Industrialization of Biology

Session 7: Advanced Molecules

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Chemical and biological catalysis

Some broad generalizations…

Chemistry	Selectivity conferred by X and Y
Biology	Selectivity conferred by R and R´

Expanding the biological reaction space

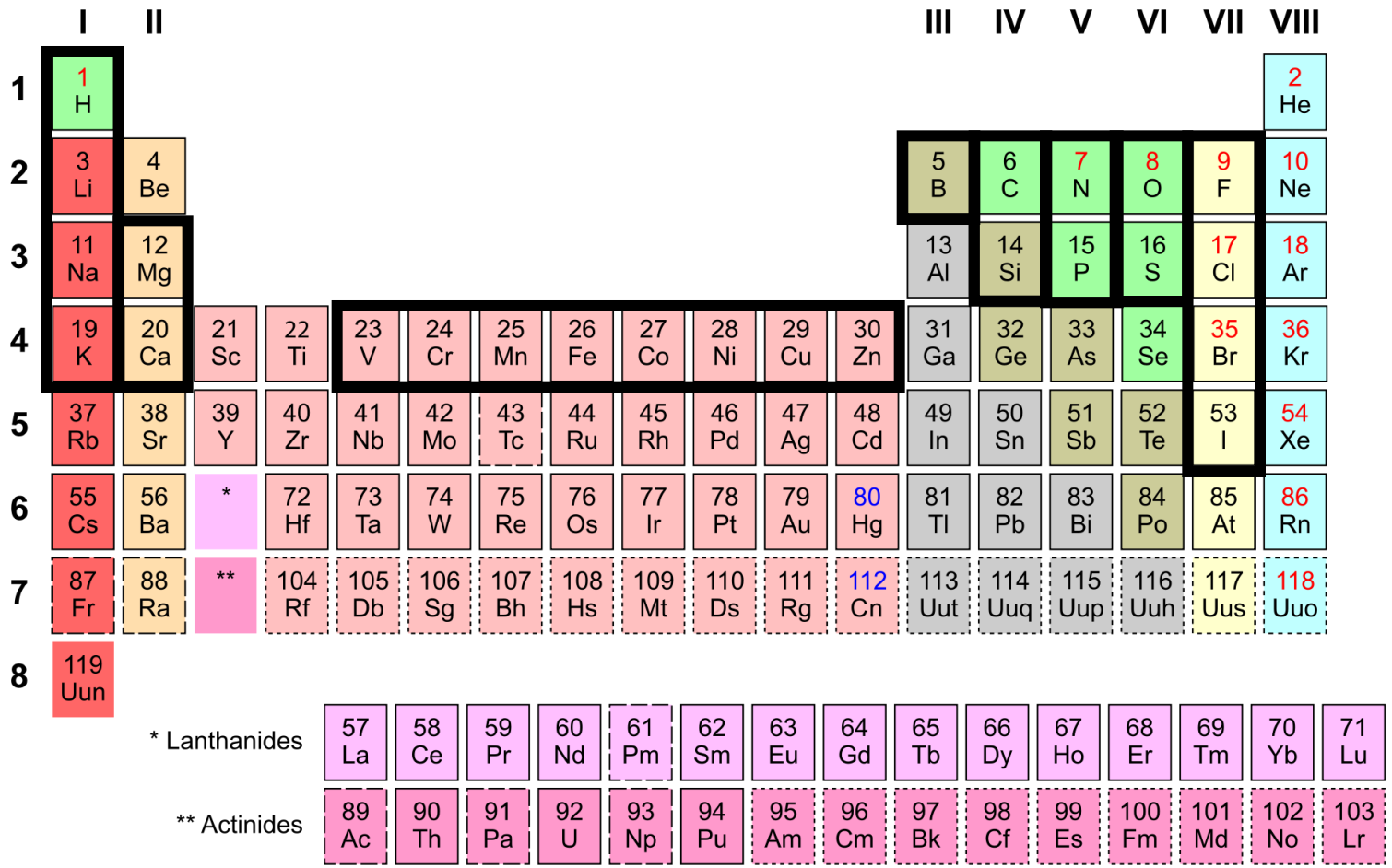
How do we integrate chemical and biological catalysis to design effective industrial-scale syntheses?

- Increasing the functional space of biologically-sourced small molecules (by accommodation or biosynthesis)
- Broadening the R group scope of known enzyme classes (e.g. ketoreductases)
- Designing or discovering new enzymes/active sites for chemical building blocks (e.g. diels alderases, crosscoupling reactions)

Can we take advantage of both the strengths of chemical and enzymatic synthesis?

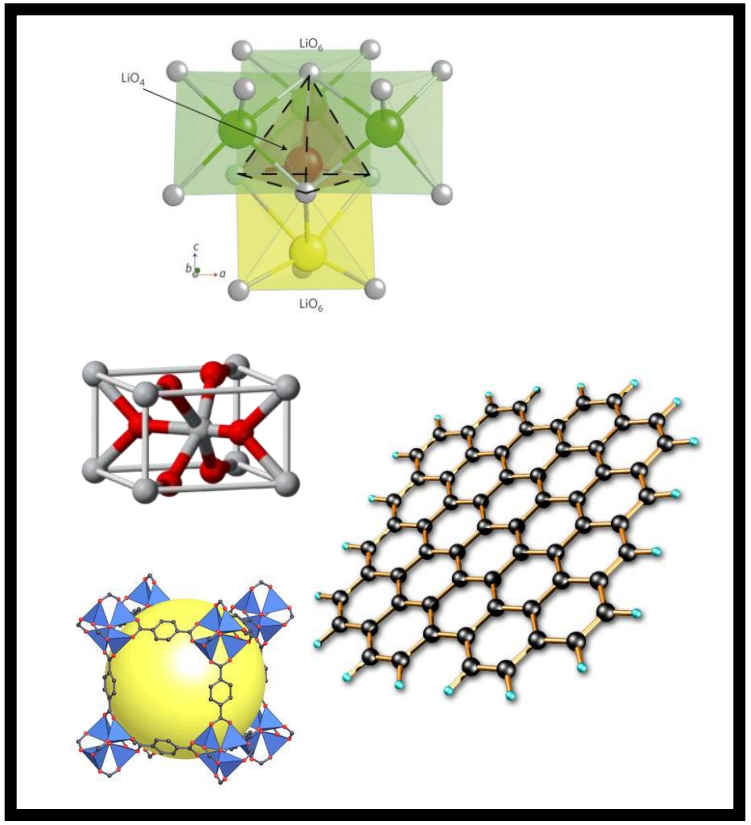
Expanding the elemental composition of cells

Cellular systems have constructed an enormous range of function from a limited set of elements

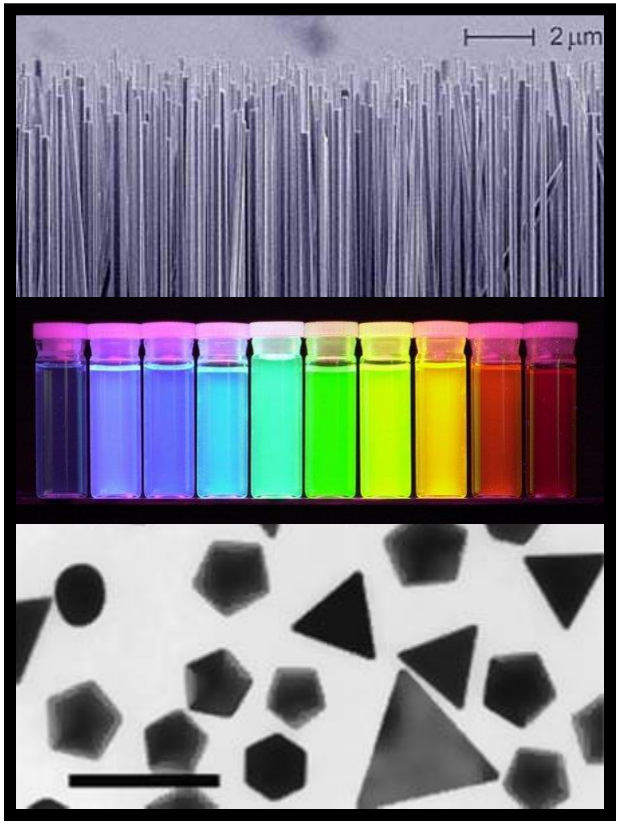


The diversity of inorganic function is broad

Inorganic materials have a diverse range of functions that respond and interact with signals that are orthogonal to typical cells

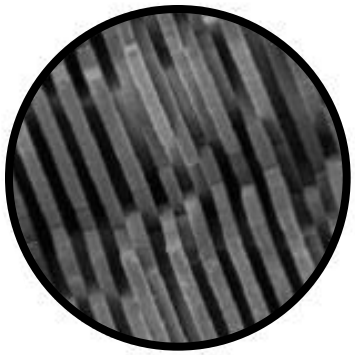


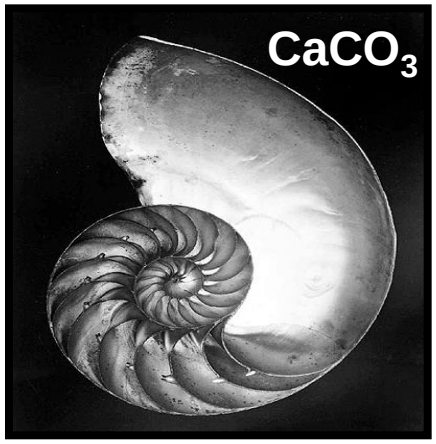
control of elemental composition and structure

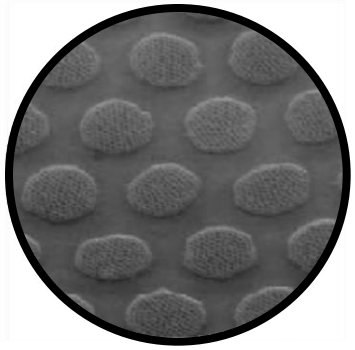


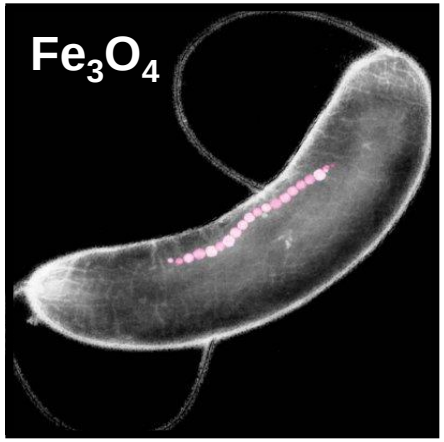
control over size and shape

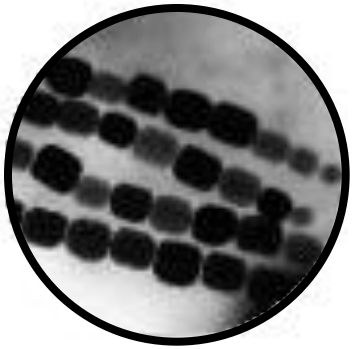
Biomaterials: Nanoscale self-assembly











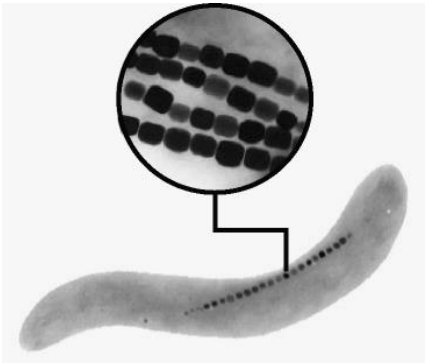
Novel material properties and functions emerge from nanoscale features

Addadi, Aizenberg, Belcher, De Yoreo, Dove, Kröger, Mann, Nagasawa, Weiner, Wilt, Veis, Zhang, and others

Synthetic biology and new materials

The best understood biomineralization systems involve the production of structural materials based on calcium (bone, nacre)

What about transition-metal based functions?



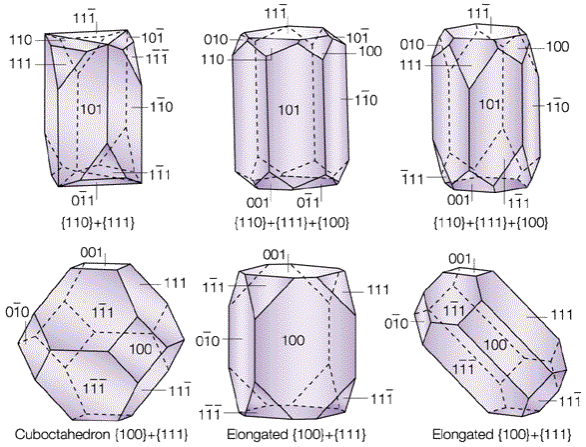
magnetotactic bacteria

unique biological features

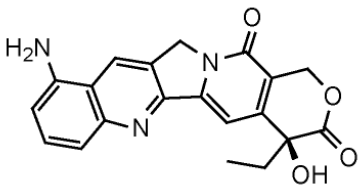
transition-metal based (magnetite)
mixed-valent
pure material (not composite)

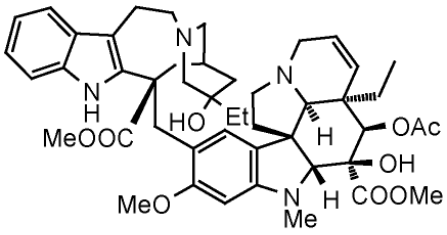
unique chemical features

genetically-determined shape
narrow size distribution (30-80 nm)
single magnetic domain
defectless



Natural products and pharmaceuticals

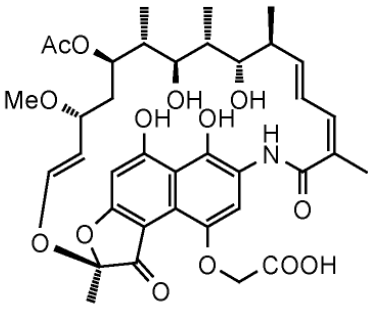




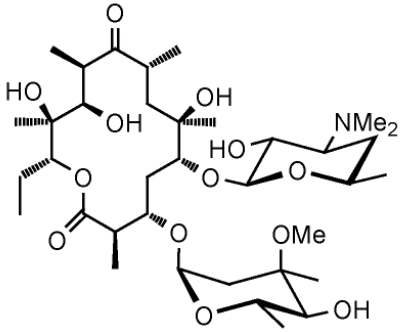
cam

4,000-5,000 organohalogens

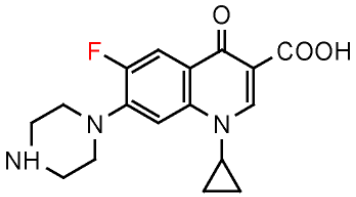
~20 organofluorines

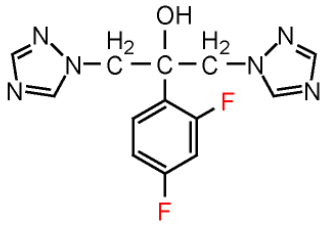


rifamycin B



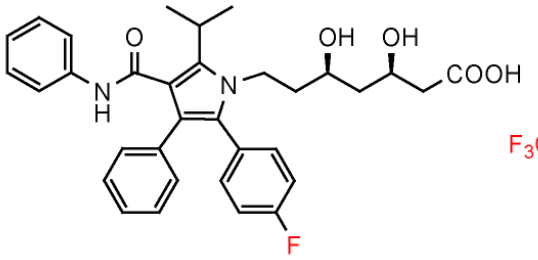
erythromycin A



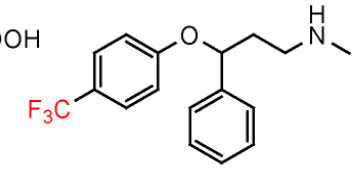


20-30% pharmaceuticals contain F

3 out of 5 top-selling drugs



Lipitor

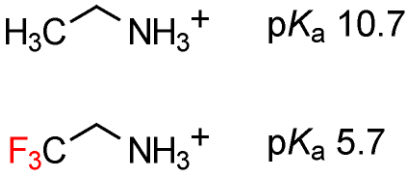


Prozac

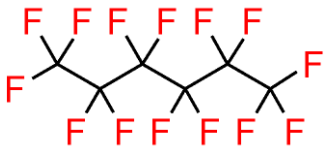
natural product drugs

synthetic drugs

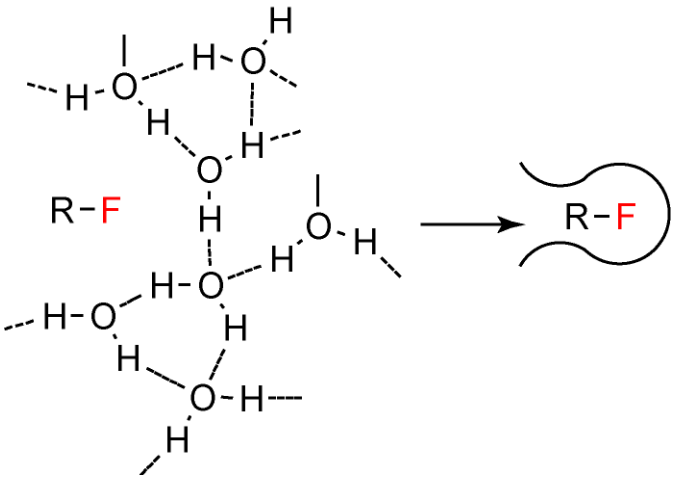
Fluorine and drug design



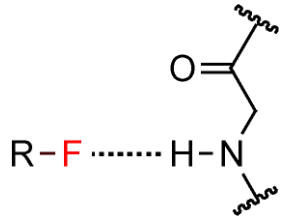
protonation state



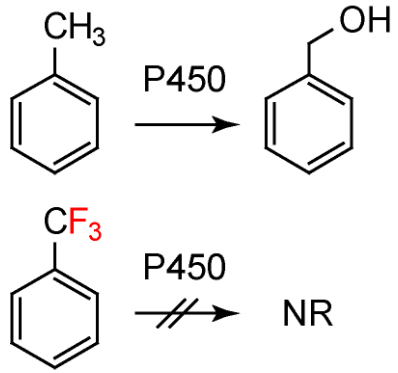
lipophilicity



desolvation



dipolar interactions

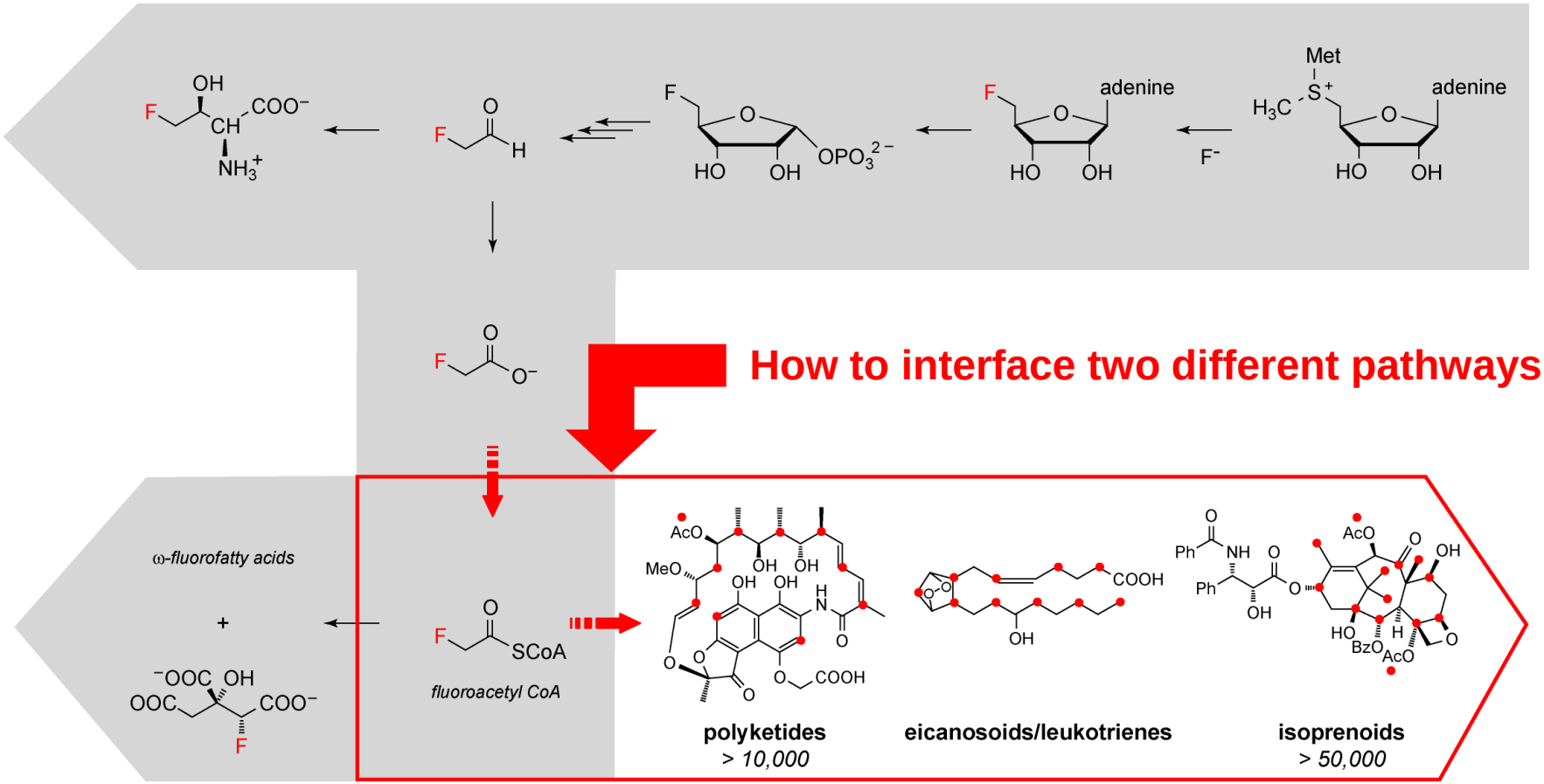


metabolism

Synthetic methods can limit our ability to incorporate fluorine into complex molecules

Synthetic biology of fluorine

natural pathways for biosynthesis of simple organofluorine precursors



engineered pathways for creating complex bioactive organofluorines

Some questions ...

- How do we identify common inefficiencies in synthetic chemistry related to stereo- or regio-chemistry?
- How do we determine whether chemical or biological steps are the most economical or resource-efficient?
- How do we design and optimize enzymes for new reaction spaces?
- How do we identify and rank the most effective semisynthetic routes?