Radiochemistry Research at the University of Iowa

Separations, Characterization, Fate and Transport, Nuclear Forensics, Geochronology, Molecular Imaging and Nuclear Medicine…

Michael K. Schultz PhD
Department of Radiology
Department of Radiation Oncology
(Free Radical Radiation Biology Program)
Department of Chemistry

Summary

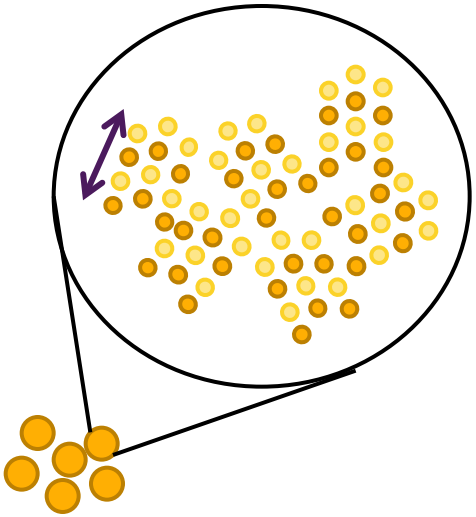
- Overview of Radiochemistry Research at Iowa
  - ✓ Researchers and Applications
- Actinide Research
  - ✓ Np Colloids, fate and transport
  - ✓ Actinide environmental speciation/fractionation
  - ✓ Nuclear forensics and radiochemical separations research
- Radiochemistry for Molecular Imaging and Nuclear Medicine
  - ✓ Molecular targeting
  - ✓ Radiochemical separations for Ga-68 imaging
- Proposed degree programs at Iowa

Radiochemistry at Iowa – Interdisciplinary and Collaborative

Researcher	Department	Research Area
Tori Forbes PhD	Chemistry	Actinide fate and transport/colloids
Michael Schultz PhD	Radiology Radiation Biology Chemistry	Nuclear Forensics, Environmental Radiochemistry, Radiopharmaceuticals
Thomas Schnell PhD	Engineering	UAVs, Event Monitoring, Homeland Security
Amnon Kohen PhD	Chemistry	Radiochemical design and synthesis
Sarah Larsen PhD	Chemistry	Nanoparticles
Chris Pigge PhD	Chemistry	Radiochemical design and synthesis
Mishtu Dey PhD	Chemistry	Biocatalysis and metalloenzymes
Hien Nguyen PhD	Chemistry	Radiochemical design and synthesis
Mark Reagan PhD	Geology	Geochronology
Yusuf Menda MD	Radiology	Nuclear Medicine
Apollina Goel PhD	Radiation Oncology	Nuclear Medicine
R. William Field PhD	Occupational and Environmental Health	Radon

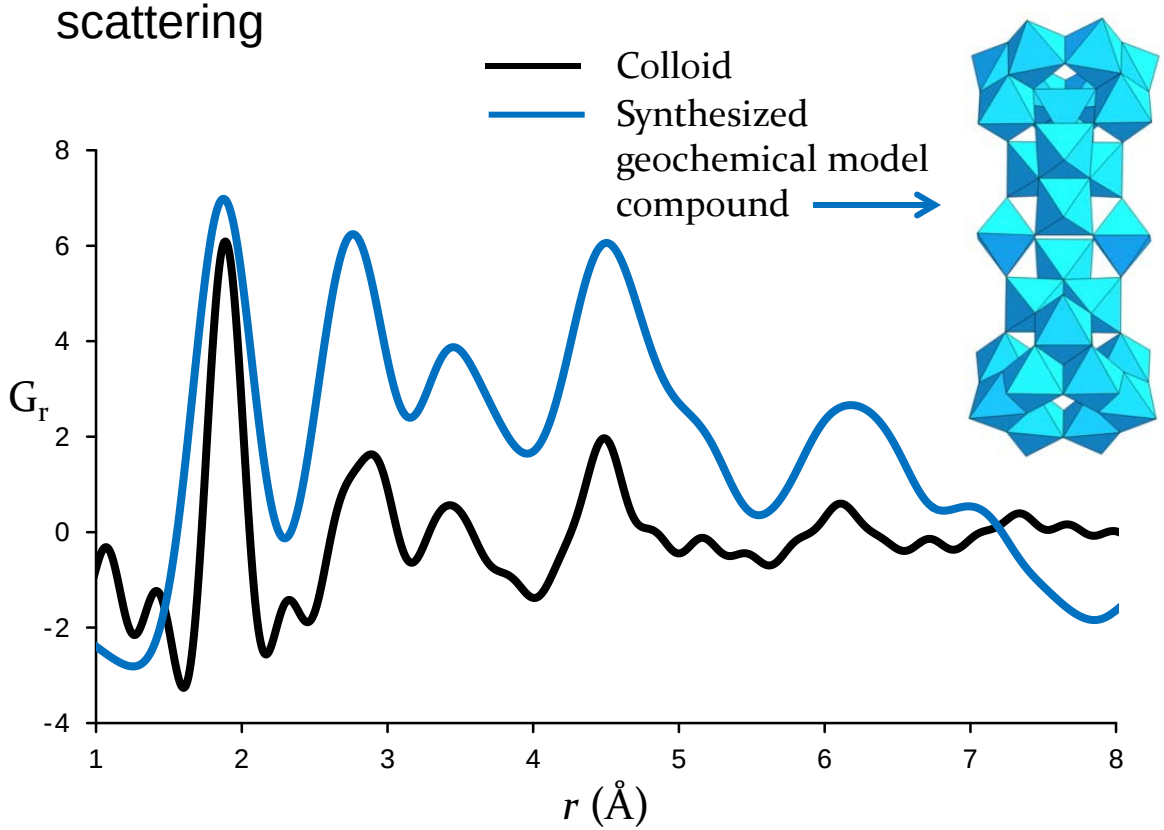
Radiochemistry at Iowa
Examples

Forbes Research Group – Department of Chemistry, University of Iowa



Characterizing adsorption of actinides onto colloidal particles

Colloidal particles contain small nanodomains of structural coherence that can be characterized by comparing synthesized geochemical model compounds to PDF analysis of high energy X-ray scattering

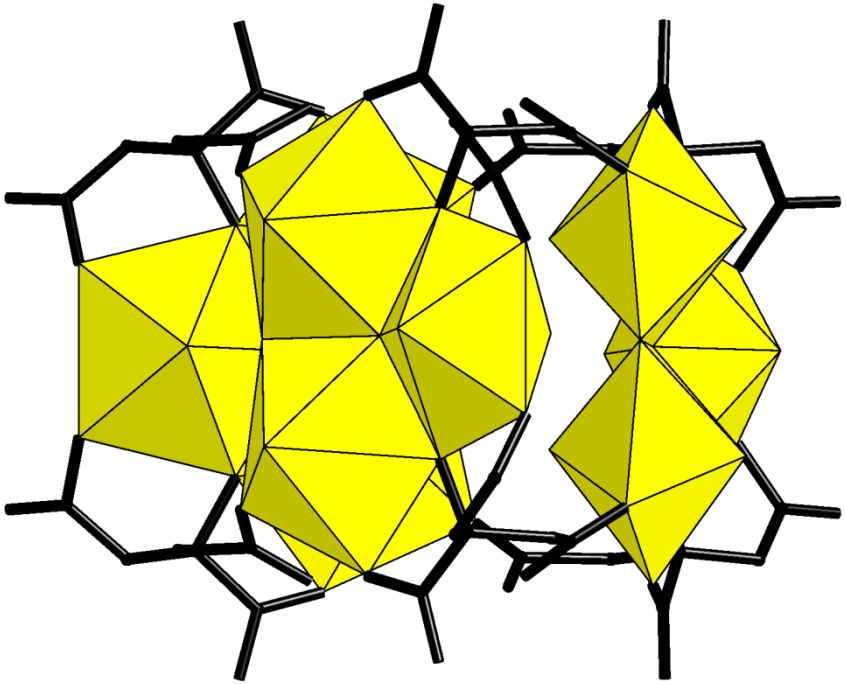


Currently we are synthesizing and structurally characterizing geochemical compounds that containing actinides bound to the surface of the particles to gain a molecular-level understanding of actinide colloidal transport

Forbes Research Group – Department of Chemistry, University of Iowa

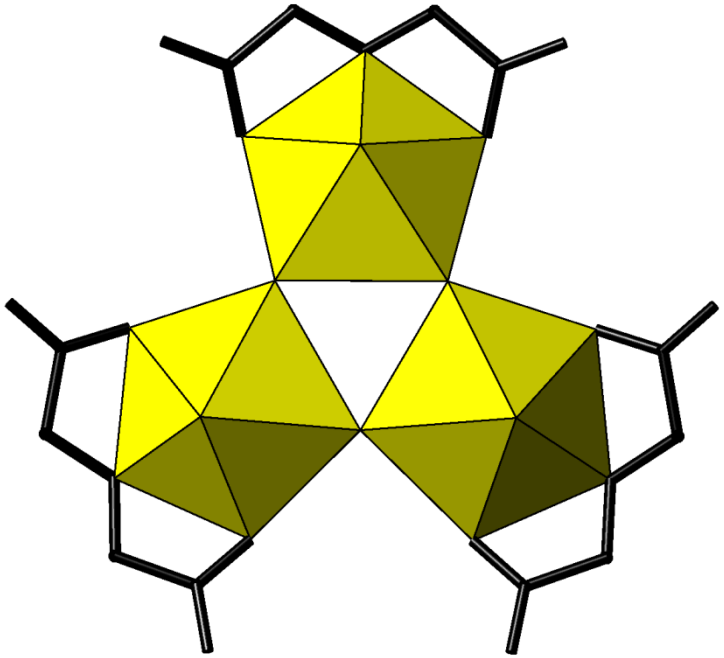
Characterizing uranium complexation with naturally occurring organic molecules

We use single-crystal X-ray diffraction, NMR, UV/Vis, and other techniques to characterize large molecular species present in aqueous solutions.



Nanometer sized uranyl citrate complex that forms in solution at pH 6

Unruh, Gojdas, and Forbes, In preparation



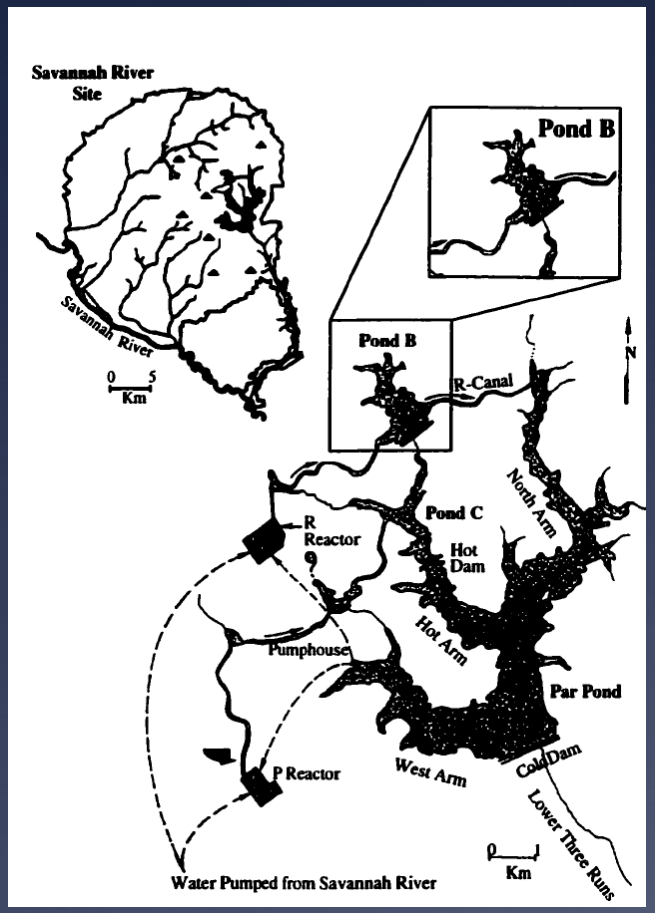
A novel uranyl trimer complexed with iminodiacetic acid

Unruh, Gojdas, and Forbes, In preparation

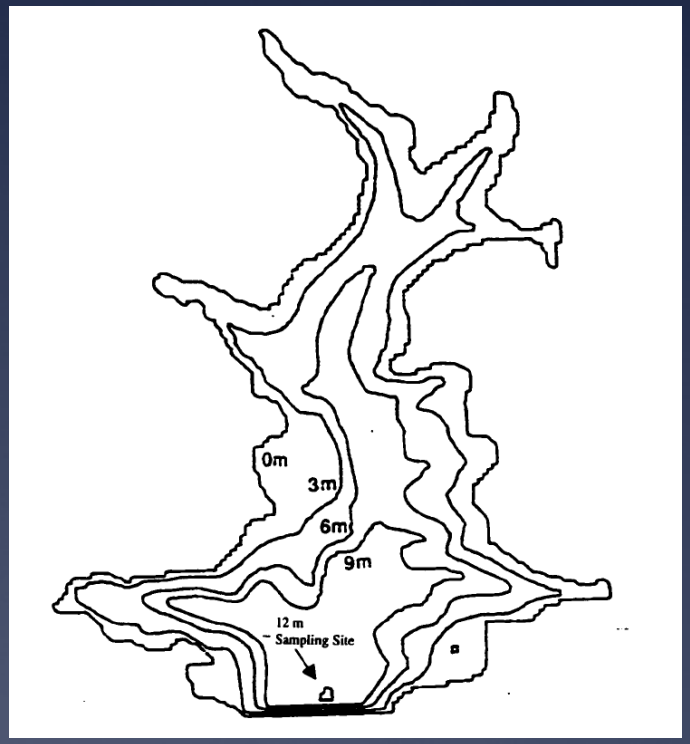
Future plans include neptunium complexation and characterization in aqueous solutions

Biogeochemistry of the Actinides

SRNL



Pond B

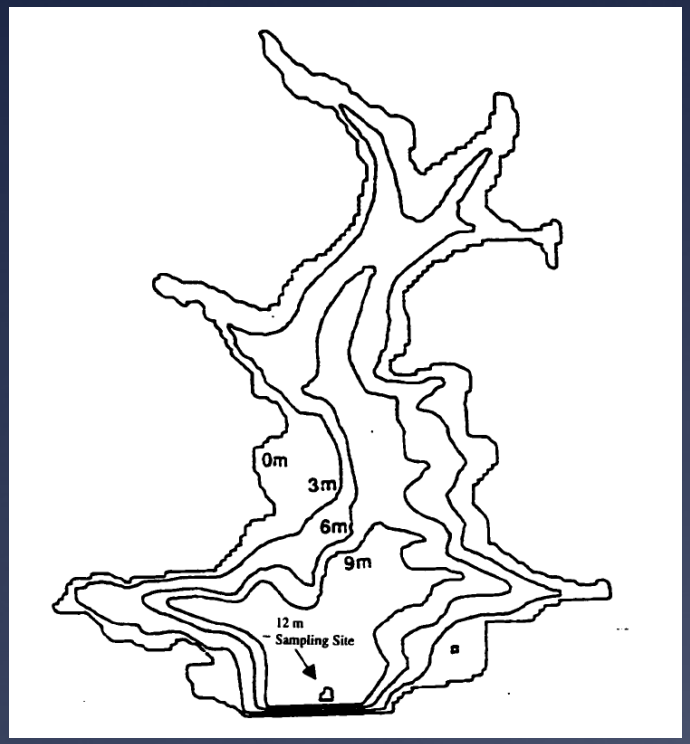


Seasonal Anoxia

Redox cycling and colloidal associations of natural/anthropogenic U, Th, Am, Pu?

Biogeochemistry of the Actinides

Pond B



Seasonal [O_2]

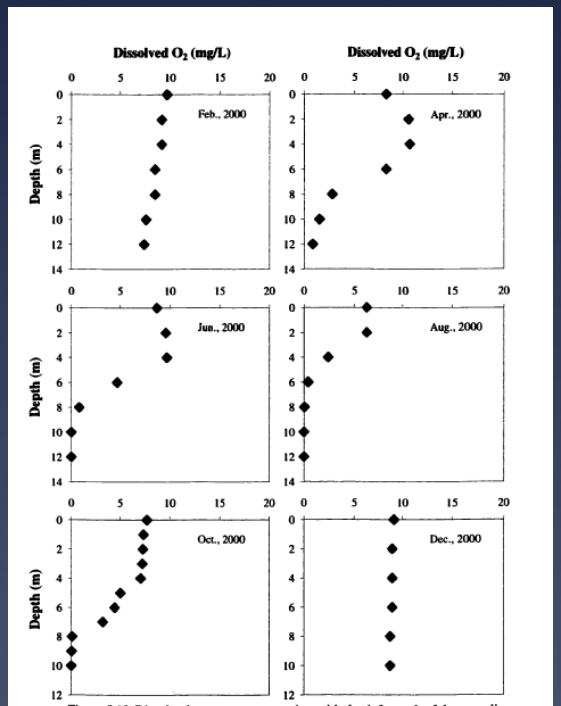


Figure 5.12 Dissolved oxygen concentration with depth for each of the sampling year 2000 samplings. Water column is well mixed in winter and stratified in summer.

Seasonal Temp

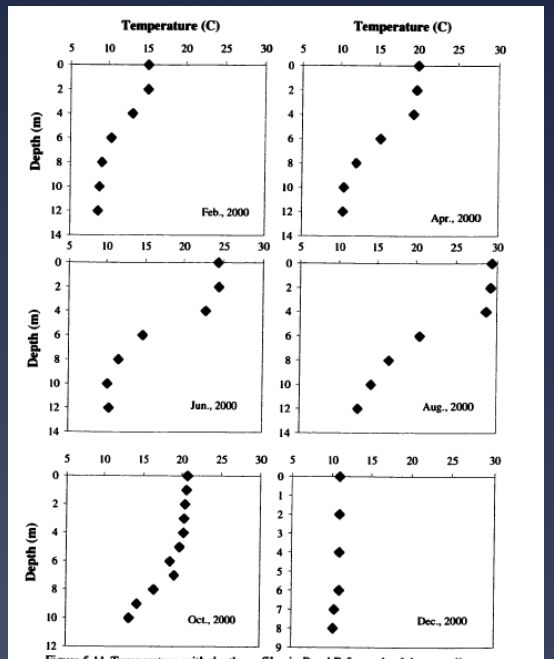


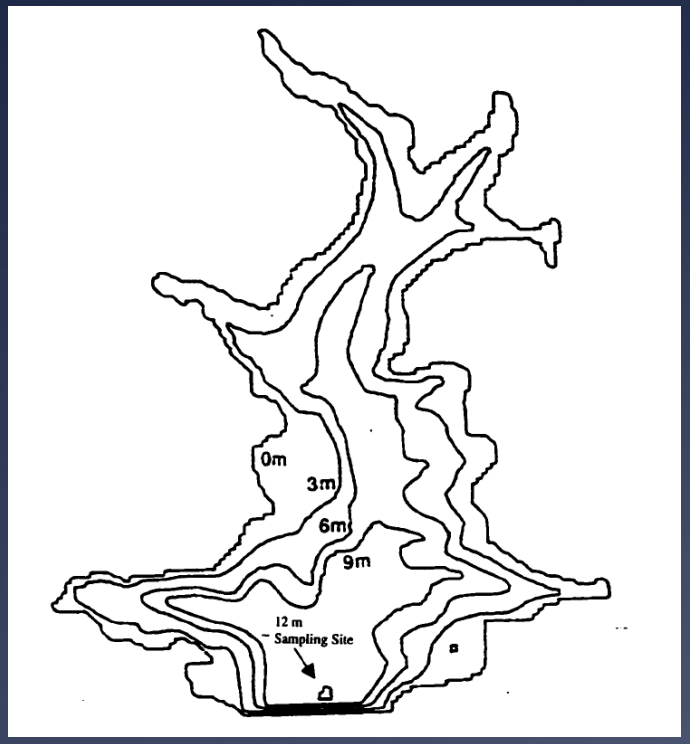
Figure 5.11 Temperature with depth profiles in Pond B for each of the sampling times for the year 2000.

Seasonal Anoxia

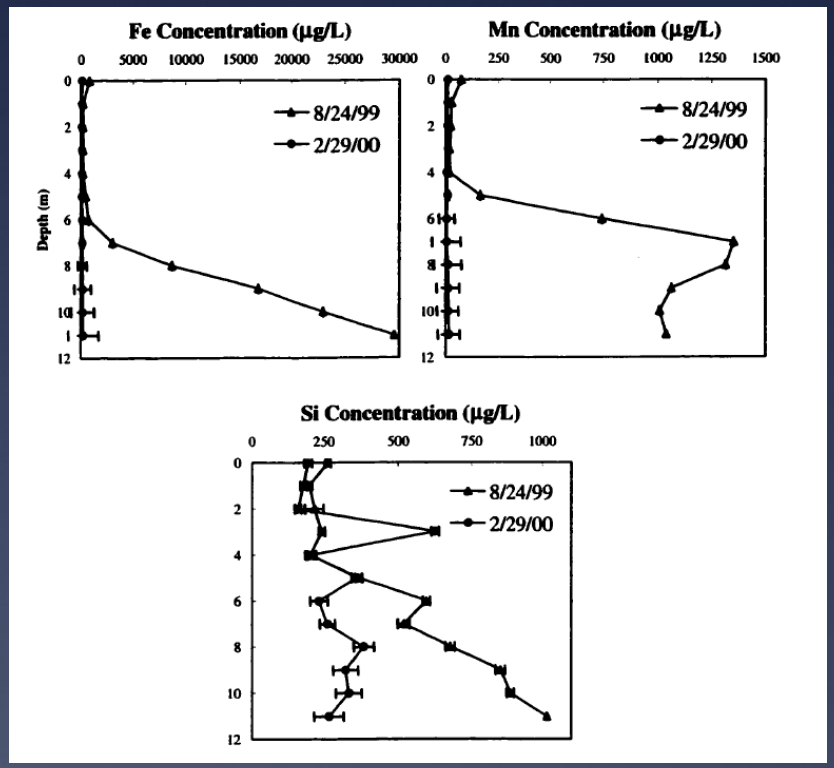
Redox cycling and colloidal associations of natural/anthropogenic U, Th, Am, Pu?

Biogeochemistry of the Actinides

Pond B



Redox Active Mn and Fe



Seasonal Anoxia

Redox cycling and colloidal associations of natural/anthropogenic U, Th, Am, Pu?

Biogeochemistry of the Actinides

Seasonal [O_2]

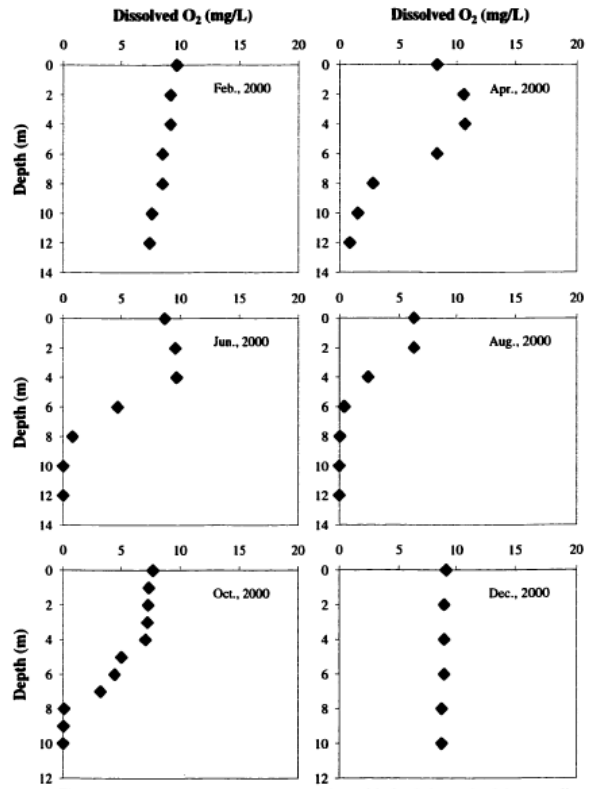
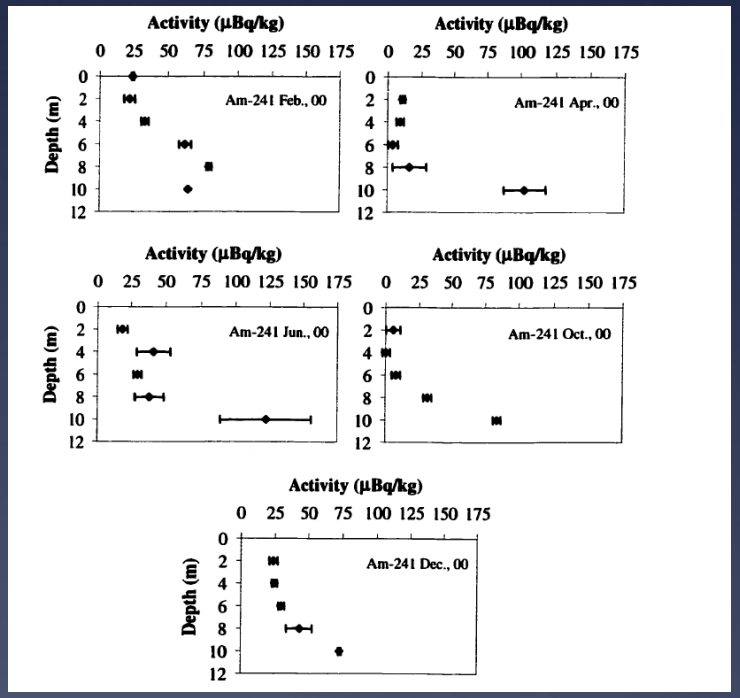


Figure 5.12 Dissolved oxygen concentration with depth for each of the sampling year 2000 samplings. Water column is well mixed in winter and stratified in summer.

Am-241



Seasonal Anoxia

Redox cycling and colloidal associations of natural/anthropogenic U, Th, Am, Pu?

Biogeochemistry of the Actinides

Seasonal [O_2]

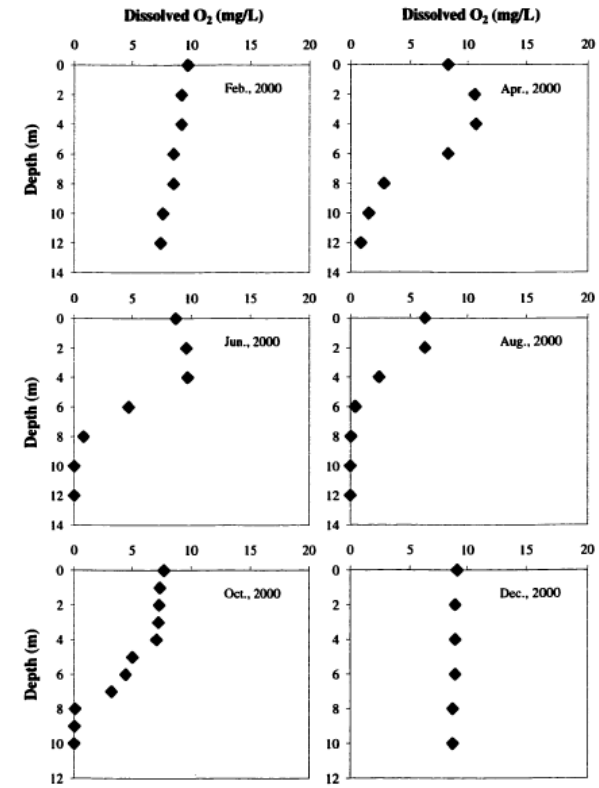
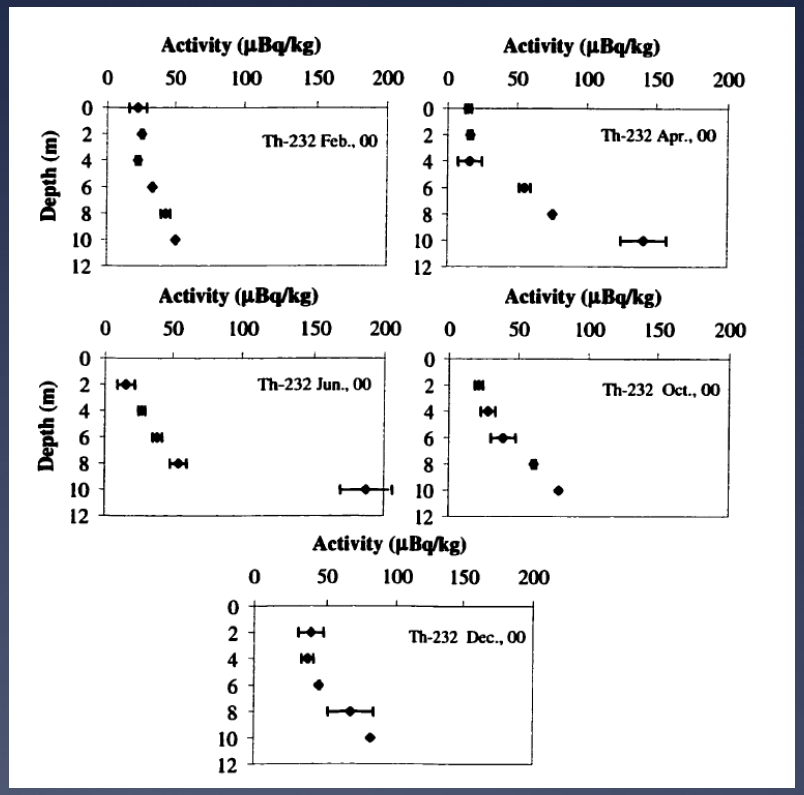


Figure 5.12 Dissolved oxygen concentration with depth for each of the sampling year 2000 samplings. Water column is well mixed in winter and stratified in summer.

Natural Th-232

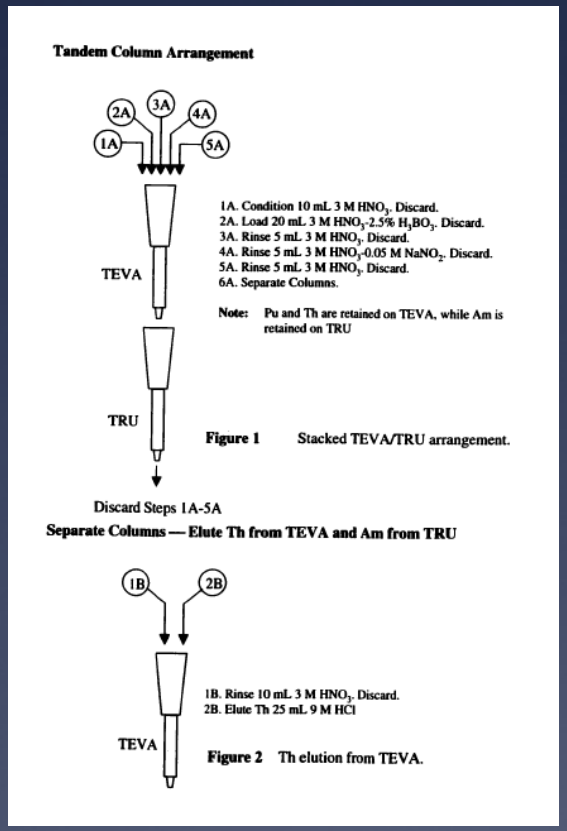


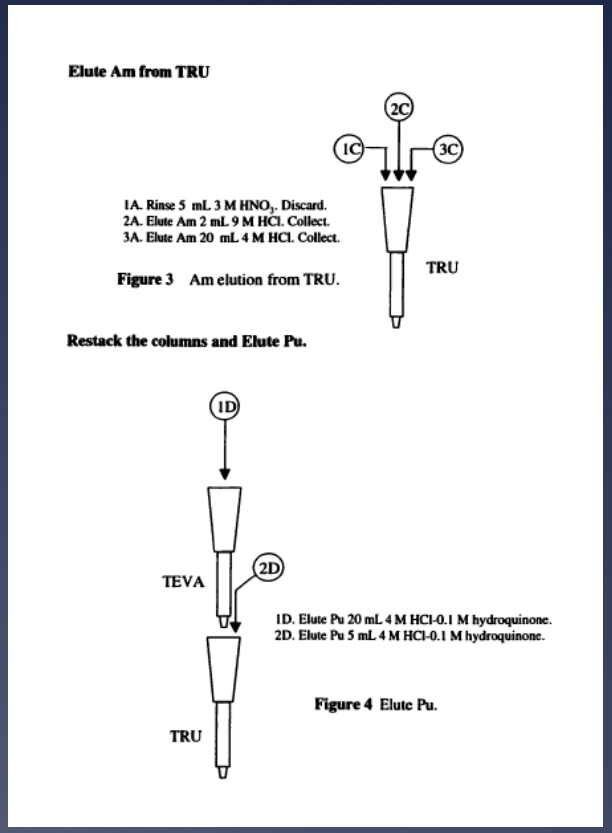
Seasonal Anoxia

Redox cycling and colloidal associations of natural/anthropogenic U, Th, Am, Pu?

U, Th, Am, Pu in the presence of high [Fe/Mn]

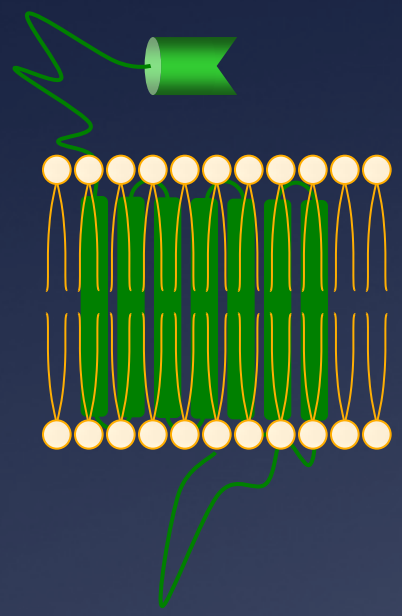
- 50 L Water Sample
- $Fe(OH)_3$ ppt
- MnO_2 ppt
- LnF_3 ppt
- 5 mL 3 M HNO_3 – H_3BO_4
- TEVA – TRU
- Split TEVA TRU

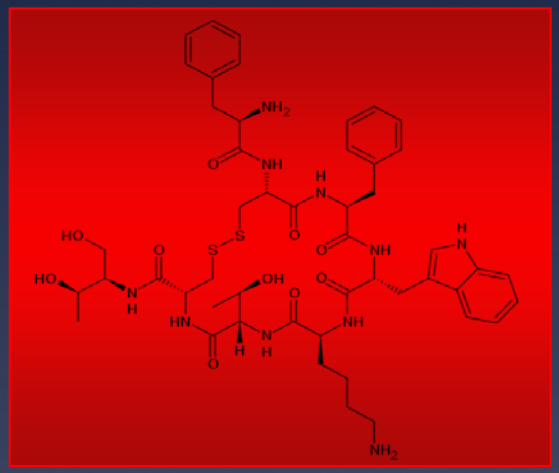


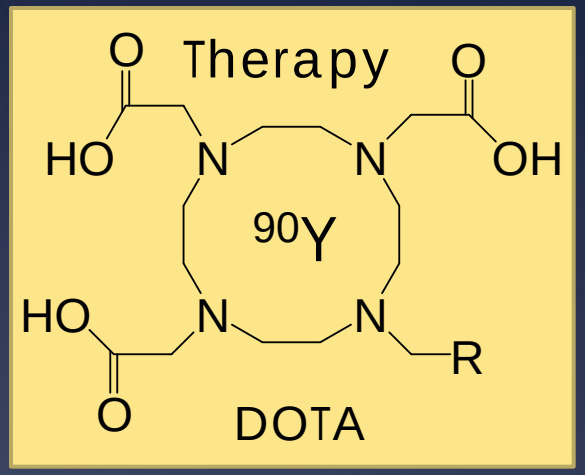


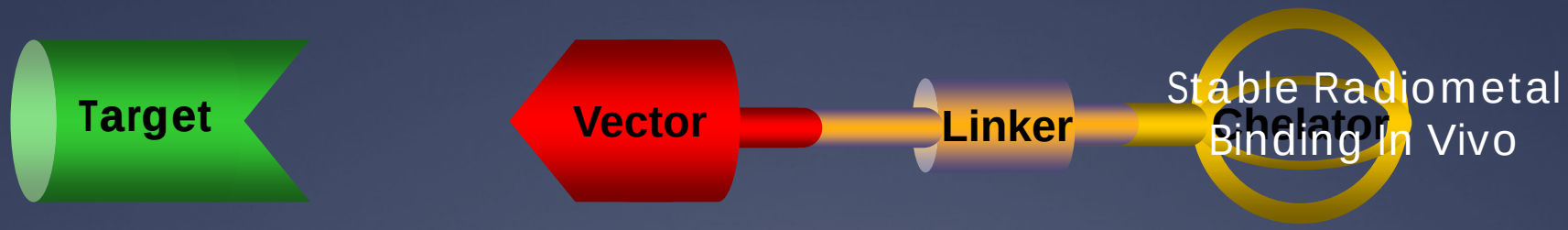
- Avg Yield 70%

Targeted Molecular Imaging and Therapy









Maintain High Affinity

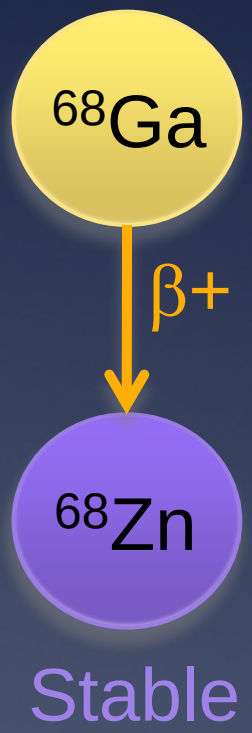
Imaging
- ^{64}Cu, ^{68}Ga

Therapy
- ^{90}Y, ^{177}Lu

Courtesy Helmut Maecke, University Hospital, Basil CH

Why Gallium-68?

- No need for on-site cyclotron
  - ✓ Still need PET/CT!
- Half Life = 68 minutes
  - ✓ Matches peptide pharmacokinetics
- β^+ Emission Intensity = 88% (^{68}Zn, stable)
  - ✓ ^{64}Cu = 18% (^{64}Ni)
- β^+ End Point Energy = 1.8 MeV
  - ✓ ^{18}F = 634 keV
  - ✓ ^{64}Cu = 653 keV
- "Surrogate" for therapeutic radionuclides
  - ✓ ^{90}Y, ^{213}Bi, ^{177}Lu
- Generator technologies have matured.



Parent/Daughter Relationships

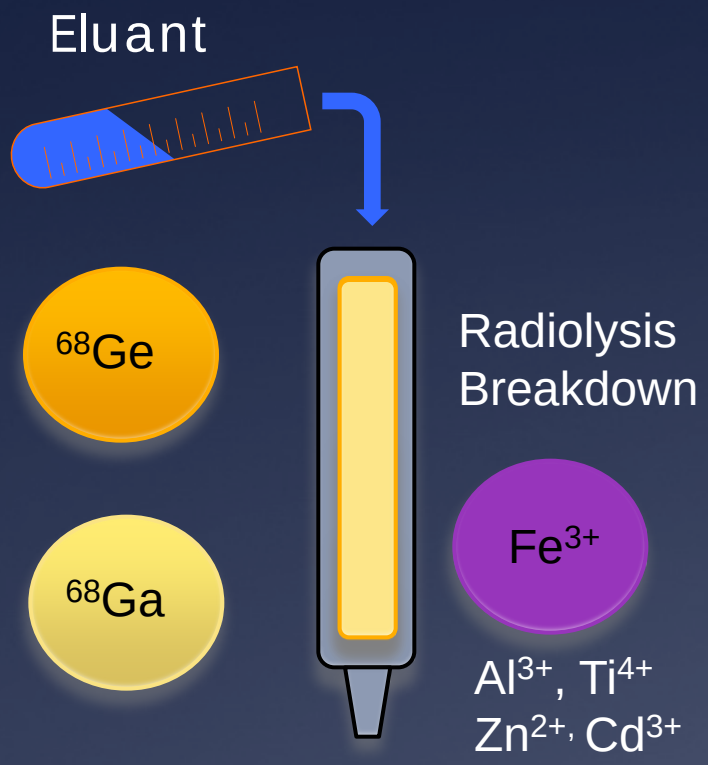
- Germani

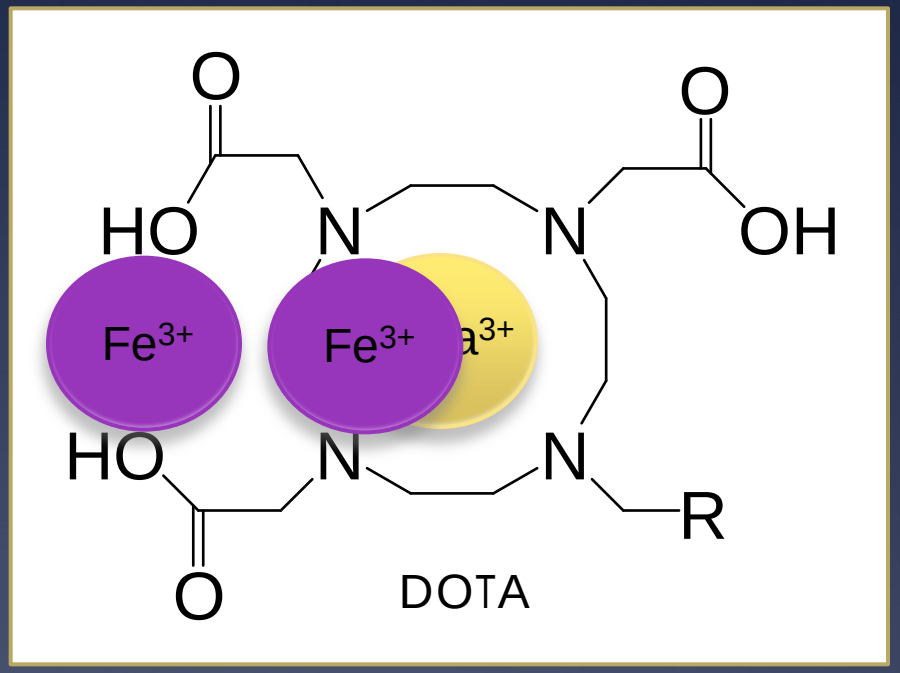
  - ✓ Cyclot 271 days
    - ^{66}Zn(
    - ^{69}Ge(

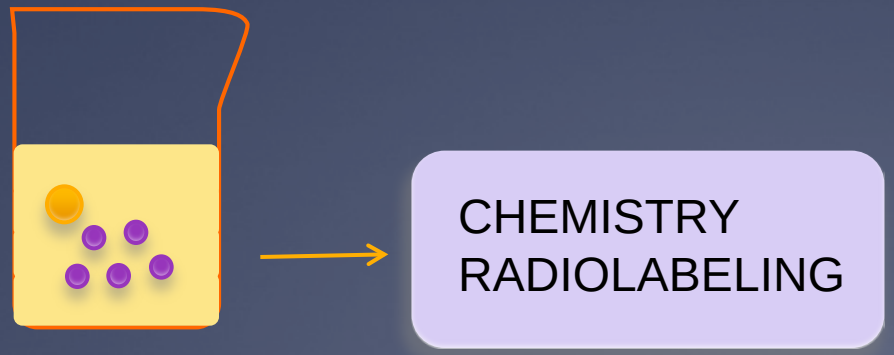
- Long live Ga
- Short lived daughter
- Periodic Use/Continuous Basis

$T_{1/2}$ = 68 minutes

Impurities and Interferences







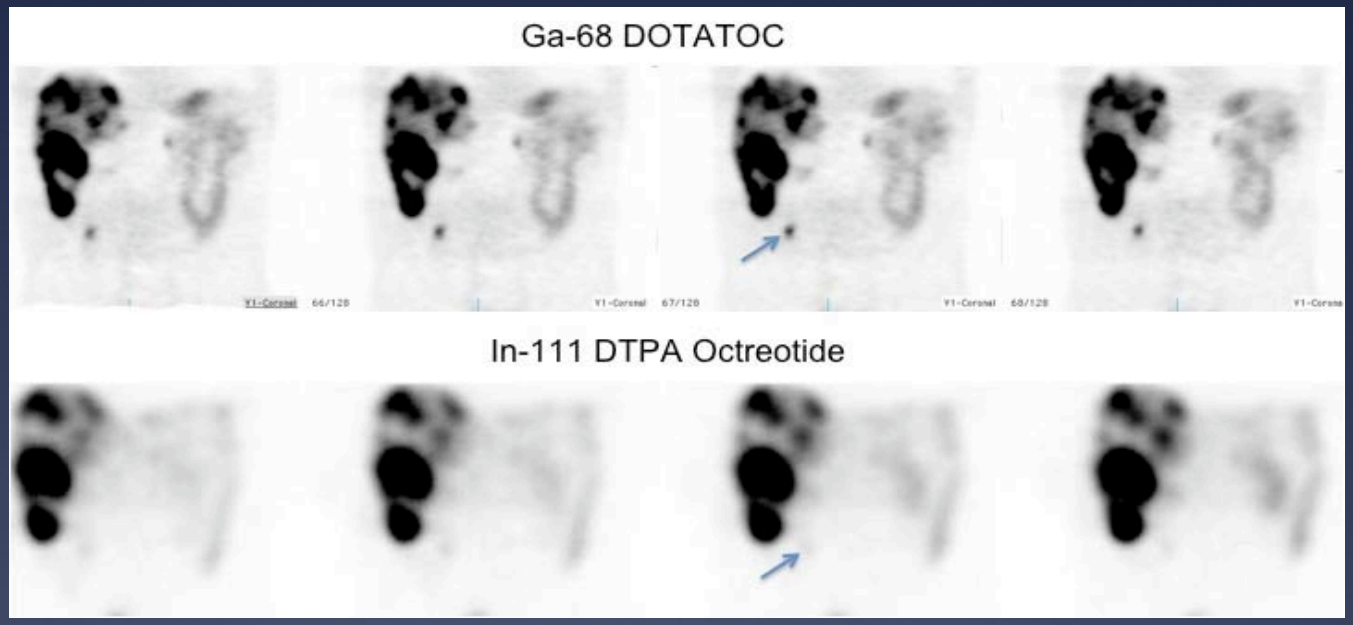
Interferences
Decrease Yield

[^{68}Ga]DOTATOC Imaging

Identifying an unknown primary tumor.

Gallium-68 DOTATOC PET

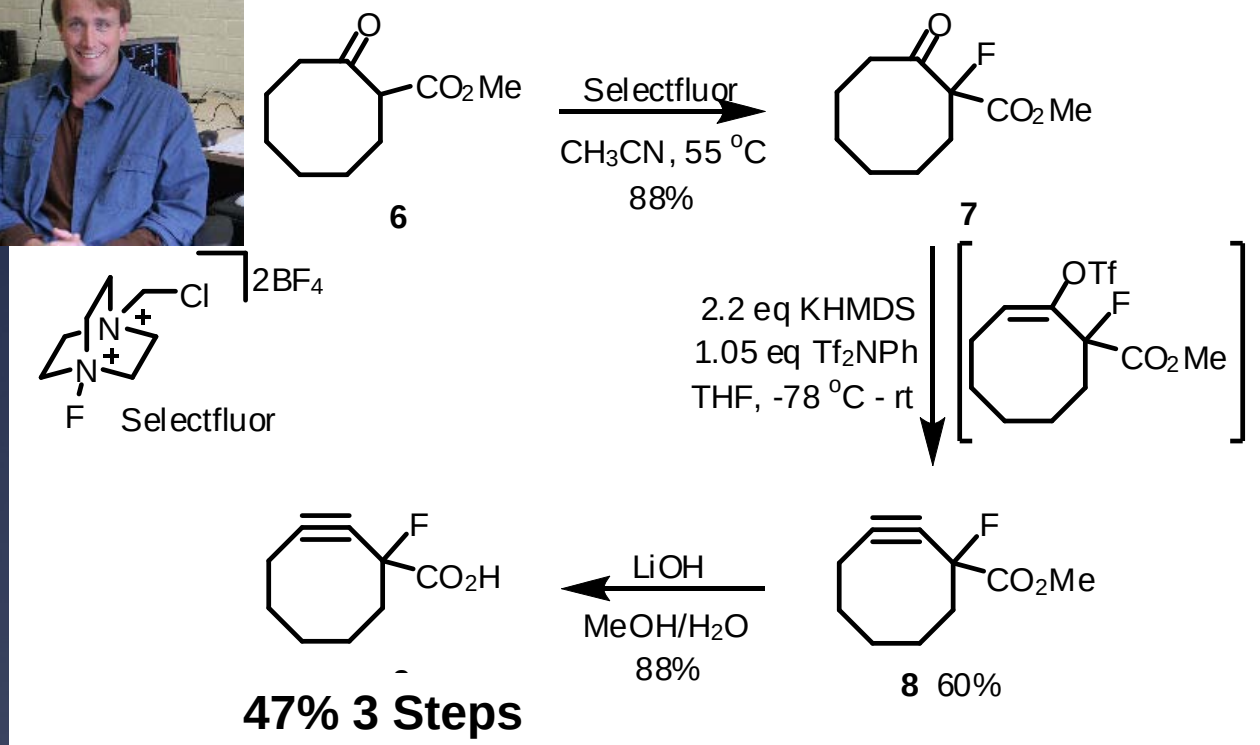
Indium-111 Octreoscan SPECT



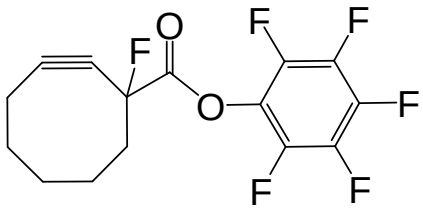
Not identifiable by SPECT.

New Separations Technologies

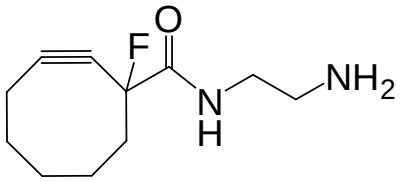
Linchpin for coupling to new chelator technologies for separations radiochemistry



Reactive Variants



PFP-ester



Primary amine

Schultz MK, Parameswarappa SG., Pigge FC, 2010 Org. Let., 12(10).
Martin et al., (Pigge, Schultz), Bioorg. Med. Chem. Let., 2010, 20(16).
Baumhover et al. (Schultz), Bioorg. Med. Chem. Let., 2011.

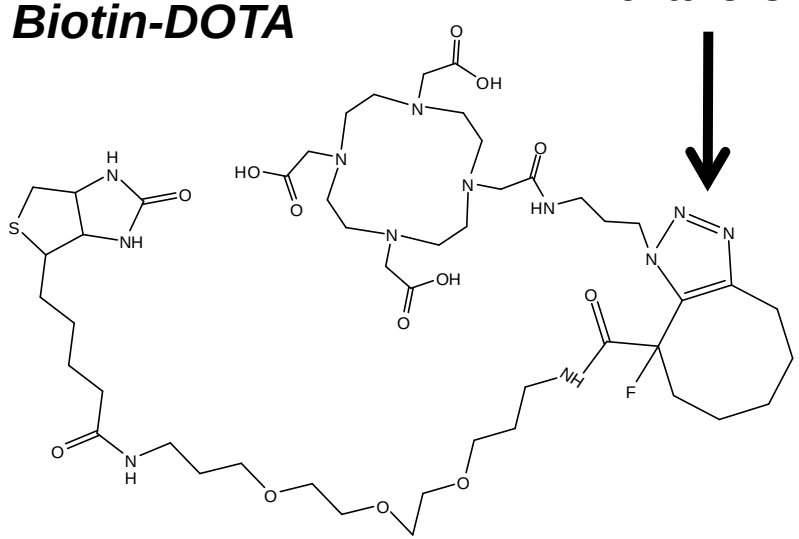
KHMDS

New Separations Technologies

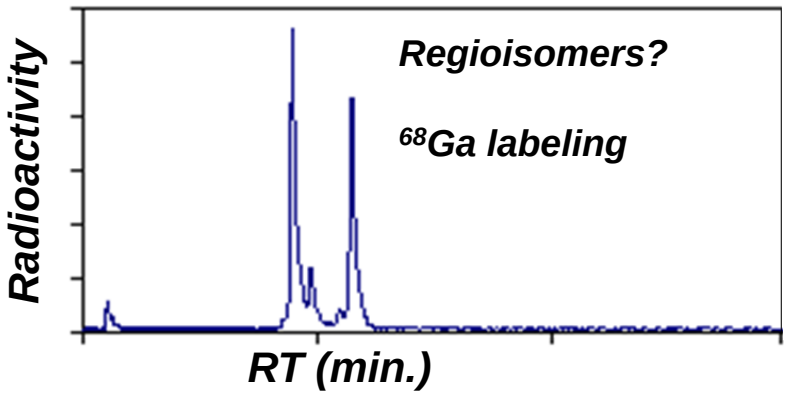
Supremely selective highly stable coupling for separations technology development

Biotin-DOTA

fused triazole



Ga-68 labeling



Potential for adapting these approaches for separations technologies is largely unexplored. (new chelators for actinides)

Schultz MK, Parameswarappa SG., Pigge FC, 2010 Org. Let., 12(10).
Martin et al., (Pigge, Schultz), Bioorg. Med. Chem. Let., 2010, 20(16).

Proposed Radiochemistry Degrees at Iowa

- BA Track
- 5 Yr Professional MS
- PhD

- Radiopharmaceutical Sciences
- Environmental Monitoring
- Homeland Security/Safeguards
- Nuclear Energy
- Academic Geochronology

Thank you!

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Richard Baum MD PhD

- Dirk Mueller PhD
- Inge Klette

University Hospital Freiberg, Germany

Helmut Maecke PhD

- Melpomeni Fani PhD

Collaborators

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Blanca Schafer MS

Susan Walsh

Len Watkins PhD

Kathy Thedes-Reynolds MS

Sue O'Dorisio MD PhD

Thomas O'Dorisio MD

David Bushnell MD

Yusuf Menda MD

Laura Boles Ponto PhD

Michael Graham MD PhD

John Sunderland PhD

My Lab

- Nicholas Baumhover PhD
- Kyle Kloepping

Support

Dance Marathon

Holden Comprehensive Cancer Center

Department of Radiology, PET Center