent effort at Lawrence Livermore National Laboratory (LLNL) has led to the developement of a data digitization pipeline to simulate radionuclide sorption that is amenable to both ML as well as traditional surface complexation modeling. With the LLNL Surface Complexation/Ion Exchange (L-SCIE) database that is already available, we have begun developing mechanistic surface complexation and ML models of radionuclide retardation specific to the nuclear waste disposal problem. In this presentation, we will introduce this novel approach to mining community data to develop robust models of radionuclide reactive transport.

NUCL

Corrosion resistance of boron-doped diamond in chloride and fluoride molten salts

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Nuclear power is a clean, reliable source of energy that can help mitigate the effects of global climate change, but safety and waste management concerns often overshadow its potential. Generation IV Molten Salt Reactors (MSRs) use liquid salt fuel systems to eliminate a primary safety concern: core meltdowns. MSRs also consume used nuclear fuel waste as a form of fast reactor technology. Electrochemical methods can probe several fundamental aspects of molten salt chemistry so long as the electrodes can

withstand the molten salt environment for prolonged periods of time. Boron-doped diamond (BDD) is expected to be resilient against harsh molten salt environments, given its sp^3-carbon structure. As such, BDD could potentially be used for *in situ* corrosion control and monitoring in molten salt containment vessels. However, the corrosion of BDD in molten salt needs to be understood first and this has yet to be fully investigated in literature. In this study, we investigated the corrosion resistance of BDD by soaking the material in chloride and fluoride molten salts (LiCl-KCl, NaCl-KCl, LiF-KF, and FLiNaK) at 600 ^oC over 250 hours. Scanning electron microscopy (SEM) and Raman spectroscopy were used to identify topographical changes in diamond crystal structures. Electrochemical techniques like cyclic voltammetry (CV), differential pulse voltammetry (DPV), and chronoamperometry (CA) with several 1-electron transfer redox couples were used before and after salt soaking to determine the following redox and thermodynamic properties: formal reduction potential ($E°'$), electron transfer stoichiometry, diffusion coefficients (D), and electroactive surface area of the BDD. In general, little corrosion or change to the BDD was observed. This work advances the understanding of MSR chemistry, while simultaneously proving the applicability of BDD as electrode material for harsh environments.

NUCL

Highly-lipophilic sulfonamide chelators and analogs for actinide separation from caustic high-level waste

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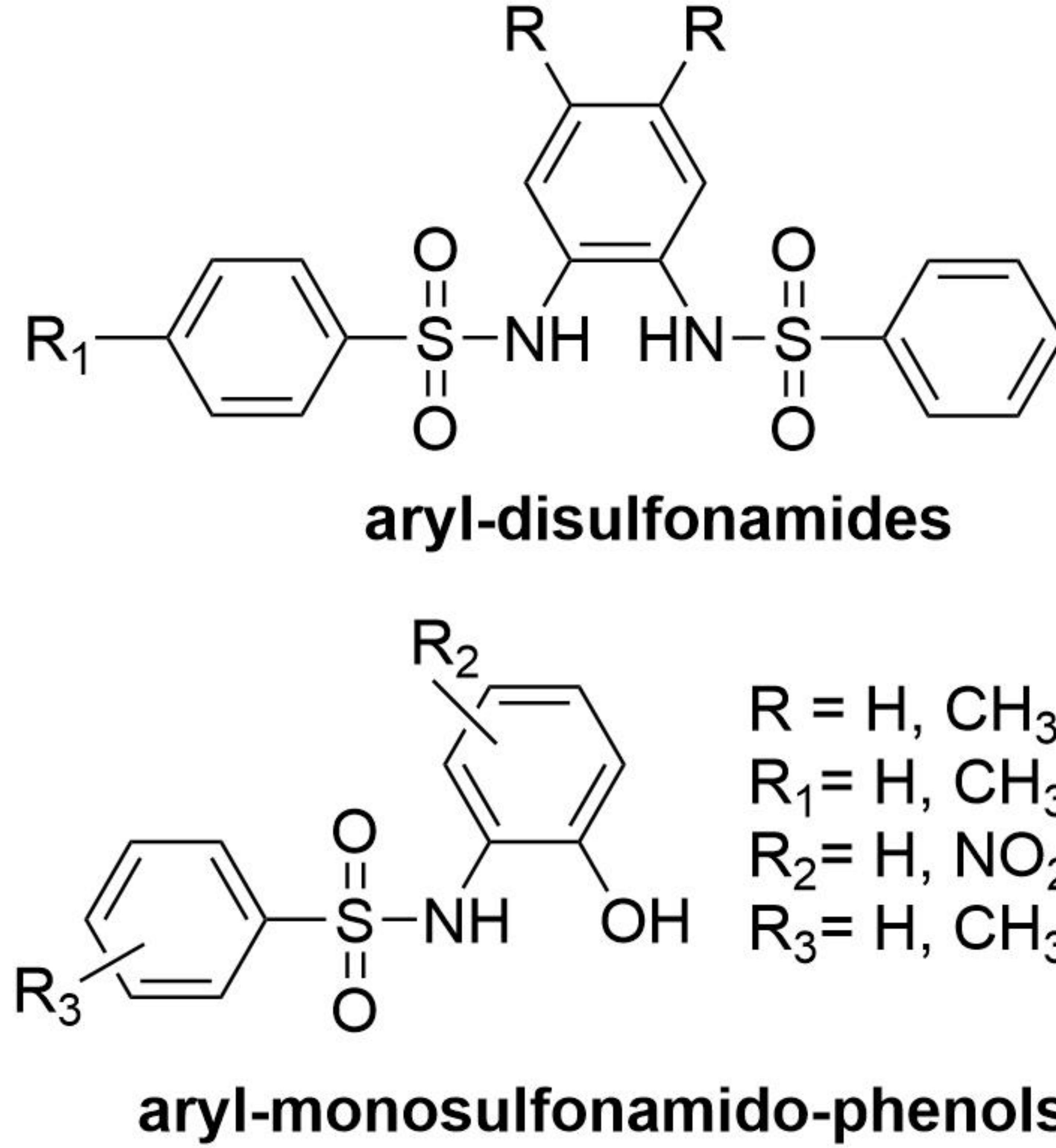
The cold war era reprocessing of nuclear fuel via the PUREX process for plutonium production has led to the generation of large volumes of caustic high-level waste (HLW) stored in underground tanks at the Savannah River Site (SRS) and the Hanford Site (HS) in the US. Current reprocessing at SRS is based on a two-step process, consisting of the Actinide Removal Process (ARP) for ^{90}Sr and actinides (An) by sorption on monosodium titanate followed by the Next-Generation Caustic-Side Solvent Extraction process (NG-CSSX) for ^{137}Cs separation. Actinide chelators compatible with the NG-CSSX process could potentially achieve simultaneous separation of Cs, Sr, and An, by a one-step solvent extraction process, reducing the contact times and amounts of titanate sorbent during the slower ARP process and thus significantly improving the efficiency of overall HLW processing. Recently, we reported effective extraction of Sm(III), used as a surrogate for Am(III), from alkaline aqueous media by *o*-phenylenediamine-derived aryldisulfonamides. Sm(III) recovery up to 81% at pH 13.0 in chlorinated solvents after just one loading-stripping cycle was demonstrated. Encouraged by these results we extended our work to *o*-(monosulfonamido)-phenol type ligands and achieved Sm(III) extraction efficiencies of > 90% at pH = 14 in dichloromethane.
The use of chlorinated solvents however, represents a major drawback for industrial

application. Hence, to facilitate application of these high- performing ligands, we have now developed and present new highly-lipophilic aryl- and alkyl-substituted disulfonamide and *o*-(monosulfonamido)-phenol derivatives, that can extract Sm(III) efficiently in process solvents, such as *n*-dodecane, *n*-dodecane/octanol from up to 2M NaOH. Preliminary experiments with some of these ligands in the actual CSSX solvent and process compatibility issues will also be discussed.



Aryl (left) and alkyl (right) sulfonamide chelators: Highly lipophilic derivatives (R_4 = dodecyl or

2-ethylhexyl) are soluble in dodecane and dodecane/octanol mixtures and can extract Sm(III) from 2M NaOH.

NUCL

SEM, EDS, and XRD analysis of synthetic trinitite as compared to authenitic and remelted trinitite samples

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In the event of a nuclear attack, the analysis of fallout debris will be crucial to the timely attribution of the nuclear materials used. As such, the synthesis and analysis of realistic, urban, melt glass has been the focus of many projects in recent years. Traditionally, these synthetic materials have been prepared using furnaces to heat the glass over several hours. A novel preparation method which uses a vacuum arc welder to simulate a nuclear fireball plasma allows for the instantaneous heating of materials to temperatures over 3000C, while in a reducing environment. In this study, the vacuum arc welder was used to prepare synthetic trinitite, as well as remelt a sample of authentic trinitite. Additionally, a sample of authentic trinitite was remelted using the more traditional MTI furnace. An authentic sample of trinitite along with the prepared samples of trinitite were then compared via SEM, EDS, and XRD analysis.

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Solid-State Analysis of Lanthanide and Actinide Diglycolamide Complexes

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Nuclear Power has some of the lowest emissions coupled with the highest energy density making it one of the most ideal options for clean energy. However, the advantages of nuclear power are hindered by the challenges of safely storing nuclear waste. Diglycolamide (DGA) ligands have shown to have a strong affinity towards Ln^{3+} and transuranic An^{3+} and are used in the separations of minor actinides from nuclear waste. Further understanding of the bonding behavior between lanthanides and actinides with variations of the DGA molecules will help to better understand the role of these ligands in nuclear waste separations. Radiolysis induced degradation of DGA ligands will compromise their separation efficiency. Studying the components found in degradation products of DGA molecules as well as complexes with *f*-elements will improve our understanding of these separation strategies. Furthermore, structural knowledge of these complexes, especially with actinides, are lacking. Here, we present crystallographic and spectroscopic data of lanthanide and actinide DGA complexes in

the solid-state along with supplementary quantum mechanical calculations. Preliminary radiolysis experimental results will also be discussed.

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Mixed N,S donor ligands for selective complexation of americium

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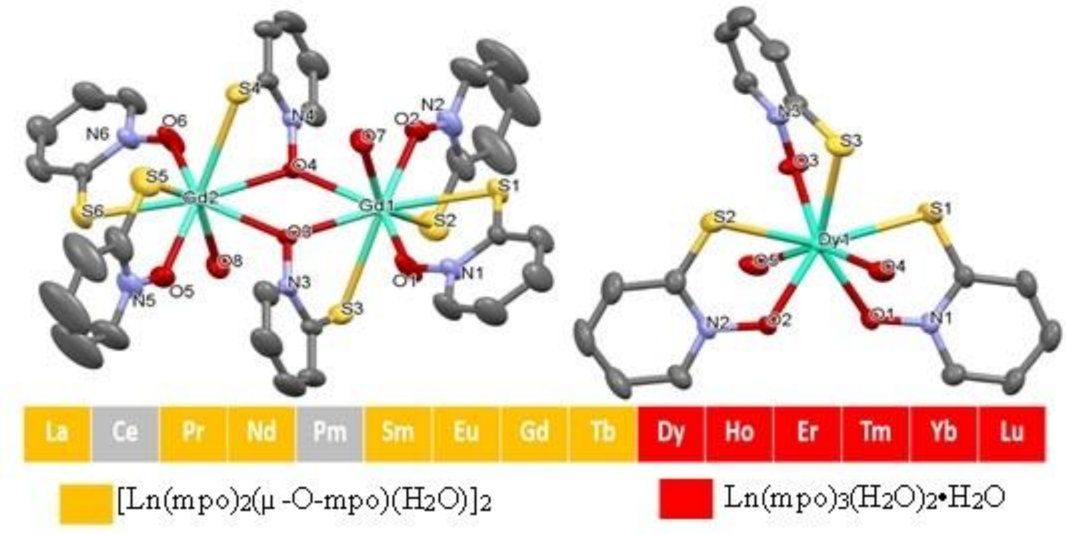
Pyridine N-oxides have long been investigated as efficacious chelating moieties of *f*-element ions and have found appreciable use in magnetic resonance imaging, luminescent labeling of biomolecules, and fluoroimmunoassays. With the goal of selectively complexing americium and curium over the lanthanides, a series of mixed S,N donor pyridine thiol complexes with lanthanides and americium have been prepared and fully characterized. The crystal chemistry, spectroscopy, and quantum mechanical analysis of bonding of this family of compounds is presented. In particular, the basis of a structural change from mononuclear to binuclear complexes across the *f*-block is explained. The presence of stronger bonding interactions in the binuclear americium compound are rationalized and compared to its isostructural Nd analogue.



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Fluorescence sensing and extraction of Ln(III) from alkaline solutions by a lipophilic dansylamide ligand based on the *o*-sulfonamidophenol framework

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The Hanford and Savannah River US DOE sites contain the majority of high-level waste (HLW) in the US, with about 100 MGal in volume and combined activity of over 400 MCi. Several approaches have been adopted to separate the waste into high activity and low activity waste forms, in order to reduce the overall volume and reduce contamination risks by disposing low level waste in cementitious form (grout) and immobilizing remaining low volumes of HLW components in solid form within glass (vitrification).

At Savannah River Site (SRS), the two sequential approaches used are the Actinide Removal Process (ARP) followed by the Caustic Side Solvent Extraction (CSSX). The ARP is a sorption process using monosodium titanate (MST) to remove Sr(II) and actinides. The CSSX process selectively extracts Cs(I) by using a calixarene extractant. Our group is focusing its efforts to CSSX-compatible additives (ligands) for combined extraction of f-elements, together with Cs(I) and Sr(II), thus reducing the amount of MST and contact time needed during the slower ARP process, and thus simplifying overall HLW processing.

We now present N-(5-(tert-butyl)-2-hydroxyphenyl)-5-(dimethylamino)naphthalene-1-sulfonamide ($\mathbf{L_D}$), which is a *o*-sulfonamidophenol ligand bearing the signaling fluorescent dansyl moiety for the sequestration and *in-situ* sensing of f-elements in HLW. We observed 92% extraction of Sm(III) (used as an experimental surrogate for actinides) from pH 13.0 into dichloromethane after one extraction/strip cycle. Addition of several Ln(III) to acetonitrile solutions of ($\mathbf{L_D}$) in the presence of organic bases showed notable fluorescence enhancements, while UV-Vis titrations in acetonitrile suggested 1:1 binding stoichiometry, with binding constant of LogK = 5.31 ± 0.33 obtained using the Hypspec program. Though we have established the stability of ($\mathbf{L_D}$) under alkaline conditions, compatibility studies of the ligand in the CSSX solvent are currently underway.

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Titanium-45 radiochemistry with THP^{Me} and TREN-CAM for development of PET radiopharmaceuticals

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The production and chemistry development of new radioisotopes are important steps in designing radiopharmaceuticals for nuclear imaging applications. Titanium-45 (^{45}Ti) is a novel radionuclide with desired physical characteristics for use in PET imaging including a moderate half-life (3.08 hour), decay by positron emission (85%) and low mean positron energy of 0.439MeV. Despite these promising characteristics, the

radiochemistry for ^{45}Ti including the development of suitable bifunctional chelators is relatively unexplored. Building on our prior work on optimized production techniques for ^{45}Ti, we aimed to explore chelators which bind efficiently under mild conditions and form complexes which are stable *in vivo*.

Radiolabeling studies of ^{45}Ti were carried with two different chelators (THP^{Me} and TREN-CAM). Radiochemistry optimization was conducted by incubating 500uCi ^{45}Ti with chelators at varying mass and pH conditions. Serum stability studies were performed in mouse serum. *In vivo* imaging studies were performed with both THP and TRENCAM labeled with ^{45}Ti and free ^{45}Ti. Dynamic PET scans were conducted for 1 hour after injection and biodistribution studies were performed immediately after imaging.

Radiolabeling optimization have shown significant binding of THP^{Me} and TRENCAM with ^{45}Ti is possible with high radiolabeling yields (>95%) for both THP^{Me} and TRENCAM achieved within 30 minutes of incubation at 37^{0}C. Excellent serum stability of ^{45}Ti with labeled chelators was observed where >95% labeled complex was intact after 6 hours of incubation. Tissue biodistribution studies demonstrated that the complexes showed rapid clearance and significantly lower ^{45}Ti in heart, lung and other key organs compared to free ^{45}Ti. This study has opened new possibilities of establishing ^{45}Ti as a novel radionuclide which hold promise for future investigations.

NUCL

Targeted Alpha Therapeutics to Combat Drug Resistant Pathogens

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Prior to the Antibiotic Era, infectious disease was leading cause of human morbidity and mortality throughout human history. However, with the advent of the first antibiotics pathogens evolved resistance mechanisms. Multidrug resistant pathogens are a pressing human health concern as the pace of now antibiotic development has slowed. Alpha-emitting radionuclides coupled with native metabolic targeting offers a new avenue for antimicrobial/antibiotic development. Here, we examine the chemistry of thorium combined with bacteria-specific siderophores as targeting vectors to kill pathogens such as *Pseudomonas aeruginosa*. Siderphore-based targeting is an attractive strategy that has garnered recent interest owing to intrinsic specificity and requisite nature for bacterial survival. We demonstrate efficacy with the alpha therapeutic Th^{IV}-227 chelated by a variety of siderophores as a promising antimicrobial strategy to fight multidrug resistance infections.

NUCL

Albumin-binding Lutetium-177-labeled LLP2A derivatives as theranostics for metastatic melanoma

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Very late antigen-4 (VLA-4) is a trans-membrane integrin protein that is highly expressed in aggressive forms of metastatic melanoma. This integrin plays a key role in tumor growth, angiogenesis and metastasis by facilitating cancer cell adhesion and migration. LLP2A, a small-molecule high affinity, peptidomimetic, itself does not inhibit cancer cell proliferation and survival, and therefore is an ideal candidate for imaging and delivery of therapeutic payloads. We previously demonstrated the utility of 177Lu-DOTA-LLP2A as a therapeutic agent against metastatic melanoma in mice in combination with immune checkpoint inhibitors, although tumor growth was marginally inhibited with no cures. We hypothesize that failure to diminish tumor burden after 177Lu-DOTA-LLP2A therapy was due to the rapid renal clearance of the dose from the blood and tumor thereby decreasing efficacy. To improve the pharmacokinetic profile, we designed and synthesized novel analogs of DOTAGA-LLP2A with a 4-(p-iodophenyl)butyric acid (pIBA) albumin binding moiety. We demonstrate the feasibility of this albumin binding strategy by comparing in vitro cell binding assay, in vivo biodistribution performance, and therapeutic efficacy of 177Lu-DOTAGA-PEG4-LLP2A (**1**) to the albumin binding 177Lu-DOTAGA-pIBA-PEG4-LLP2A (**2**). In vitro cell binding assay results for 1 and 2 showed K_d of 0.4 and 1.75 nM and B_{max} of 200 and 315 fmol/mg respectively. Our in vivo biodistribution data for both tracers exhibited specific uptake in tumor, spleen, thymus and bone due to endogenous organ expression of VLA-4. Tumor uptake for **1** was highest at 1 h (~15 %ID/g) and **2** at 24 h (~27 %ID/g). Clearance from the tumor for **1** occurs at 24 h (<5 %ID/g) while **2** is retained for up to 168 h (~10 %ID/g). Compound **2** also exhibited much longer blood circulation time compared to **1**. Preliminary therapeutic efficacy studies (30 MBq; 800 mCi/mouse for each compound 1 & 2) showed a notable inhibition of tumor growth for compound **2** compared to **1** with tumor volumes of 0.122 and 1.24 cm^3 at 14 and 7 days post dose injection, respectively. Collectively, the in vitro and in vivo data suggest that modifying LLP2A with an albumin binder (pIBA) offers similar VLA-4 receptor binding qualities as the non-albumin binding molecule and provides a remarkable improvement in renal clearance and tumor retention and inhibition. Further efficacy studies are ongoing.

NUCL

Tb-161 and Lu-177 labeling chemistry of DOTAGA-PEG4-LLP2A and Lumi804-PEG4-LLP2A as VLA-4 targeted theranostics

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Very late antigen 4 (VLA-4) is a transmembrane non-covalent heterodimer, which is overexpressed in certain types of cancer cells and is associated with tumor growth and metastasis. Previous studies have shown that ^{177}Lu-DOTA-PEG4-LLP2A provides marginal therapeutic efficacy in B16F10 melanoma tumor-bearing mice. Terbium-161 [6.89 d half-life, β^-:100%, $E_{\beta max}$ = 594 keV, γ emissions: 48.9 keV (17.0%) and 74.6 keV (10.2%)] has physical and chemical properties that are comparable to the clinically established isotope Lu-177 [6.65 d half-life, β^-:100%, $E_{\beta max}$ = 497 keV, γ emission: 208 keV (10.4%)]. In contrast with Lu-177 however, Tb-161 decays with co-emission of ~12 Auger and conversion electrons (≤50 keV, vs. ~1 keV for Lu-177), and along with its low energy β^- particle, results in a higher total electron-to-photon ratio of Tb-161 (5.9) than Lu-177 (4.8). For internalizing radiopharmaceutical therapy agents, higher abundance of low-energy electrons may enhance the killing of tumor cells. Bifunctional derivatives of the macrocyclic chelator DOTA represent the current state-of-the-art for radiolanthanide-based agents. However, fully in-cage chelation of lanthanides by DOTA is slow and sensitive to the presence of transition metal impurities (e.g., Zn^{2+}, Cu^{2+}, Fe^{3+}), which lowers the achievable effective molar activity of radiopharmaceutical therapeutic agents. In contrast, Lumi804 is a recently developed macrocyclic bifunctional chelator that more readily chelates metal ions that prefer 8-coordination, such as Zr^{4+} and Lu^{3+}. A major advantage of Lumi804 over DOTA is its propensity for efficient radiolabeling at lower temperature (25 ^{o}C) and at lower pH (more favorable to aqueous metal ion stability) within 30 minutes. Herein we present our comparative study of molar activities achieved using MU Research Reactor produced Tb-161 (^{160}Gd(n,g)^{161}Gd - ^{161}Tb) and Lu-177 (^{176}Lu(n,g)^{177}Lu) labeled DOTAGA-PEG4-LLP2A (where GA = glutaric acid; **1**) vs. Lumi804-PEG4-LLP2A (**2**). Thus far, only small activity batches of Tb-161 have been produced (< 1 GBq), meaning the effects of trace metal contaminants become more important. Our preliminary labeling results showed quantitative Tb-161 labeling of compound **2** in 5 minutes at room temperature (pH 4-5). In contrast, compound **1** required heating to 95 ^{o}C for 30 minutes (pH 4-5). The highest molar activity reached thus far for **1** and **2**are 40 mCi/nmol and 200 mCi/nmol, respectively. Studies with Lu-177 labeling are ongoing.

NUCL

Using electronic structure and implicit solvent calculations to model the effect of the organic solvent on liquid-liquid extraction of lanthanides

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As the demand for pure lanthanides continues to rise in the technology sector, efficiently and responsibly obtaining them continues to be a topic of great concern. Specifically, separating lanthanides from one another in mixtures is a challenging and costly process. Liquid-liquid solvent extractions are often employed to separate lanthanide mixtures. This study sheds light on the effects of the organic phase in liquid-liquid solvent extractions by modeling the interactions of trivalent lanthanides (Ln = La, Lu) with different extractants and acids. Explicit lanthanide-ligand molecular complexes in implicit solvents served as models of three ligand-lanthanide-organic solvent extraction systems. To determine the computational models with maximum correlation to experiments, the relative free energy of the complexation reactions was computed for different organic phases. The polarizable continuum model (PCM) and the conductor-like screening model (COSMO) both produce energy values that correlate with the experimental results for the diphosphine oxide/nitric acid systems. There was no correlation when using the self-consistent reaction field (SCRF) implicit solvation model. For the diglycolamide ligand extraction of lanthanides from hydrochloric acid, COSMO and PCM provide qualitative accuracy when modeling systems with a 1:1 ligand-to-metal ratio but break down in systems with higher ligand-to-metal ratios. For systems with diglycolamide ligand extraction from nitric acid, none of the computational models reproduce the experimentally observed trend, the possible reasons will be discussed.

NUCL

Synthesis and evaluation of triarylselenonium salts as precursors for radiofluorination of arenes

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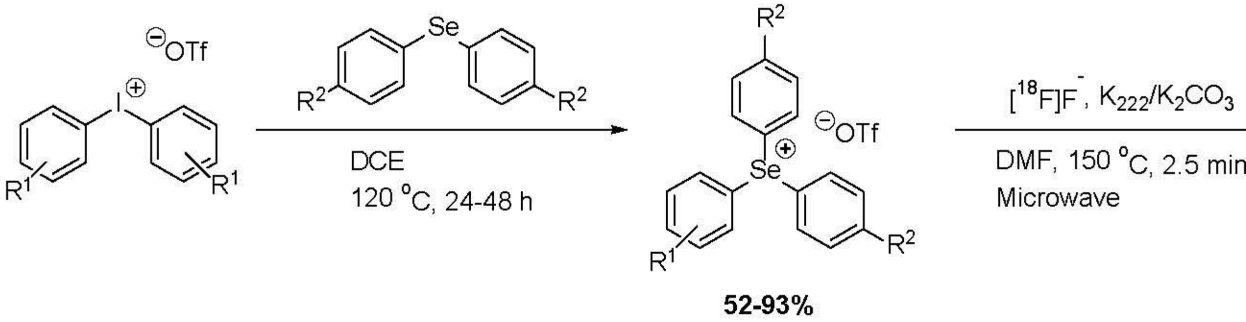
Positron emission tomography is a sensitive imaging tool that can elucidate biochemical processes *in vivo* by using ligands labeled with short-lived positron-emitters, such as fluorine-18 ($t_{1/2}$ = 109.8 min). Several methods for aryl radiofluorination have been developed, but improved and more efficient methods are still sought after. Triarylsulfonium salts are efficient precursors for radiofluorination, but their use is limited to arenes containing electron-withdrawing groups (EWGs). We recently reported that simple diarylselenones may also serve as precursors for aryl radiofluorination. Here we extend this work with regards to the syntheses of more complex salts and the investigation of ring selectivity in radiofluorination. A broad range of functionalized diphenyl-arylselenonium triflates was obtained in moderate to high yields (52-93%) from diaryliodonium salts and commercially available diphenyl selenide. **[^{18}F]1-8**, which bear EWGs or neutral groups, were produced in moderate to high radiochemical yields (RCYs) by treating the triarylselenonium salts with [^{18}F]fluoride ion in DMF. Electron-rich **[^{18}F]9-12** were produced in low RCYs with an accompanying higher yield of [^{18}F]fluorobenzene as a byproduct from a spectator phenyl group. To improve yields, two salts were made symmetrical (**[^{18}F]13-14**), which led to a three-fold improvement in RCYs (6-34%). Five selenonium salts were then compared to their respective sulfonium

analogues, and they showed higher RCYs. These results further indicate the potential value of triarylselenonium salts as precursors for [^{18}F]fluoroarenes.



⊖OTf
I⊕
R1
R1
Se
R2
R2
DCE
120 °C, 24-48 h
R2
⊖OTf
Se⊕
R1
R2
52-93%
[18F]F-, K222/K2CO3
DMF, 150 °C, 2.5 min
Microwave

Scheme 1. Synthesis and evaluation of triarylselenonium salts as precursors for radiofluorination of arenes

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Homogeneous precipitation of radioactive metals: Applications in cancer and arthritis

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Precipitation of Sn-117m and Y-90 was performed by slowly increasing the global pH of aqueous solutions of the metal. This was accomplished by the heat degradation of urea included in the solution. Using this method, homogeneous particle sizes were reproducibly prepared. The particles were shown to remain at the site of administration when injected into the synovium of rats or muscle of mice.

Particles of Sn-117m were developed to treat arthritis. After positive results in an arthritis rat model, the product was tested in dogs. The product is commercially available as a medical device for veterinary use in the US. The next step in this technology is human clinical trials.

Particles of Y-90 have been directly administered to tumors. Efficacy in dogs, horses, and one rhino will be discussed. Direct administration of radioactive colloids to tumors could increase the dose to tumors while significantly reducing the dose to normal tissues and organs.

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Measurement of the ^{230}Th(p,2n)^{229}Pa and ^{230}Th(p,3n) ^{228}Pa reaction cross sections from 14.1 to 16.9 MeV

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Actinium-225 is of interest as an agent for targeted alpha therapy and there is on-going research into methods of producing this isotope, either directly or via the decay of its parent isotopes (^{229}Th, ^{229}Pa, and ^{225}Ra). One method that has been suggested is the ^{230}Th(p,2n)^{229}Pa reaction, however, there is no available cross section data for this reaction in the literature.

This talk will discuss measurements of the ^{230}Th(p,2n)^{229}Pa and ^{230}Th(p,3n)^{228}Pa reaction cross sections, including the target fabrication and post-irradiation chemical processing, and present the results in the energy range where the ^{230}Th(p,2n)^{229}Pa reaction cross section has been calculated to peak. For these experiments, targets naturally enriched in ^{230}Th were fabricated and irradiated at Lawrence Livermore National Laboratory with proton energies ranging from 14.1 to 16.9 MeV. Chemistry development studies were performed to determine a procedure for processing the targets post-irradiation to separate the protactinium activation products. Chemical processing was followed by γ-ray spectroscopy to measure the activities of ^{228,229,230,232}Pa produced in the irradiation. Excitation functions are reported for the ^{230}Th(p,2n)^{229}Pa and ^{230}Th(p,3n)^{228}Pa reactions as well as the ^{232}Th(p,n)^{232}Pa reaction, which was used to verify the experimental conditions.