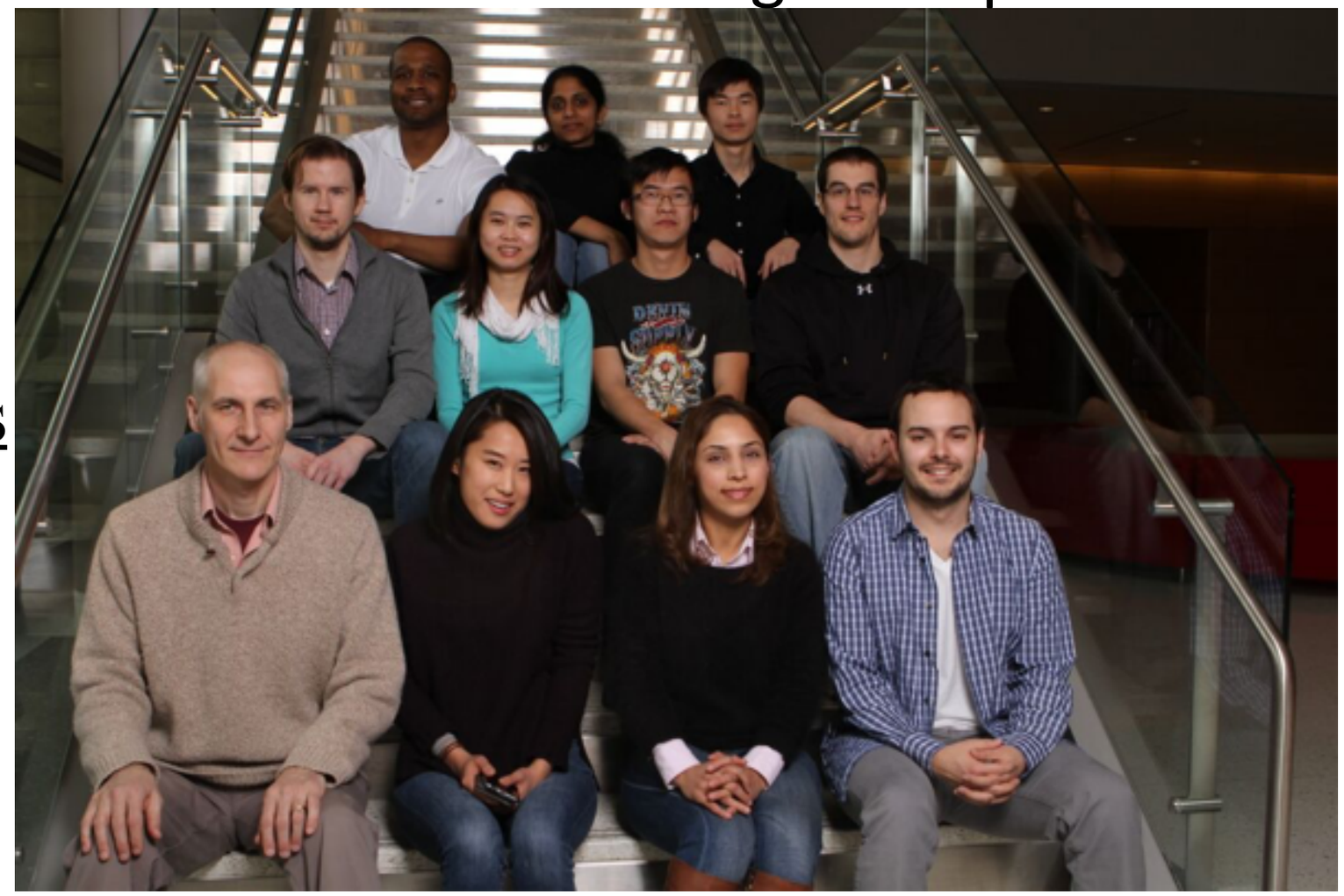
Schafmeister Group

Abiotic Biological Chemistry - ABC

Nanometer scale - Angstrom precision



PAST GRADUATE STUDENTS

Dr. Stephen Habay, Ph.D. program. Graduated 2006
Dr. Christopher Levins, Ph.D. program. Graduated 2006
Dr. Gregory Bird, Ph.D. program. Graduated 2006
Dr. Paul Morgan, Ph.D. program. Graduated 2007
Megan Macala, M.Sc. program. Graduated 2007
Chris Morgan, M.Sc. program. Graduated 2007
Laura Belasco, M.Sc. program. Graduated 2007
Dr. Sharad Gupta, Ph.D. program. Graduated 2009
Dr. Zachary Brown, Ph.D. program. Graduated 2010
Dr. Qingquan Zhao, Ph.D. program. Graduated 2014
Dr. Matthew Parker, Ph.D. program. Graduated 2015
Dr. Mahboubeh Kheirabadi, Ph.D. program Graduated 2015

CURRENT GRADUATE STUDENTS

Kavitha Akula, Ph.D. program.
Senzhi Zhao, Ph.D. Program.
Chongsong Xu, Ph.D. Program.
Conrad Pfeffer, Ph.D. Program.
J.D. Northrup, Ph.D. Program.
Jae Eun Cheong, Ph.D. Program.
Yanfeng Fan, Ph.D. Program.
Steven Fletcher, Ph.D. Program.
Melody Pham, Ph.D. Program

COLLABORATORS

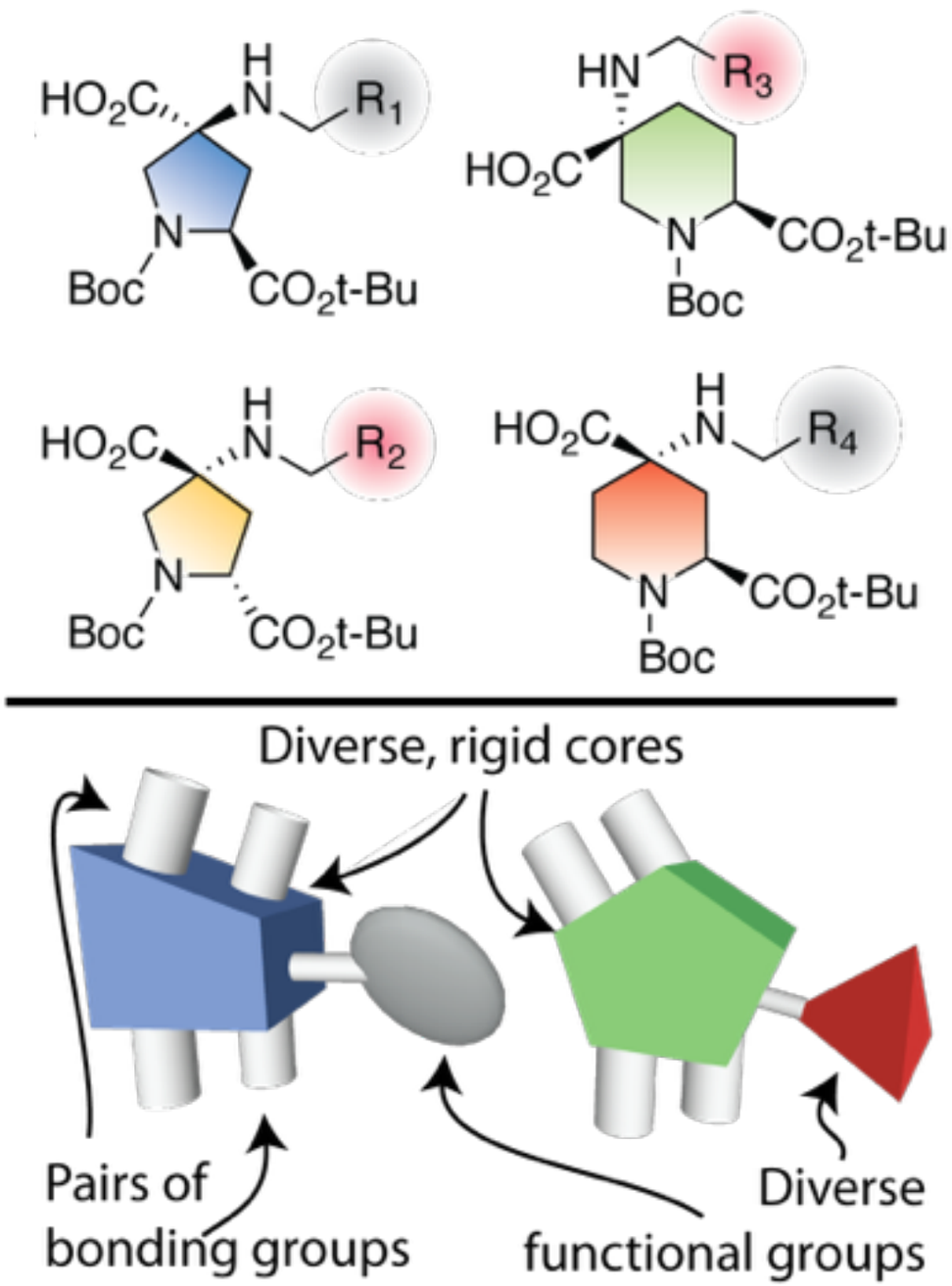
Prof. Mark Feitelson (Temple, Biology)
Dr. Alla Arzumanyan (Temple, Biology)
Prof. Ken Houk (UCLA)

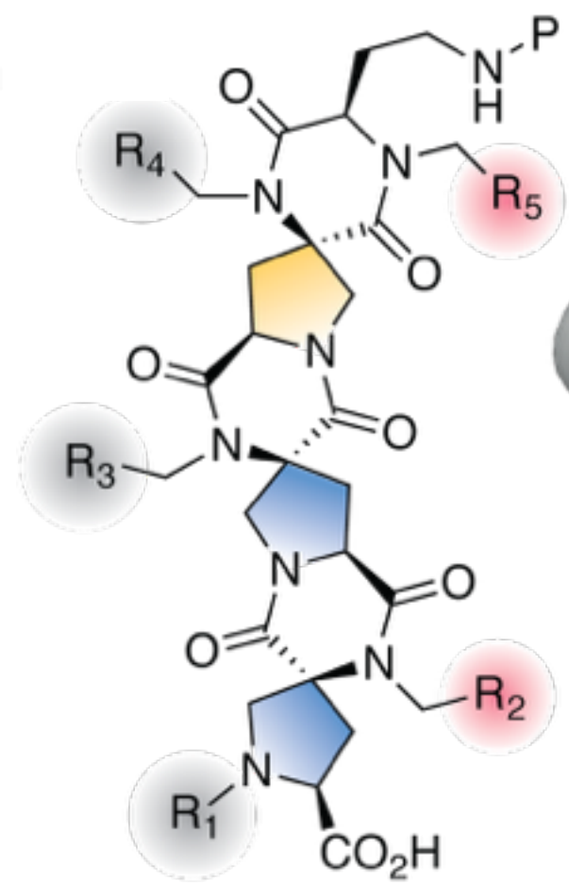
FUNDING

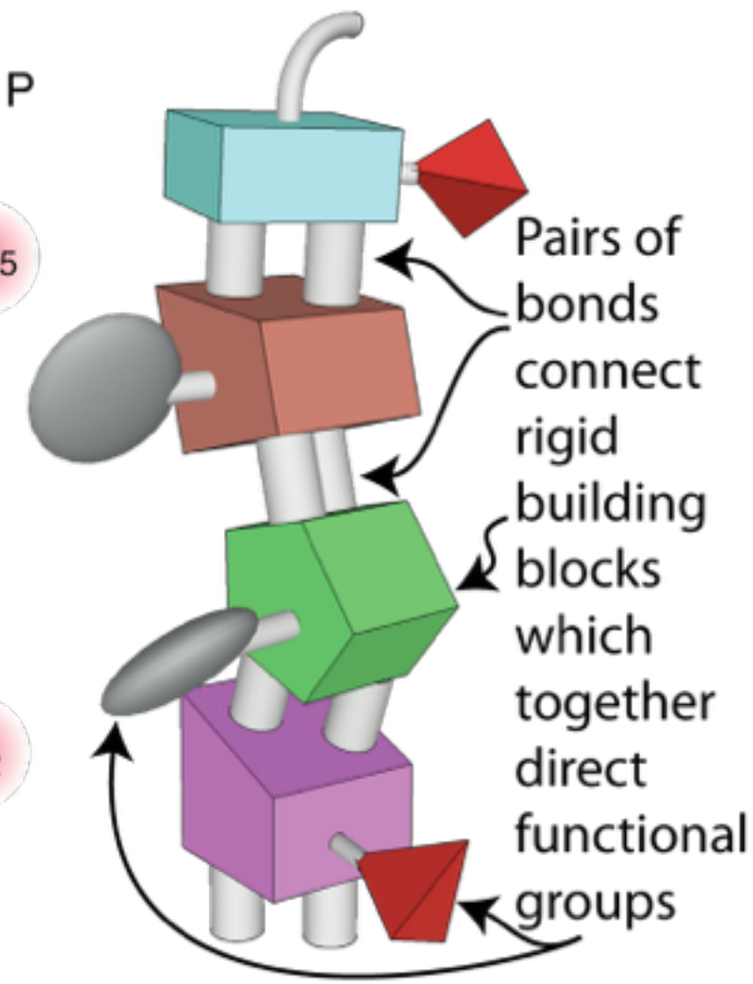
National Institute of Health, NIGMS
National Science Foundation
Defense Threat Reduction Agency (DOD-DTRA) - Dr. Ilya Elashvili
Temple University

Molecular Building Blocks amenable to Computational Design

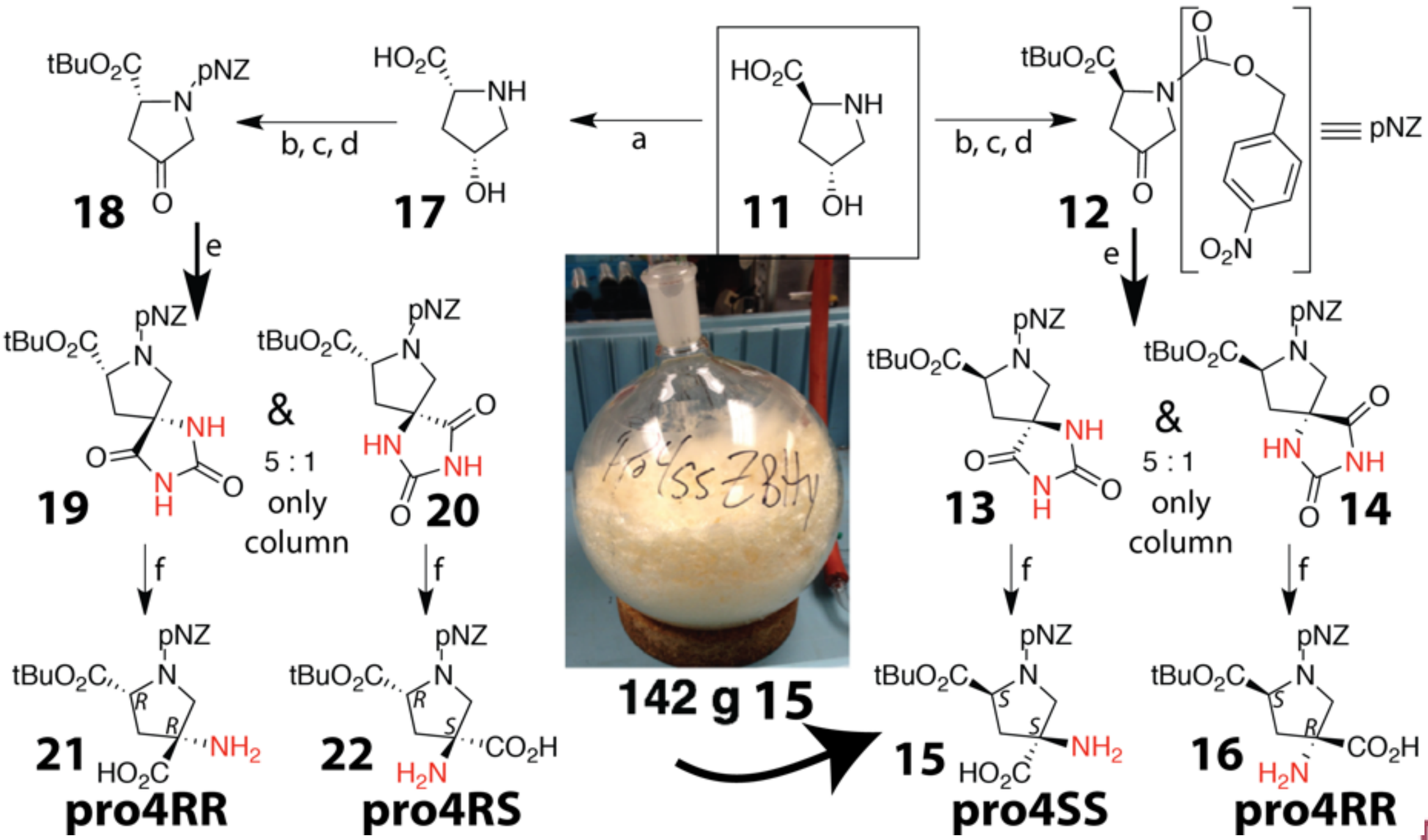
- **Spiroligomers - synthetic alternative to proteins**
- Built from rigid, cyclic, functionalized building blocks



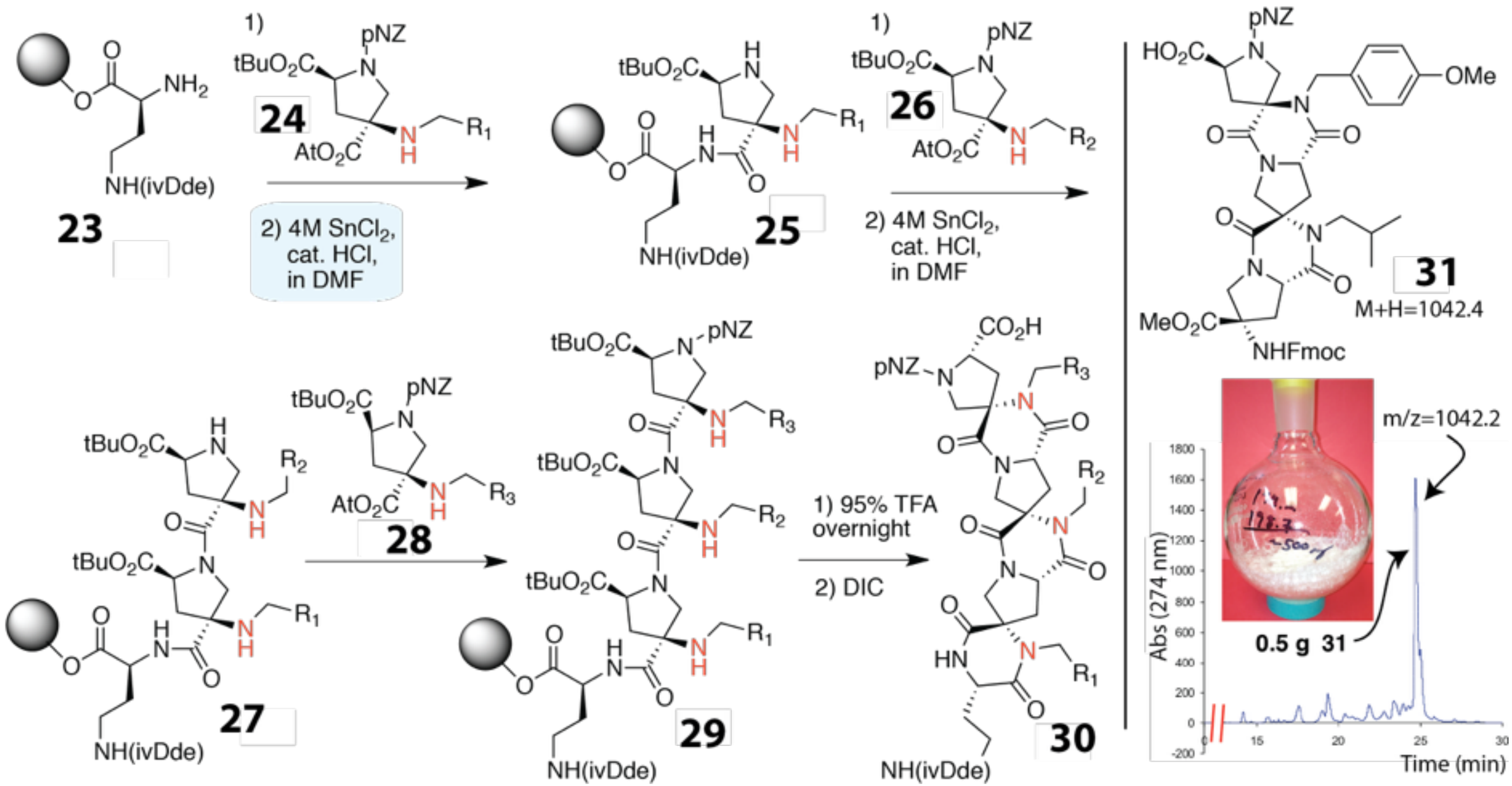




New synthetic developments enable spiroligomer nanostructure synthesis

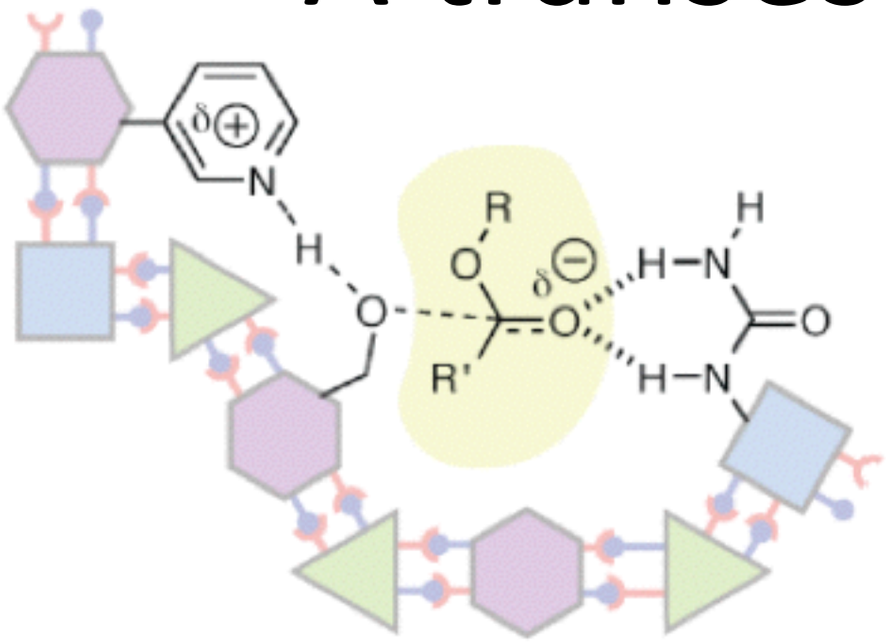


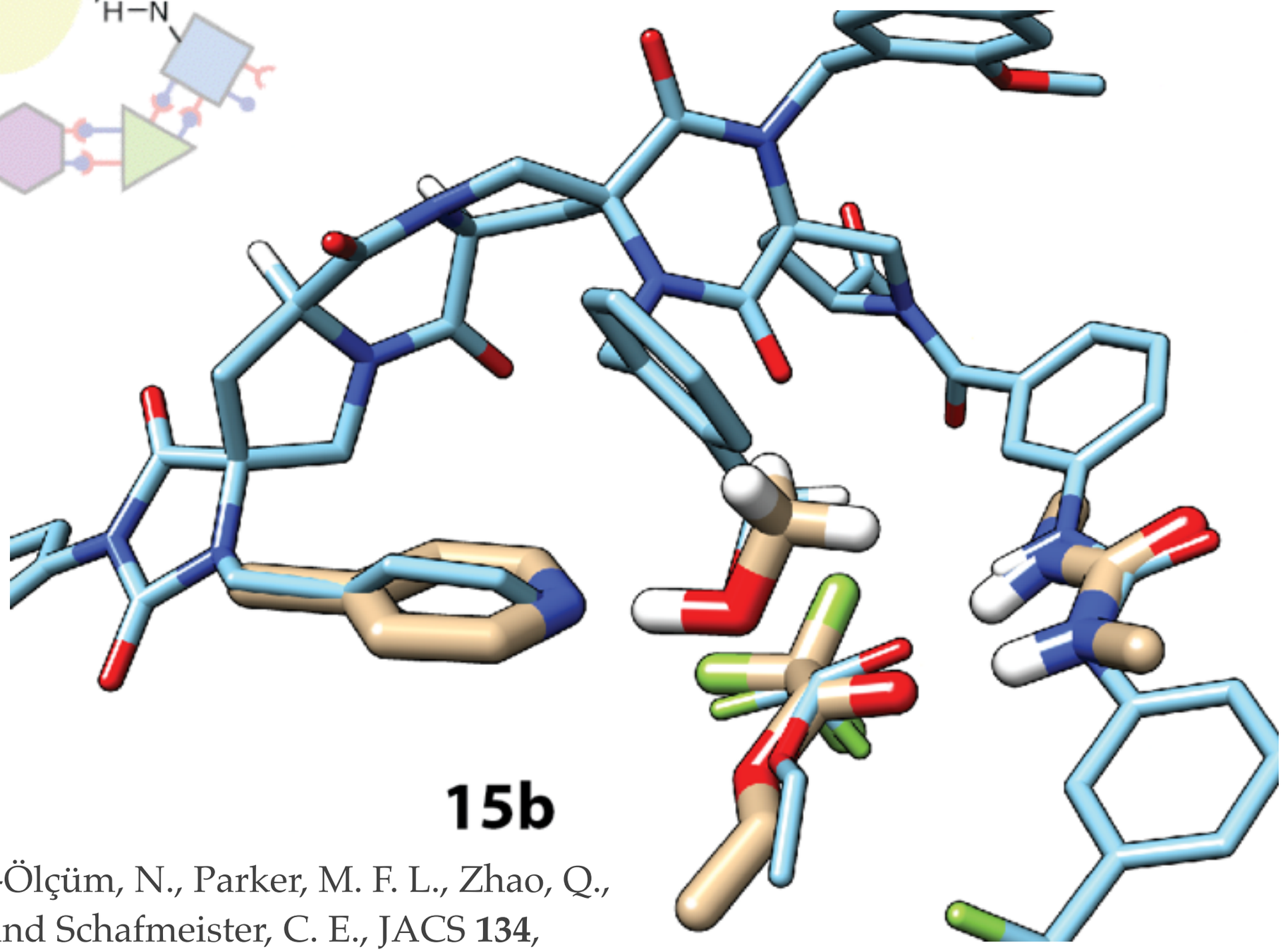
New synthetic developments enable spiroligomer nanostructure synthesis



Red nitrogens are ^{15}N labeled for Structure Determination

A transesterification catalyst





Kheirabadi, M., Çelebi-Ölçüm, N., Parker, M. F. L., Zhao, Q., Kiss, G., Houk, K. N., and Schafmeister, C. E., JACS **134**, (2012): 18345–18353. doi:10.1021/ja3069648,

New synthetic developments enable spiroligomer nanostructure synthesis

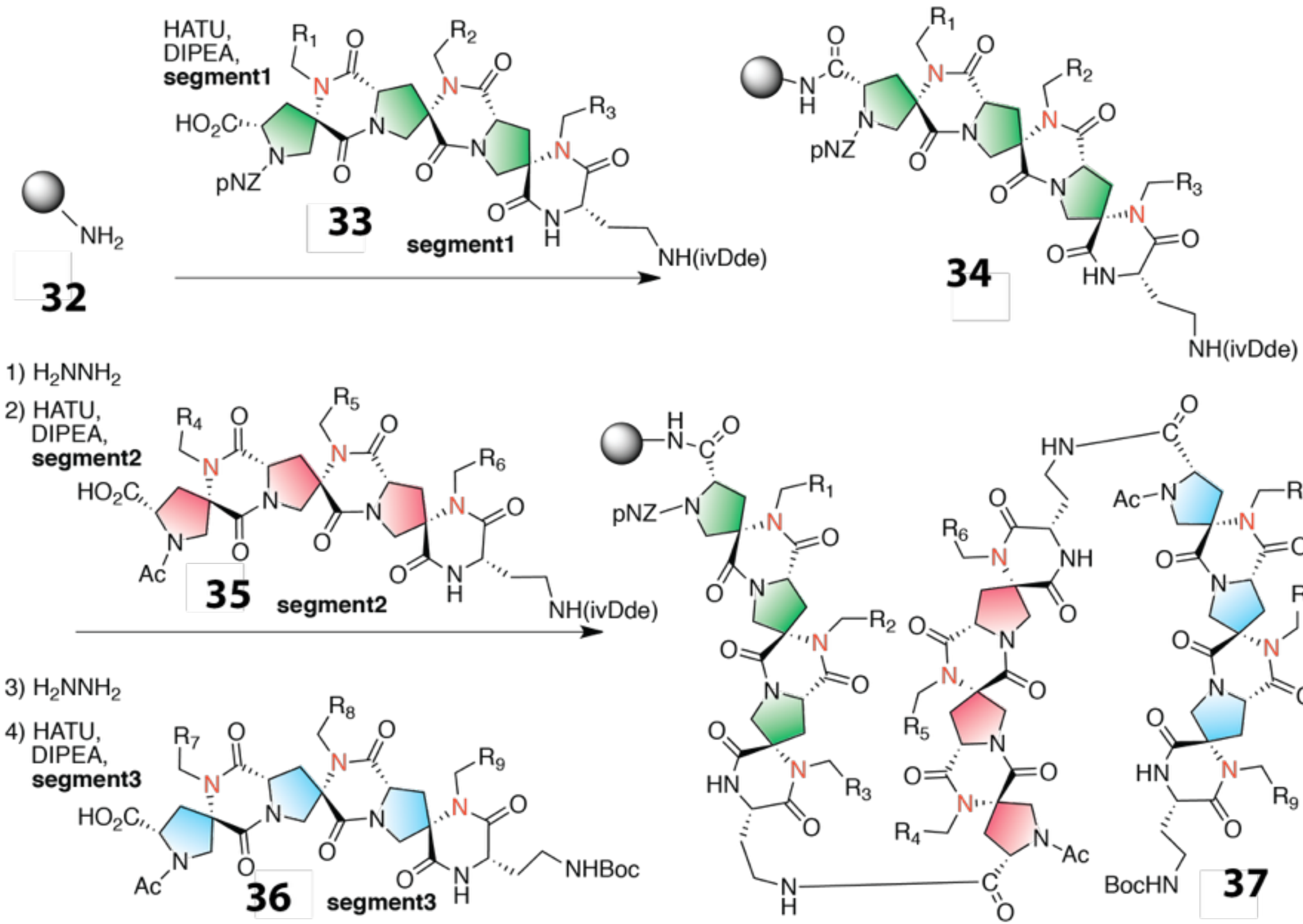
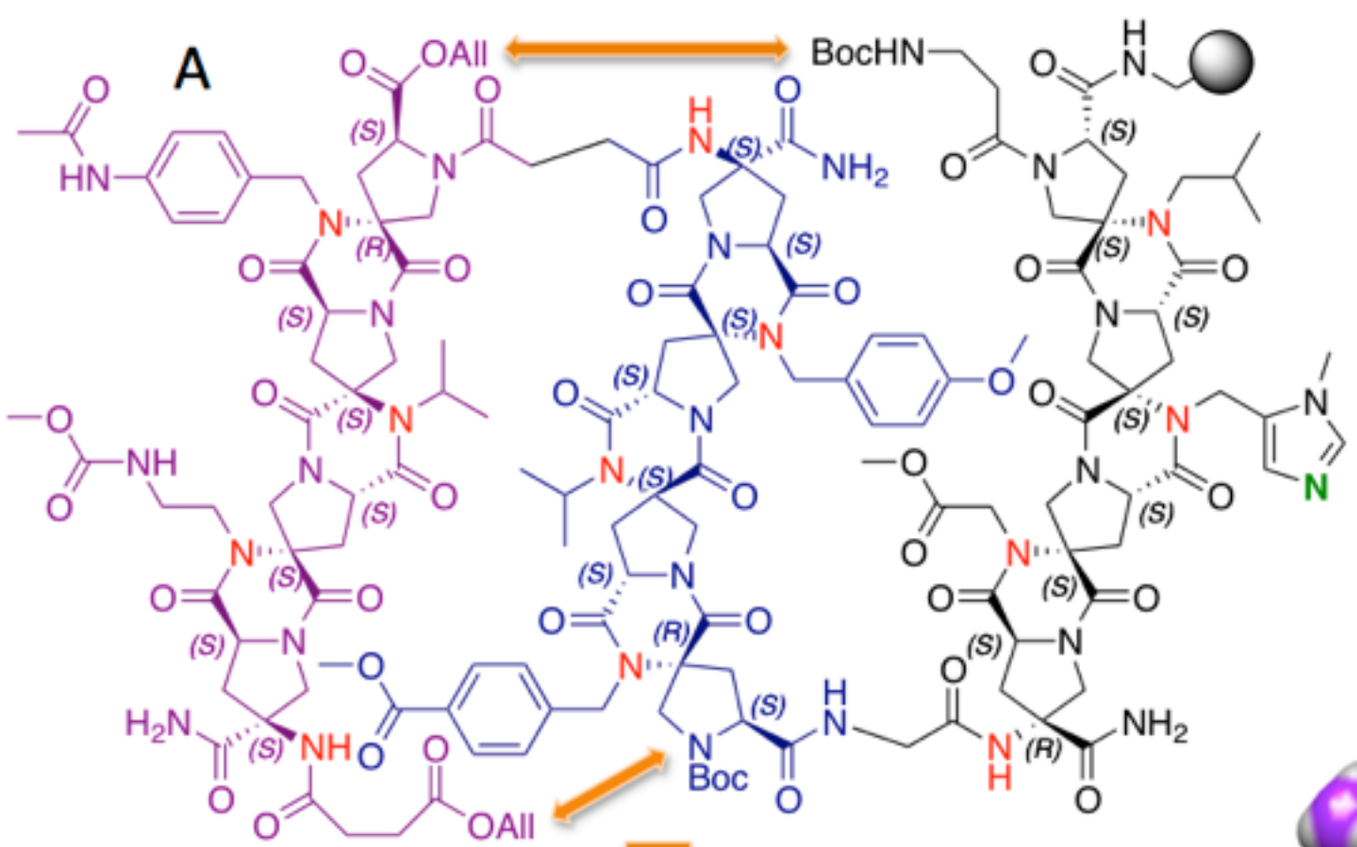
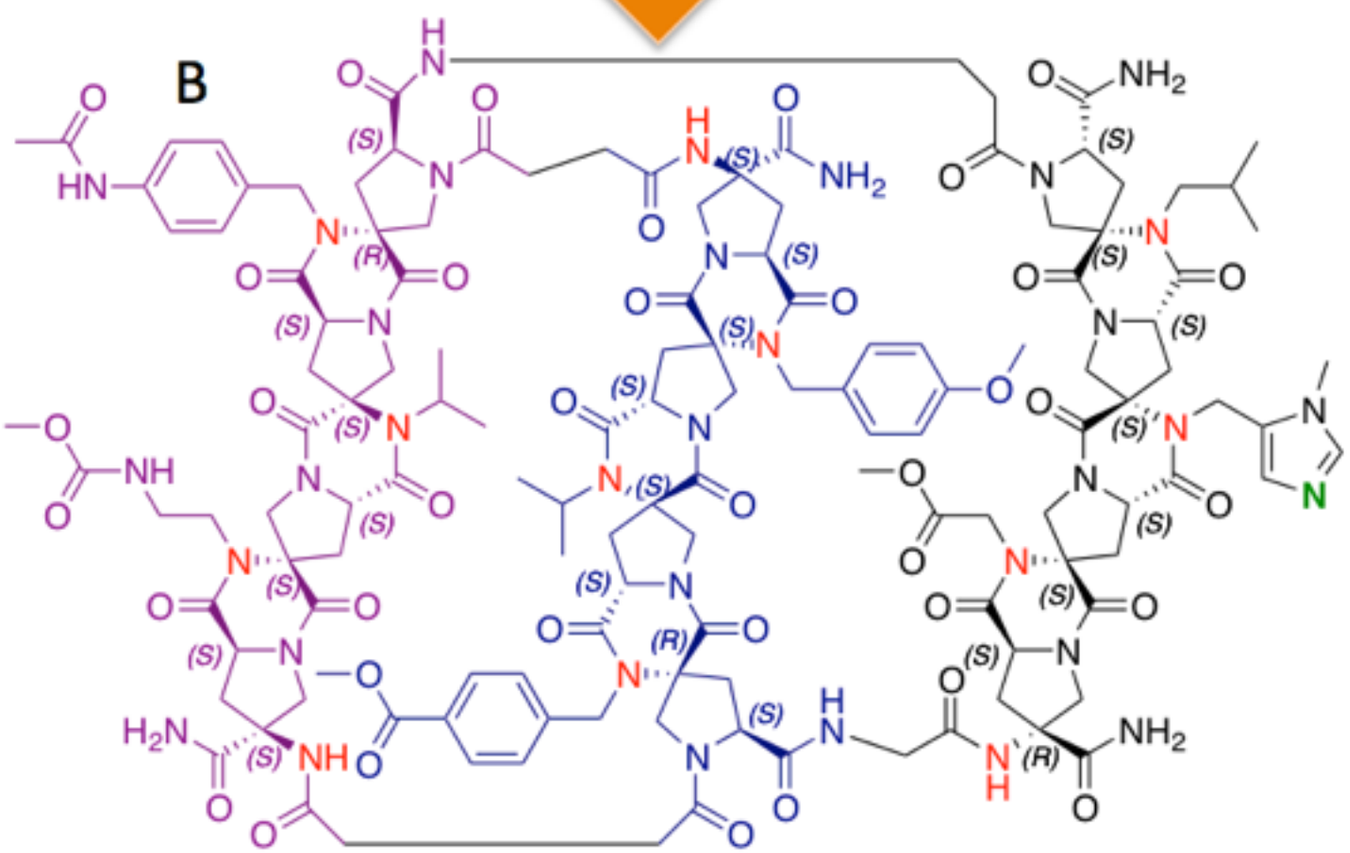


Figure 5: Overview of Catalytic Fauxtein Project

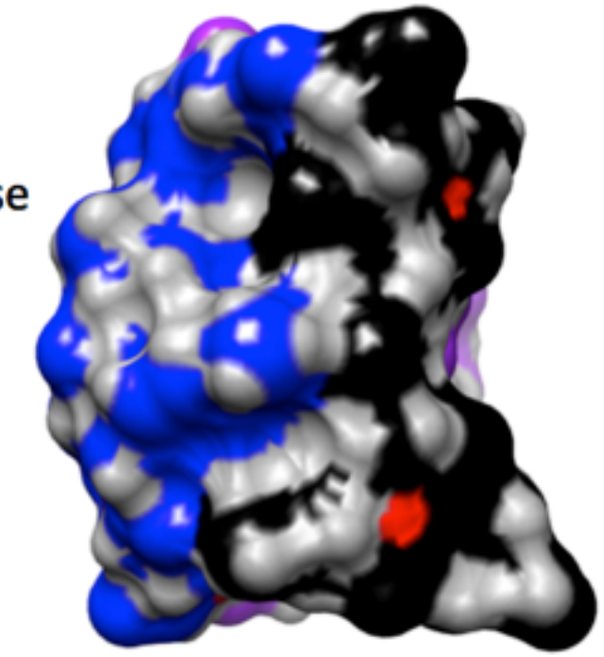


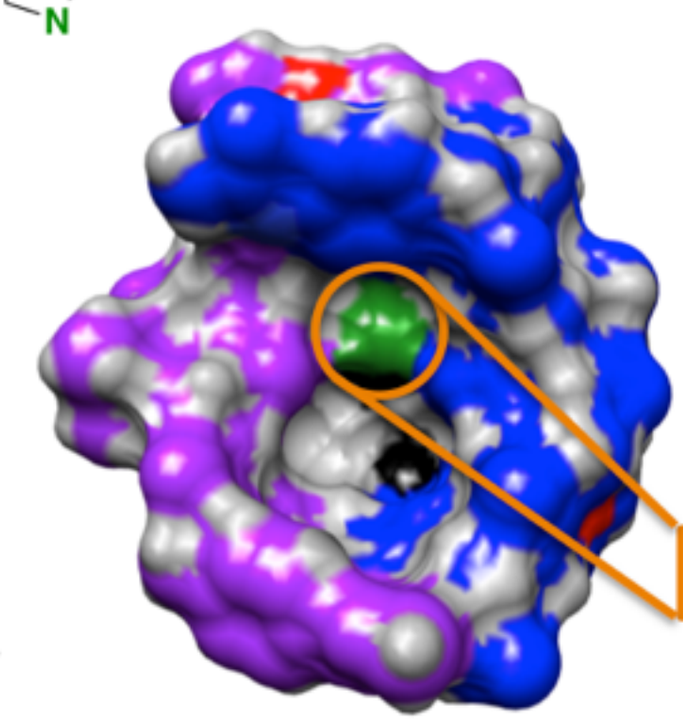
Cleavage, Deprotection & Crosslink



C

120° Counterclockwise

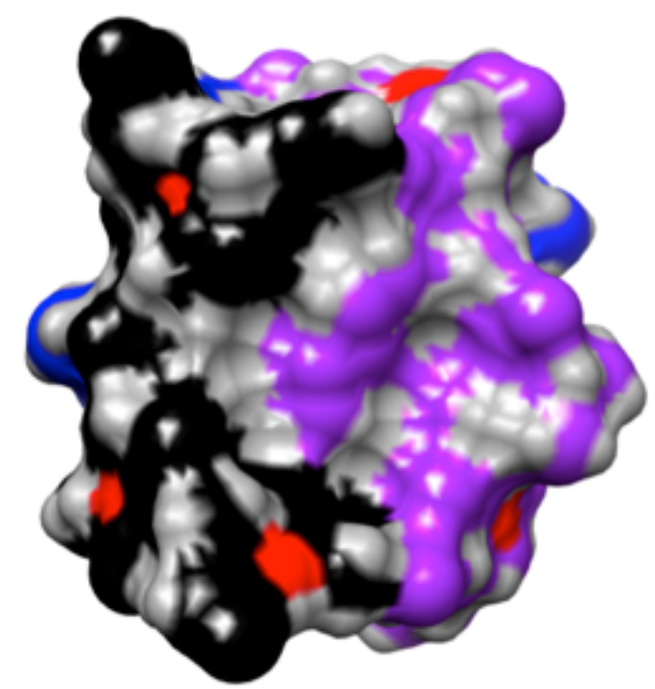


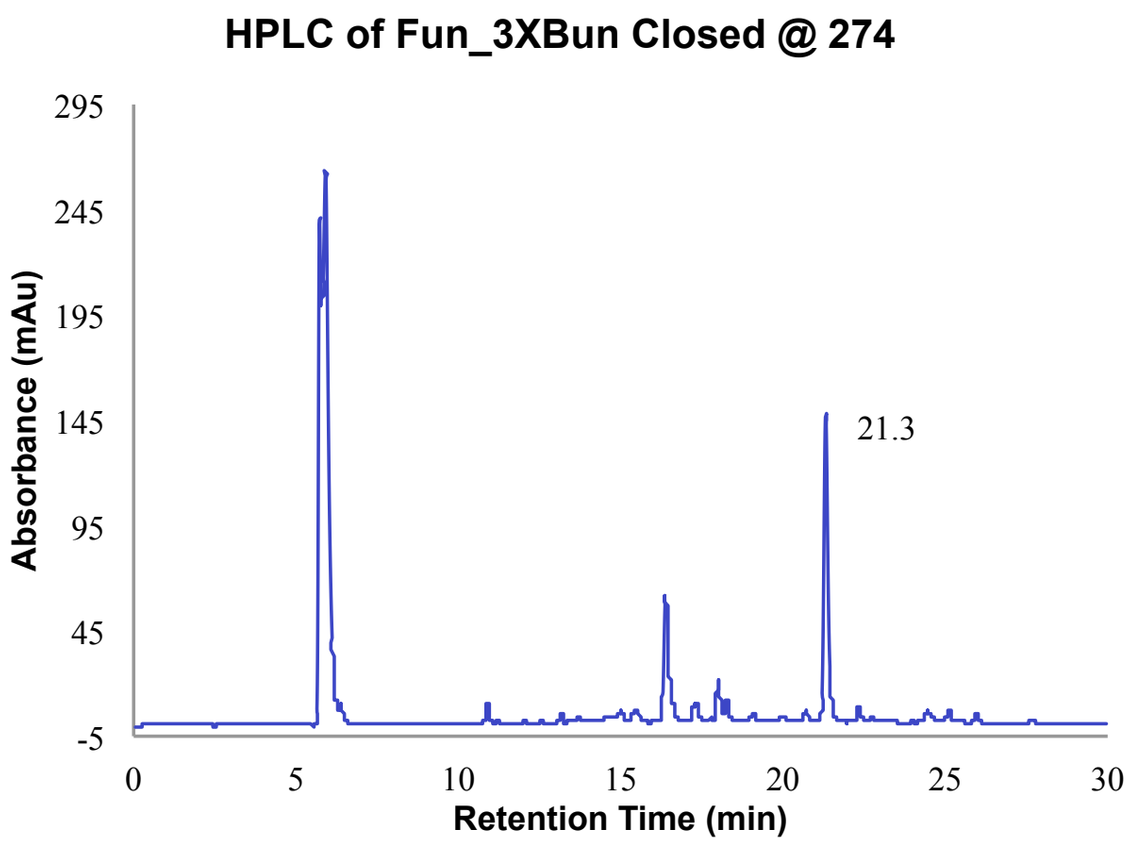


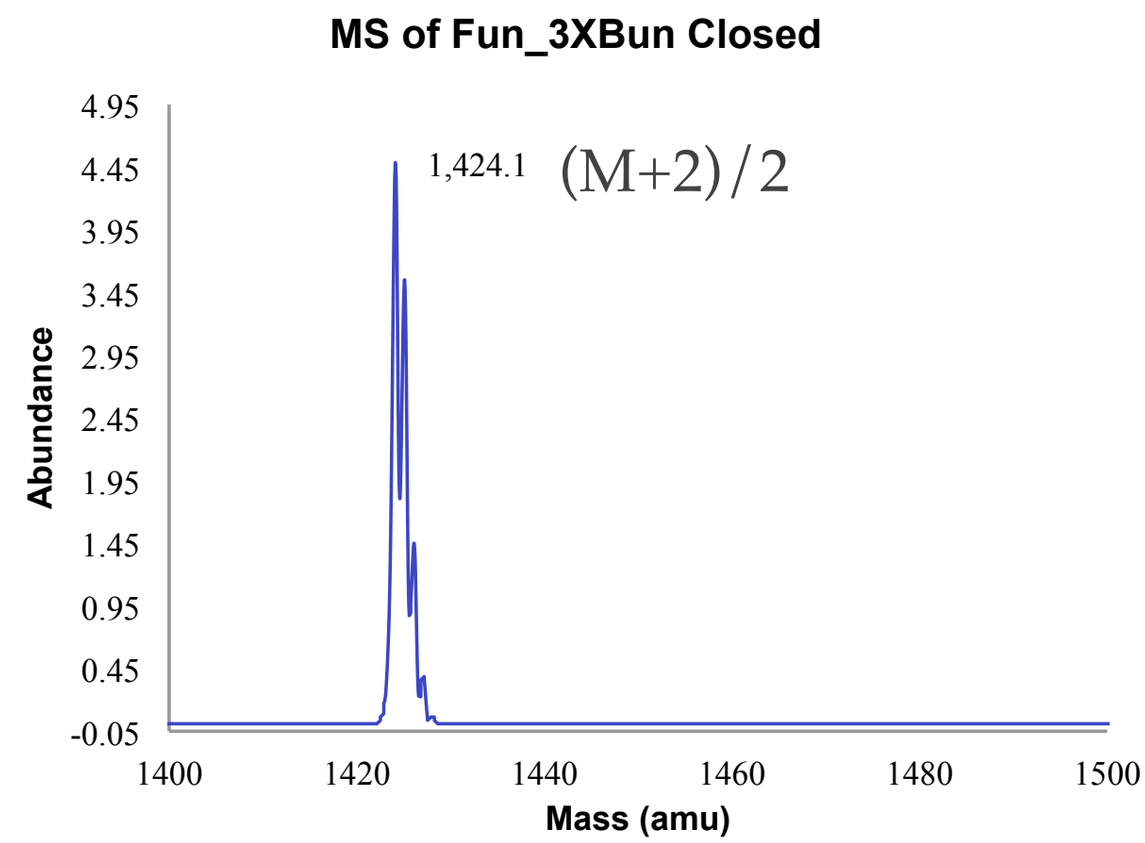
3D-Model
Hydrophobic Surface
Amber 94 Minimized

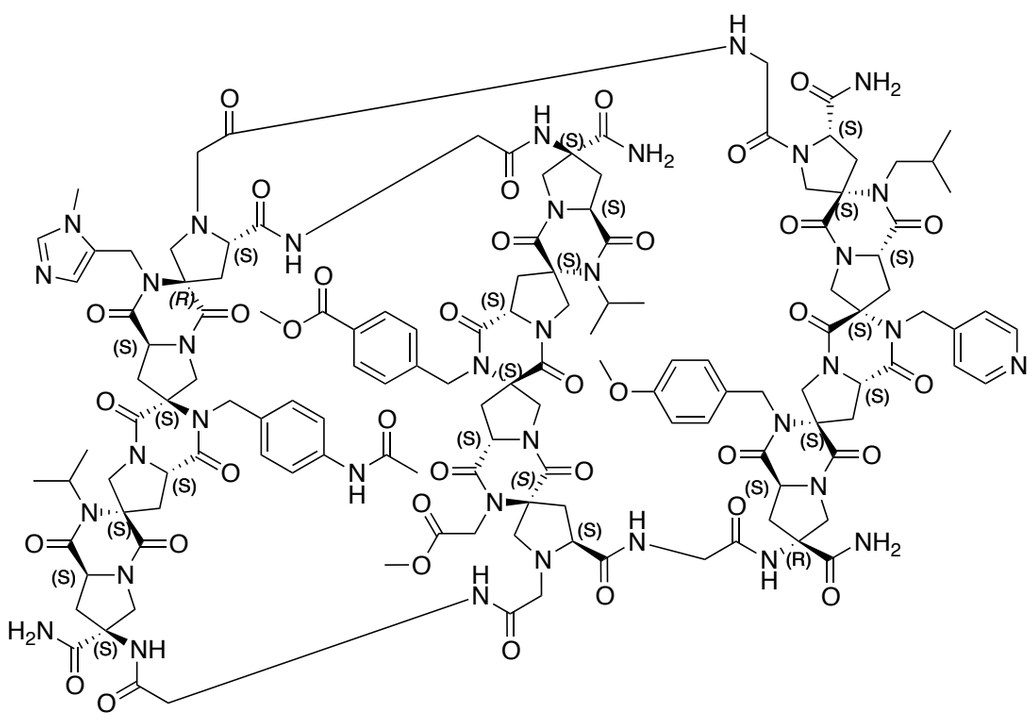
Buried Nucleophilic Catalyst

120° Clockwise

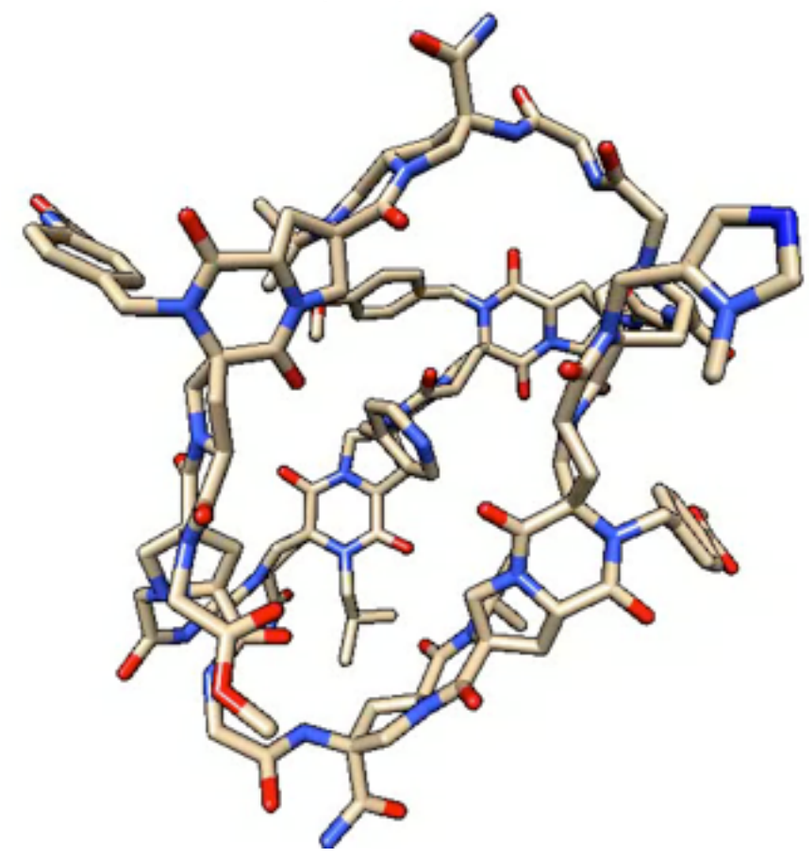






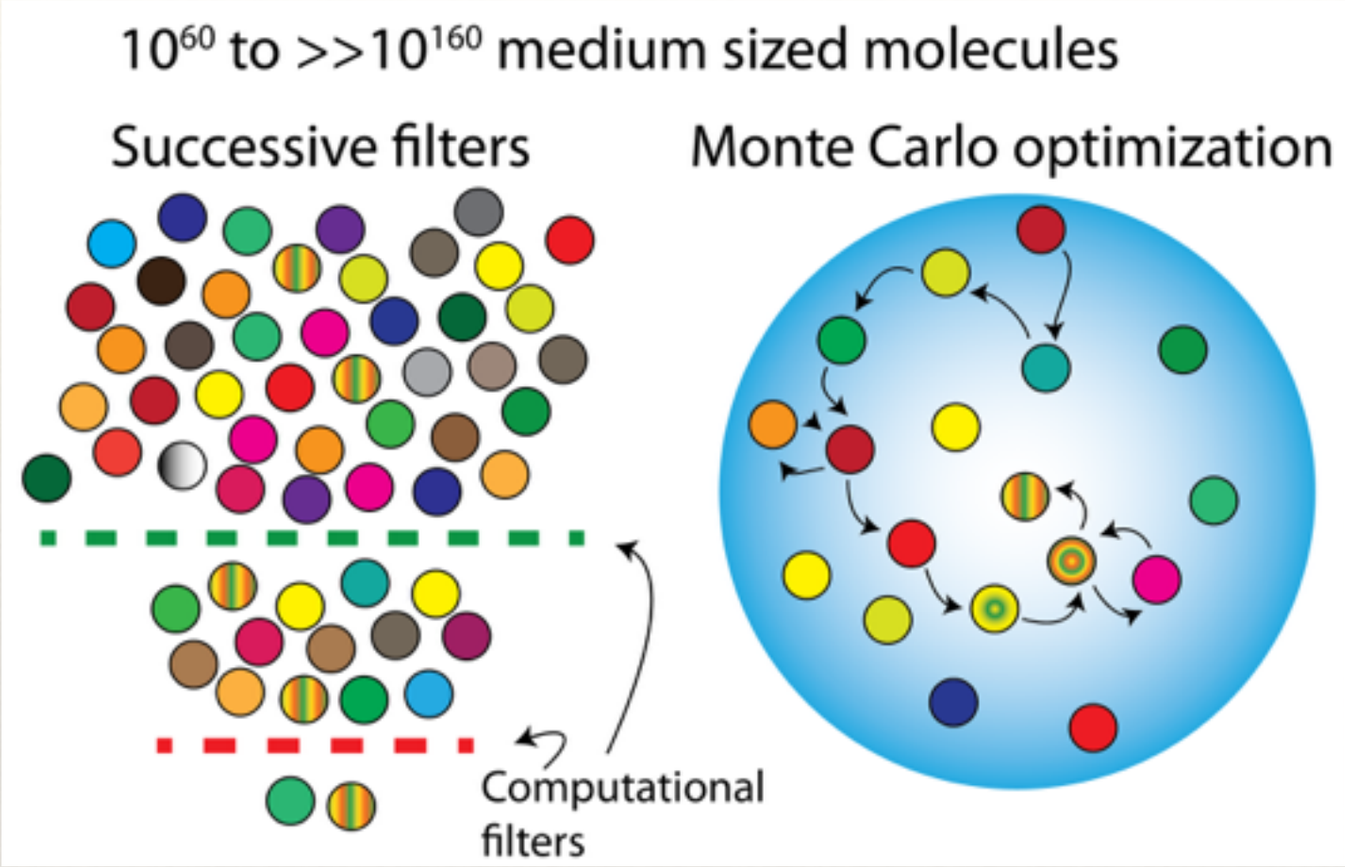


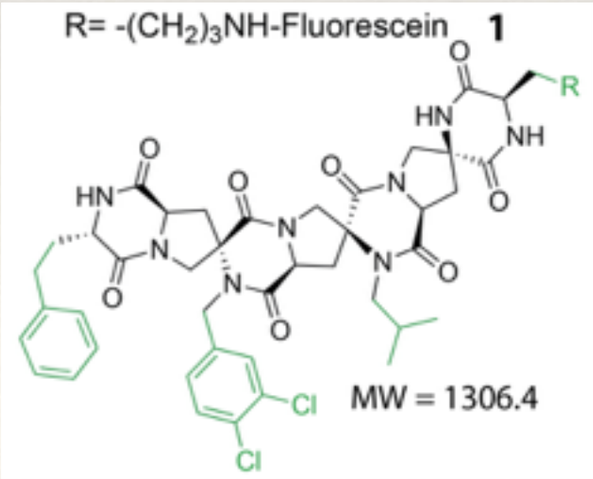
Exact Mass: 2846.15

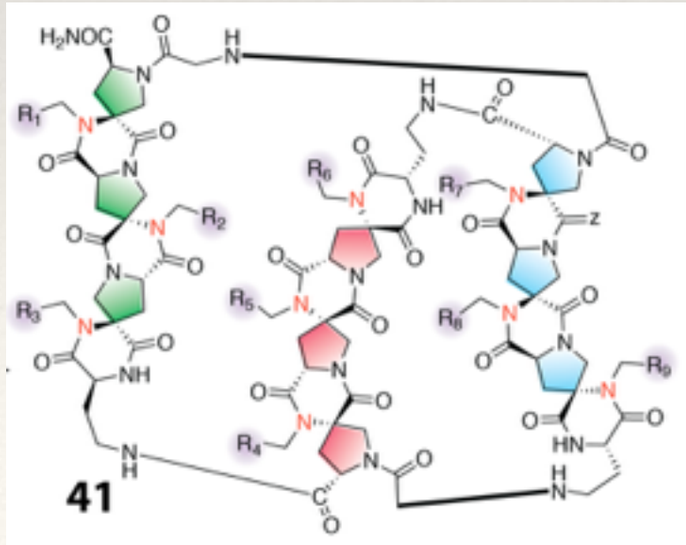


One of $2^{24} \times 50^{9} = 3.3\times10^{22}$ possible structures

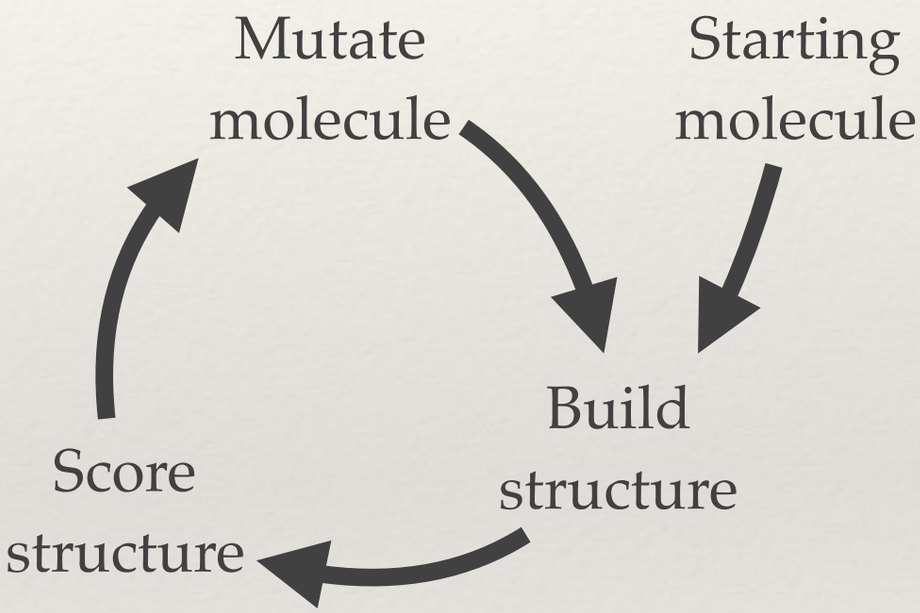
How can we design macromolecules that do things?







Monte Carlo optimization

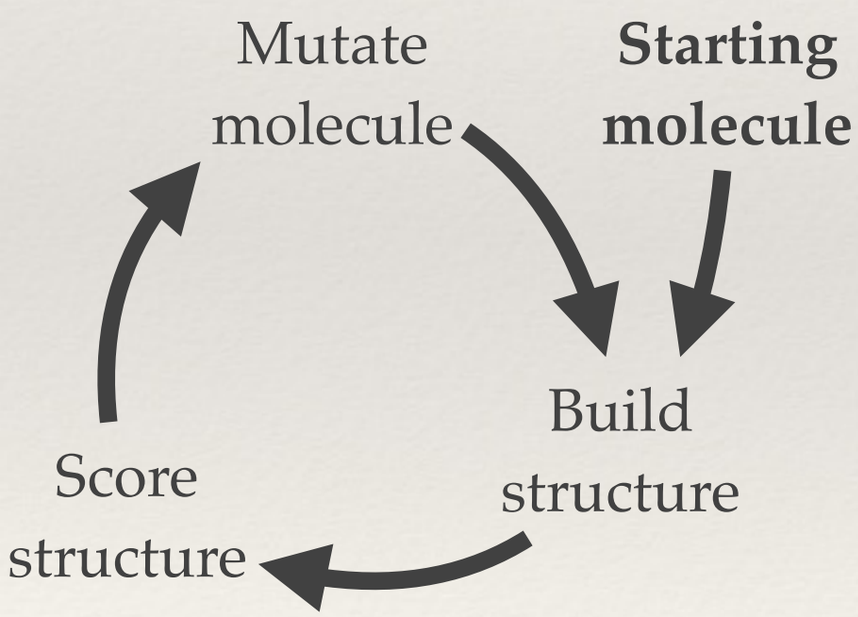


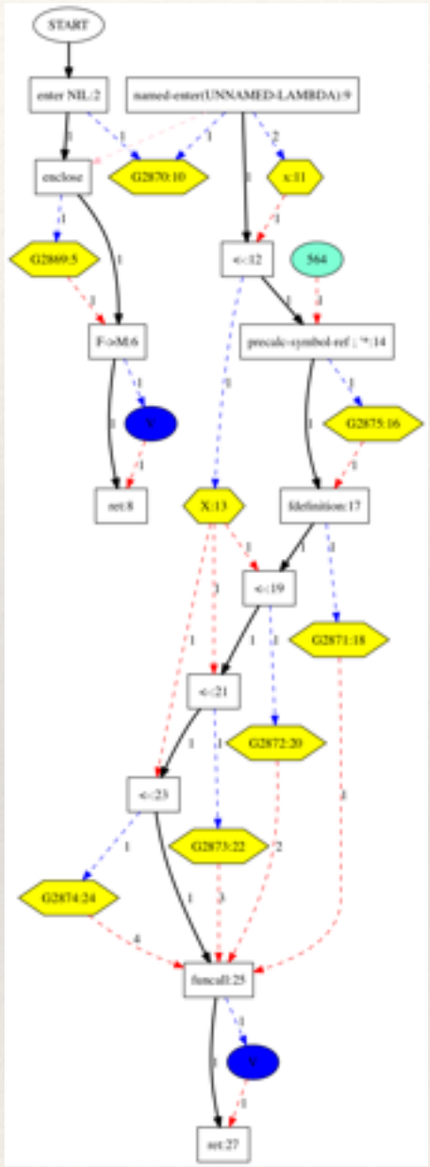
Specialized software with tightly coupled functions in the same processor

Requires a *FAST*, chemistry-aware, programming language

CANDO: fast native code for macromolecular design

Monte Carlo code





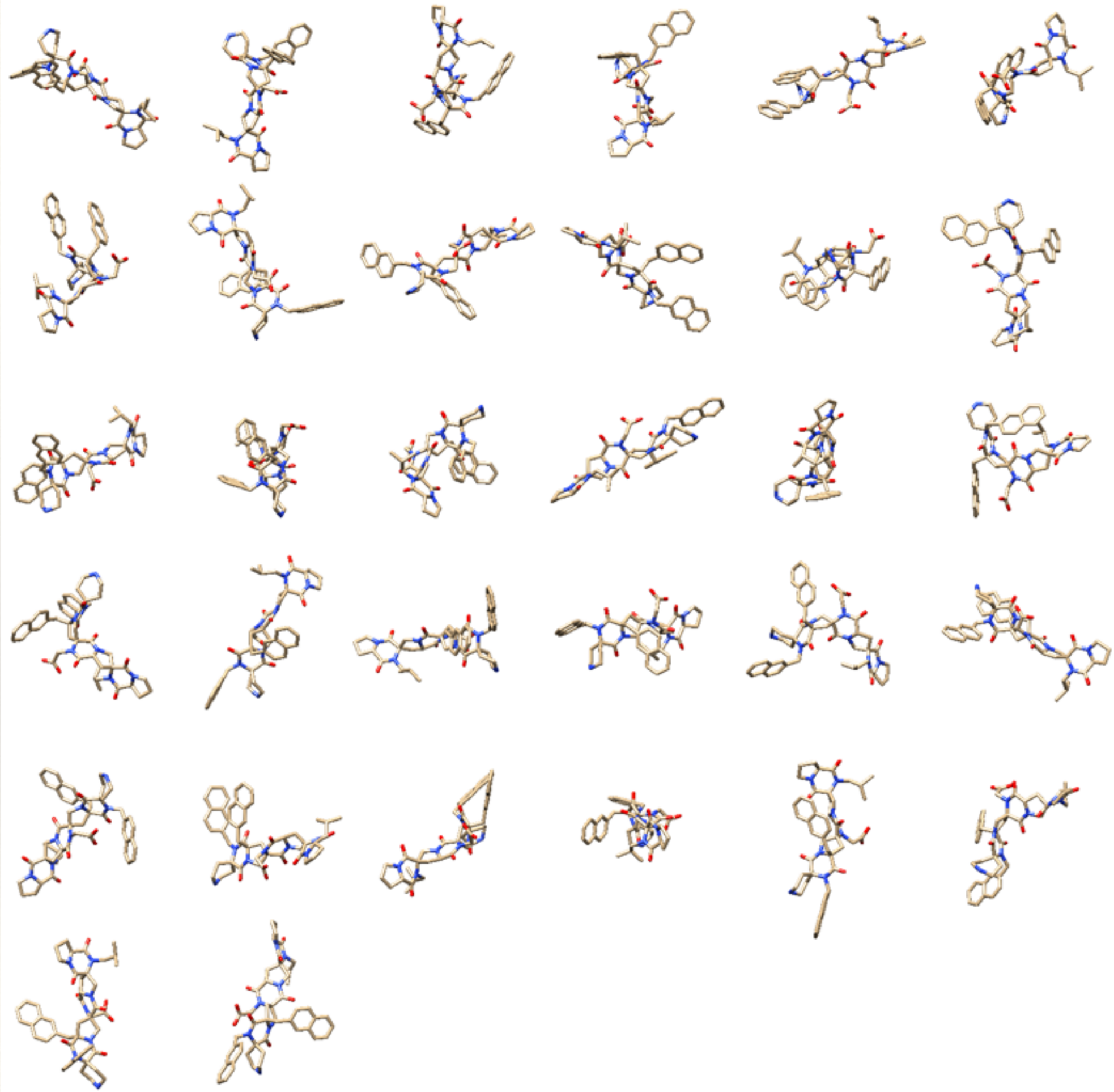
LLVM-IR (Apple, Google)

Fast native code runs on 100,000's CPUs - currently 1/4 speed of C

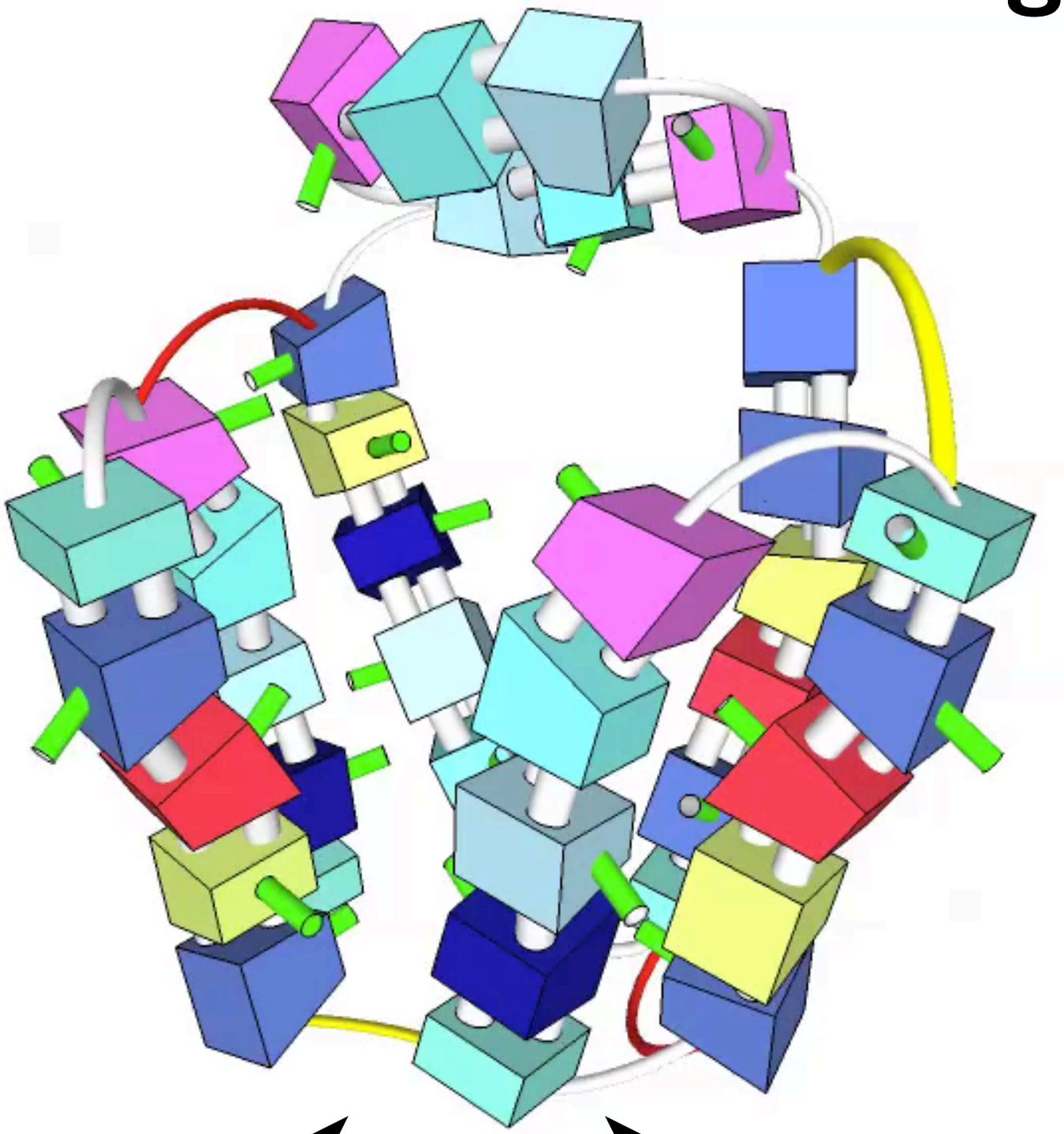
```
;;;
;;; Build starting geometry for all 32 stereoisomers
;;;
(dotimes (i 32)
  (set-stereoisomer *stereocenters* i :show t)
  (build-good-geometry-from-random *agg* *ff*)
  (save-mol2 *agg*
             (indexed-pathname #P"fuzi/run.mol2" i)))

(array-stereoisomers #P"fuzi/run.mol2" 32)
```

```
;;; 32 stereoisomers are written into fuzi/run000.mol2
;;;       … fuzi/run031.mol2
```

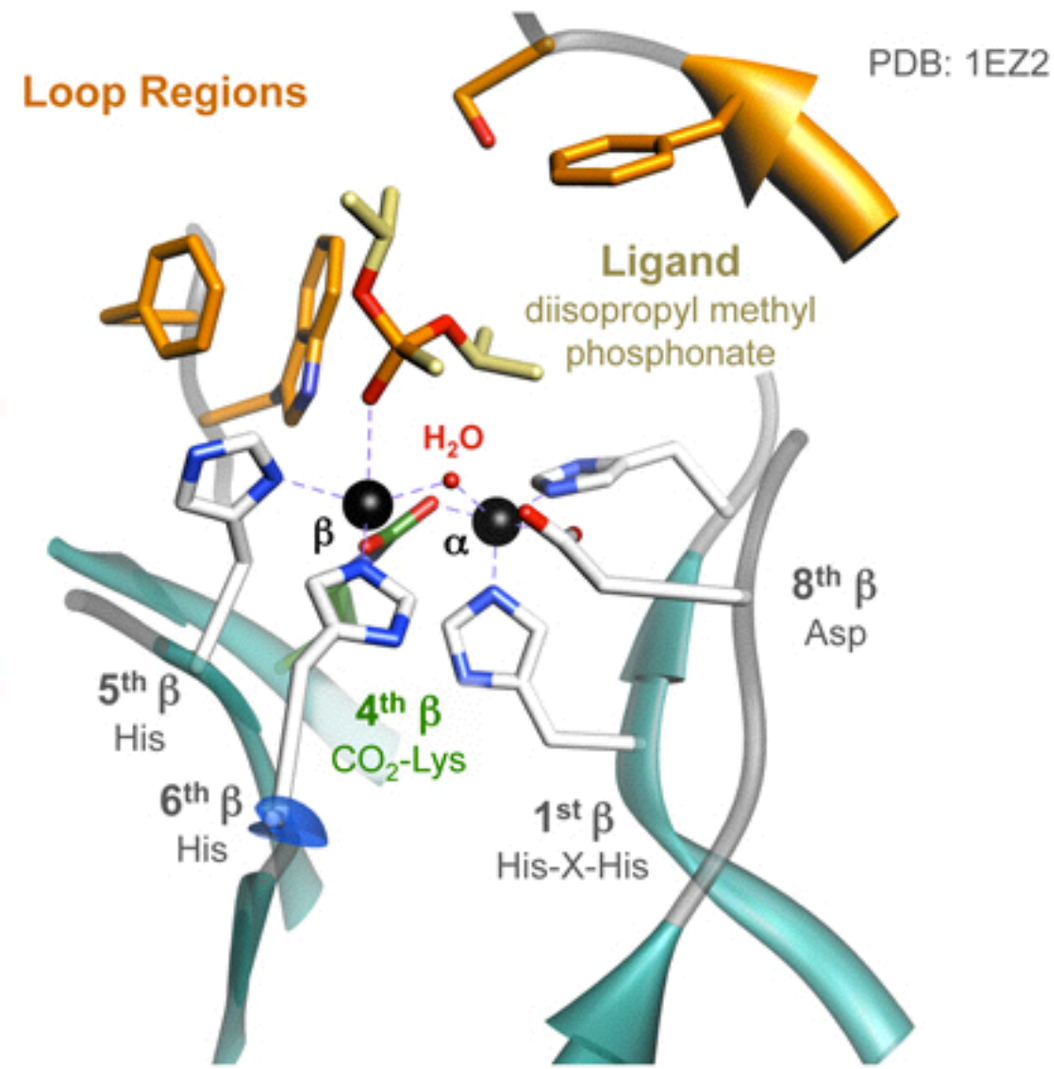


“Molecular Metaprogramming” software that designs molecules



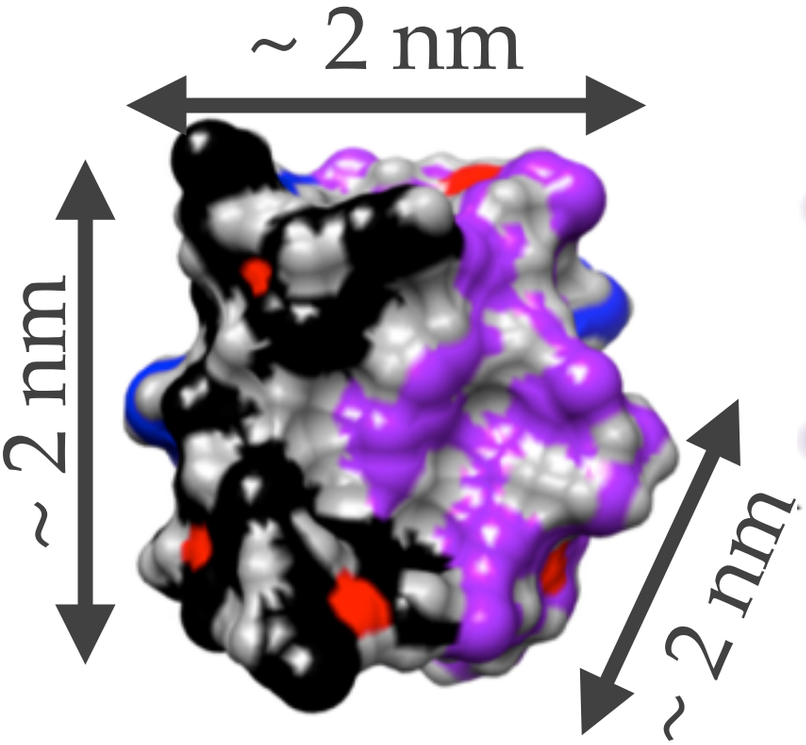
~ 3 nanometers

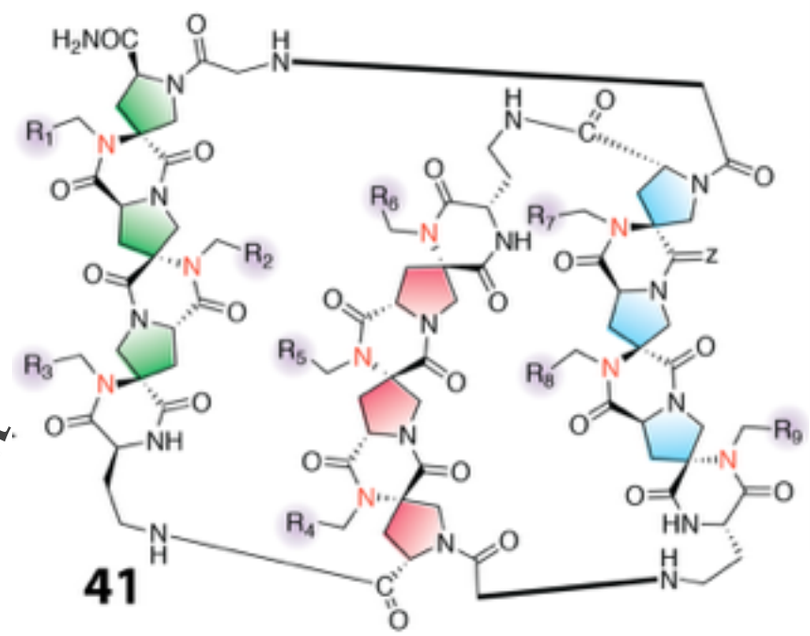
Organophosphate hydrolase

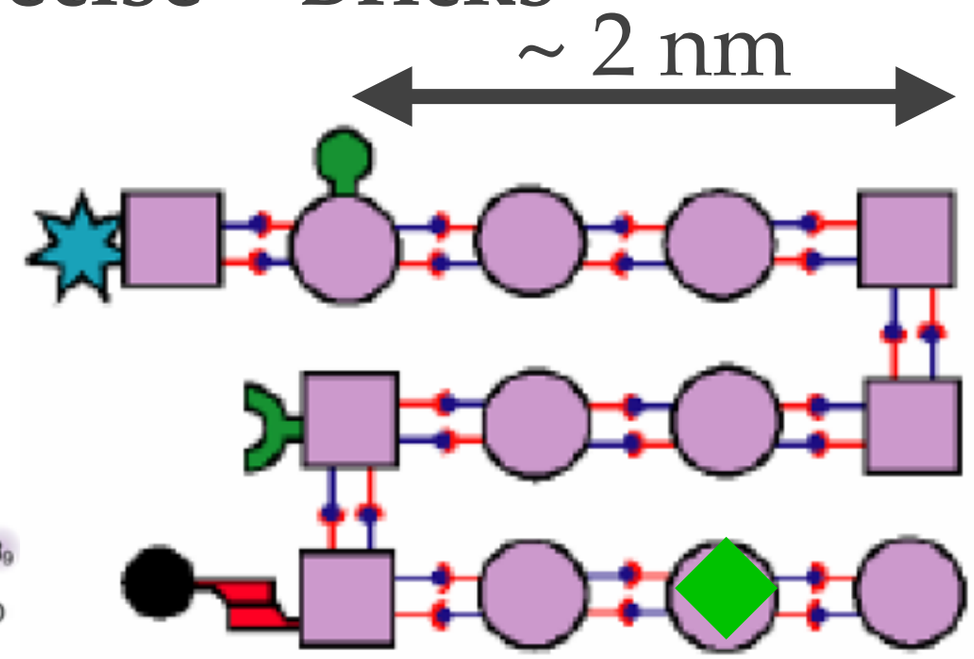


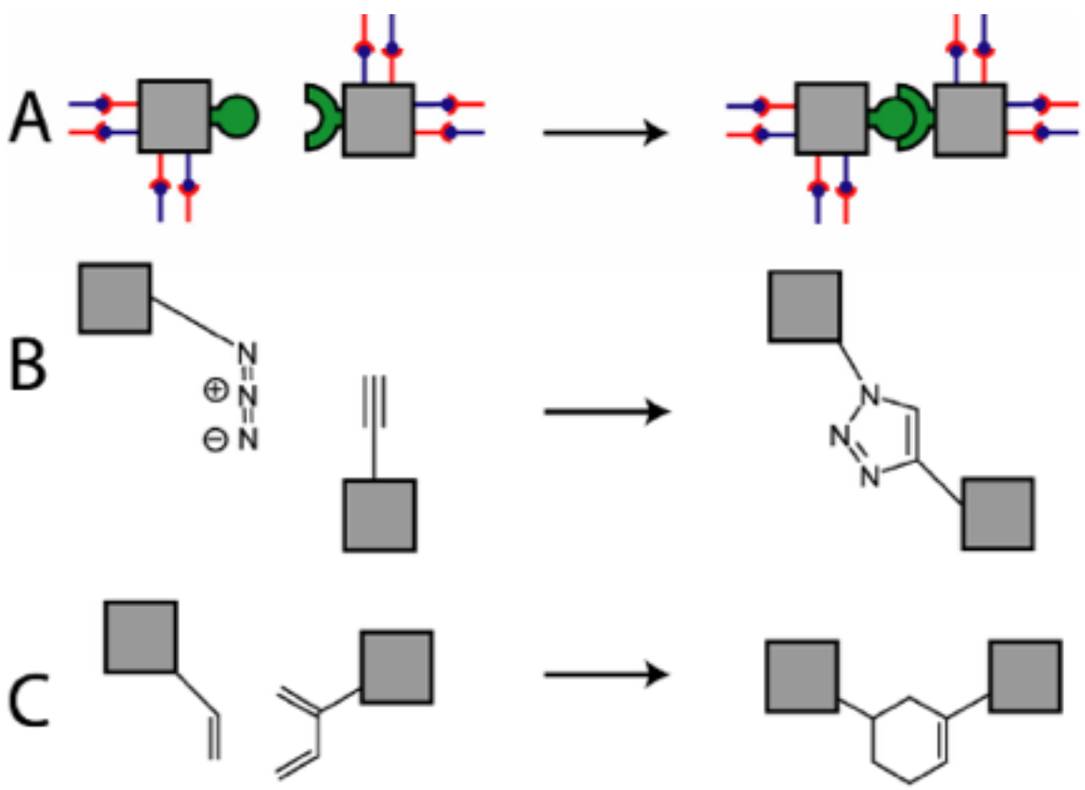
Wong, K. and Gao, J.
Biochemistry **2007**, *46*, 13352-13369.

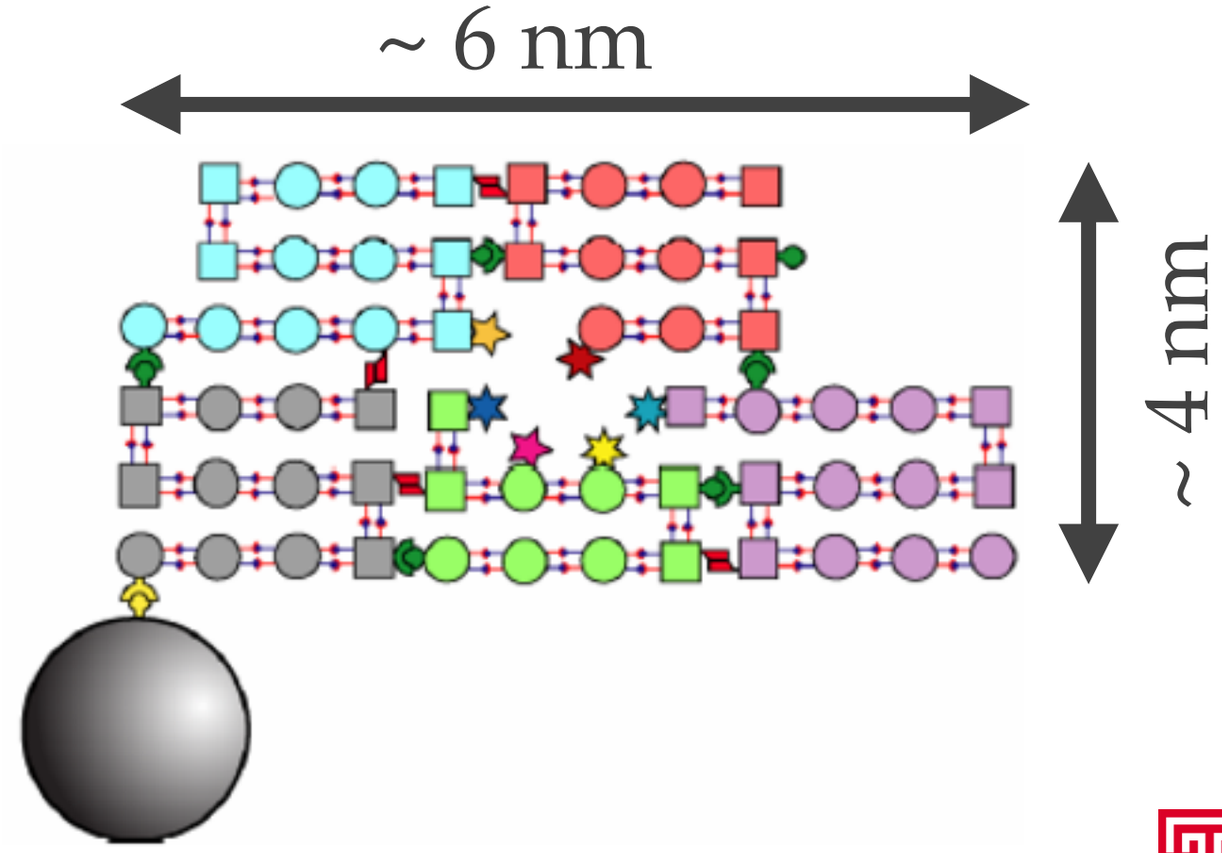
Functionalized Multi-spiroligomers are programmable, atomically precise "Bricks"



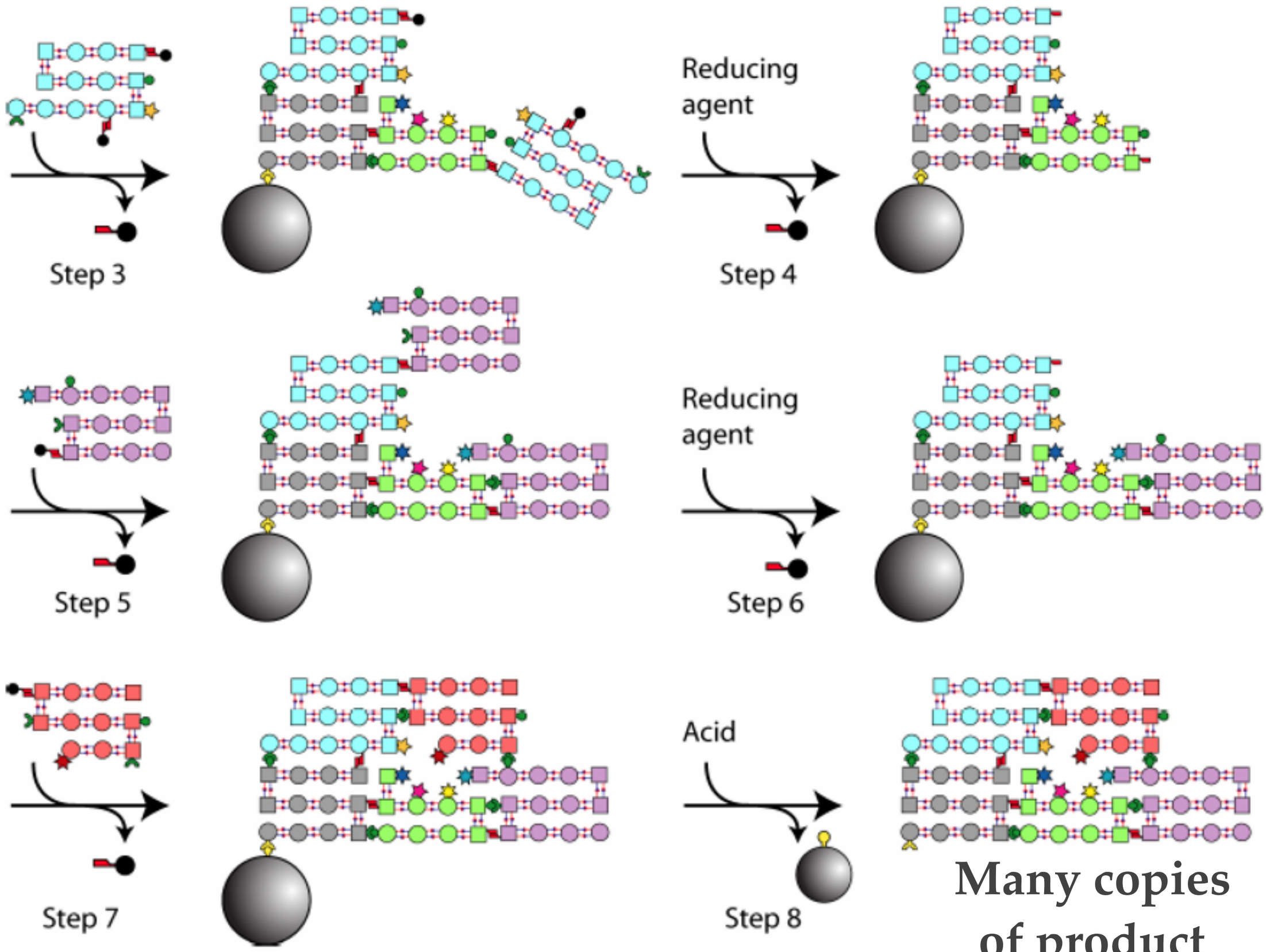




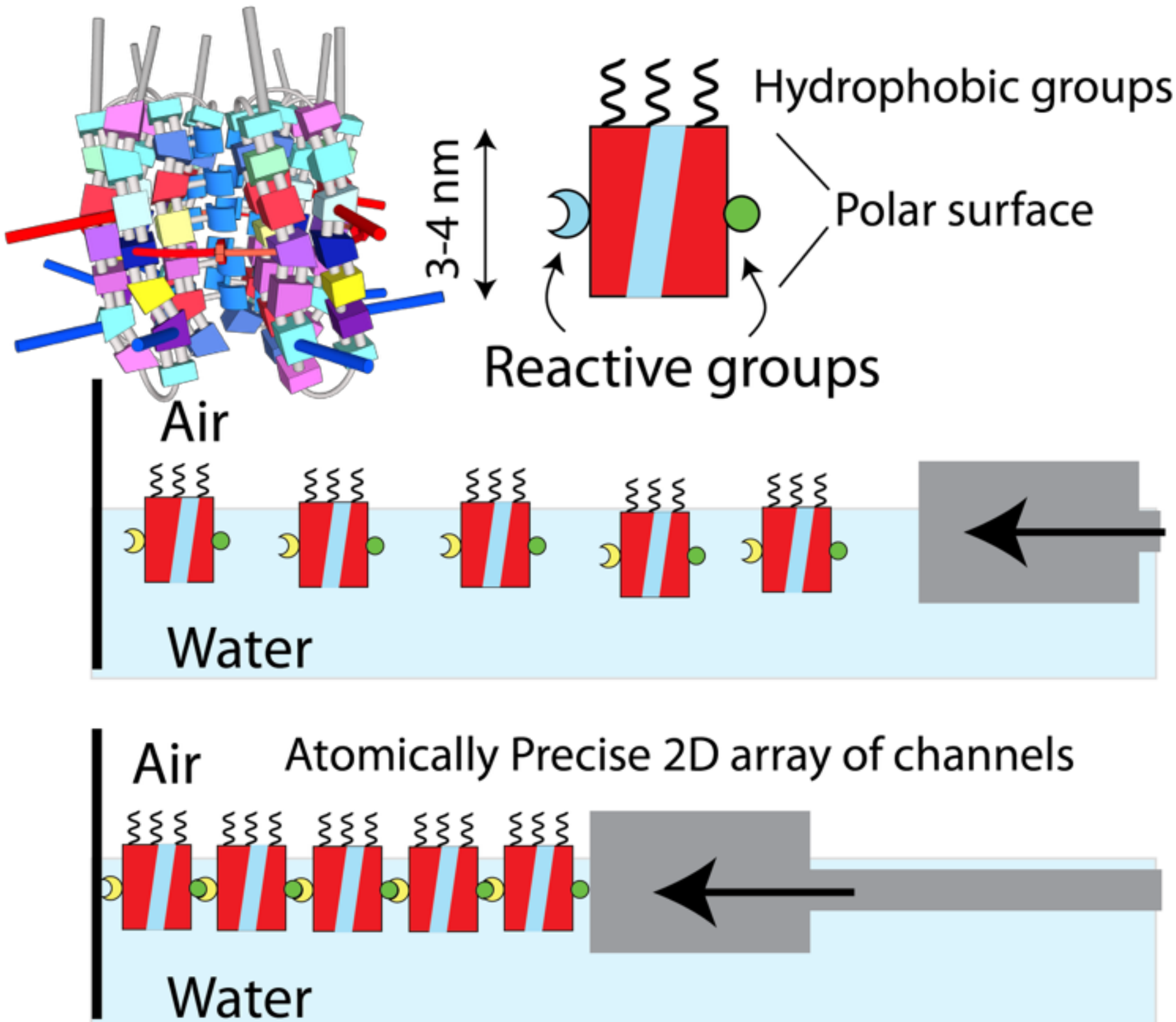




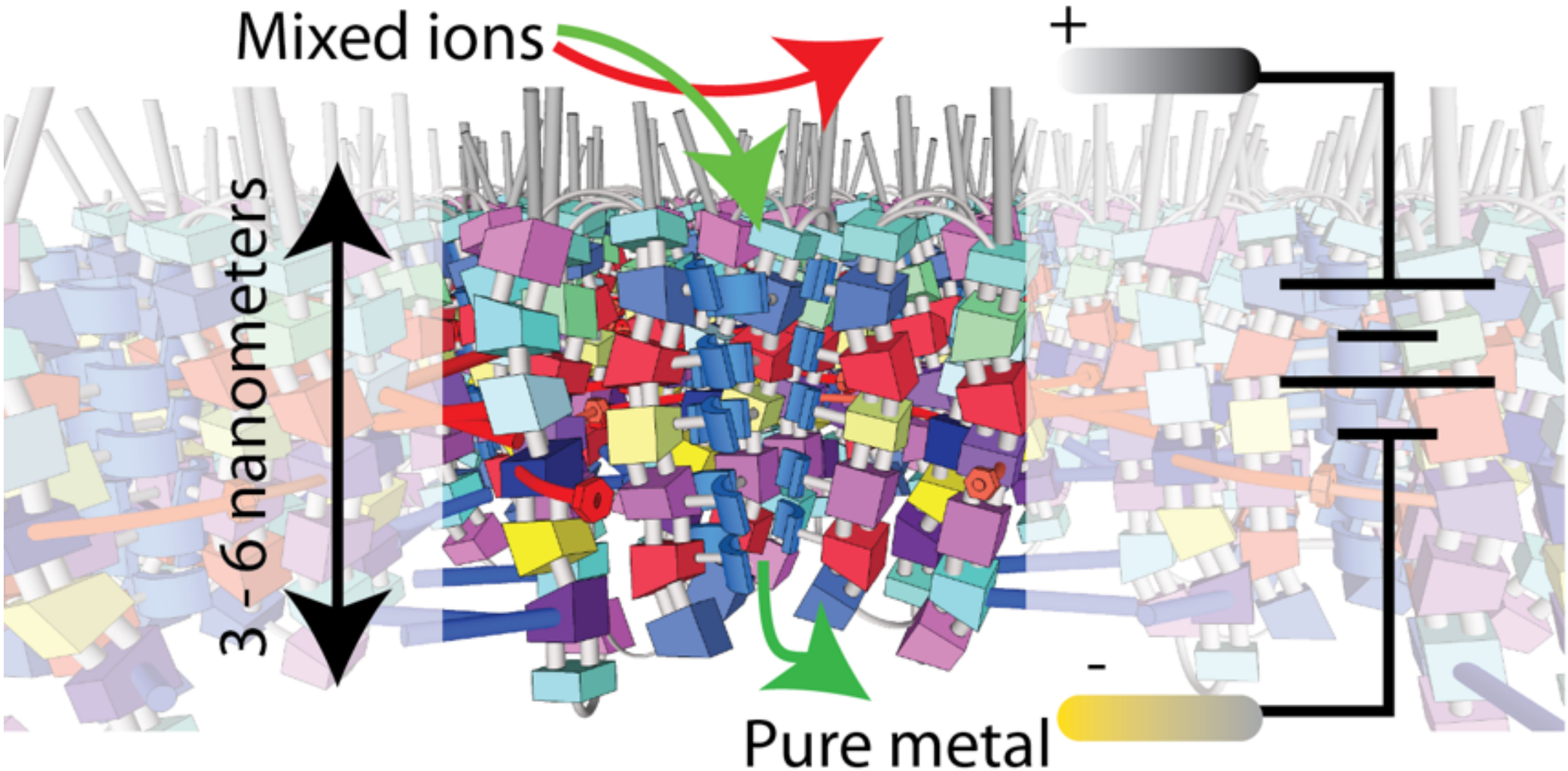
(1) Reversible Covalent "Dock and Lock"

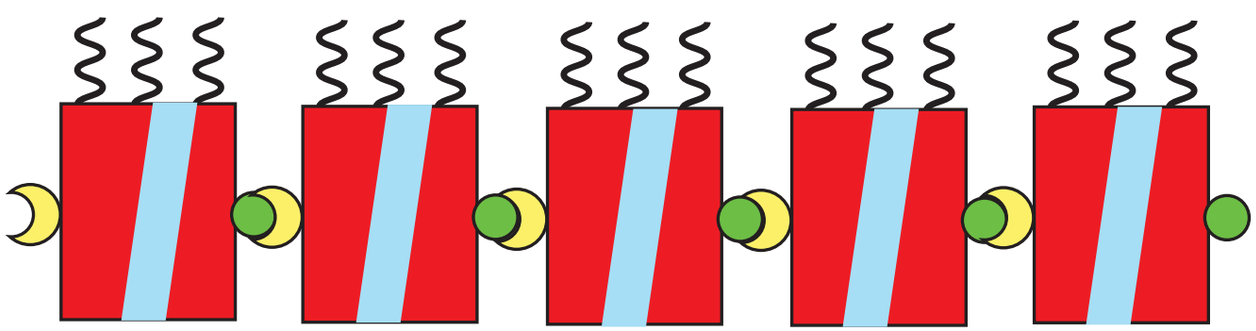


(2) LB assembly of atomically precise 2D arrays

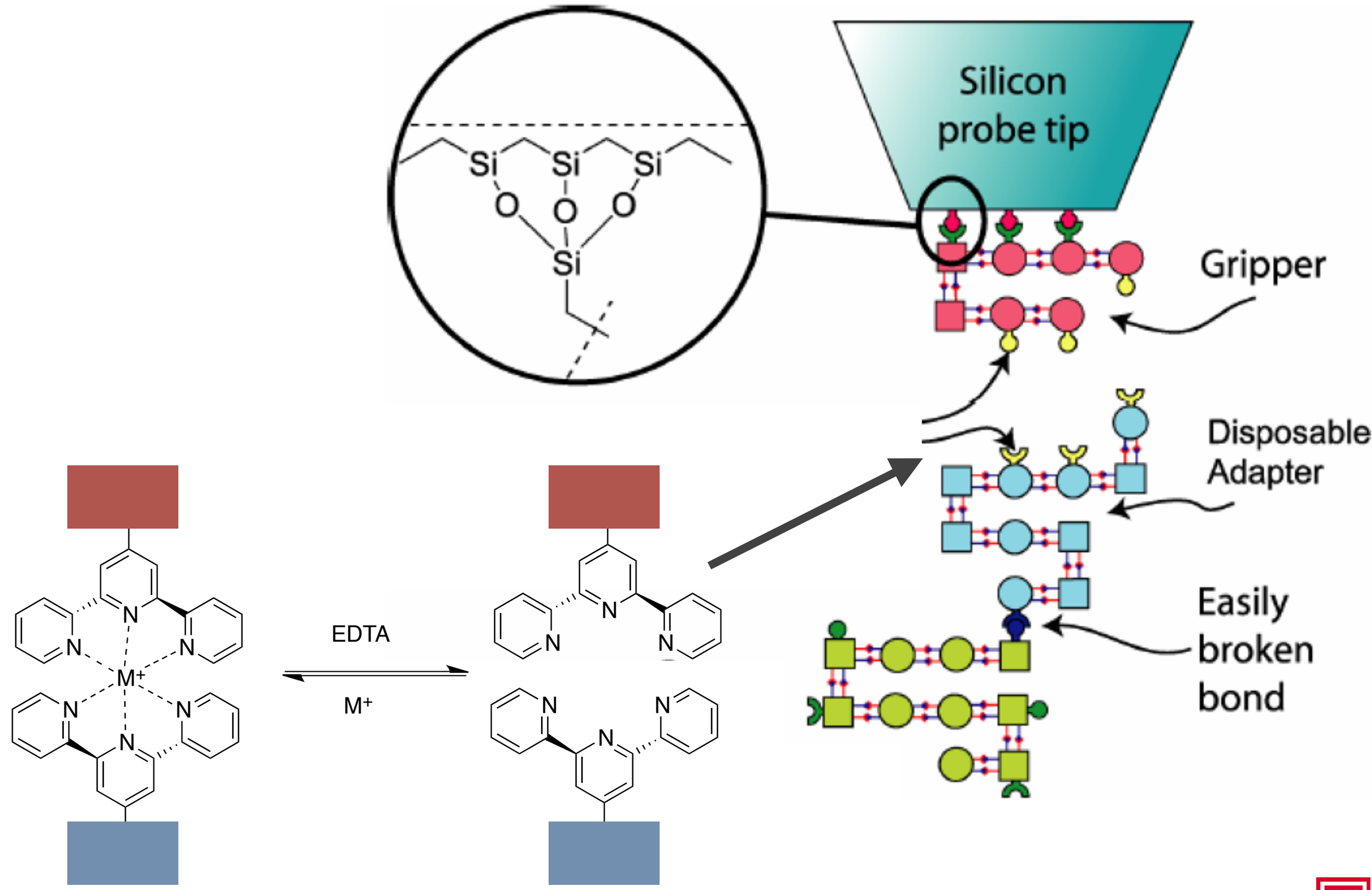


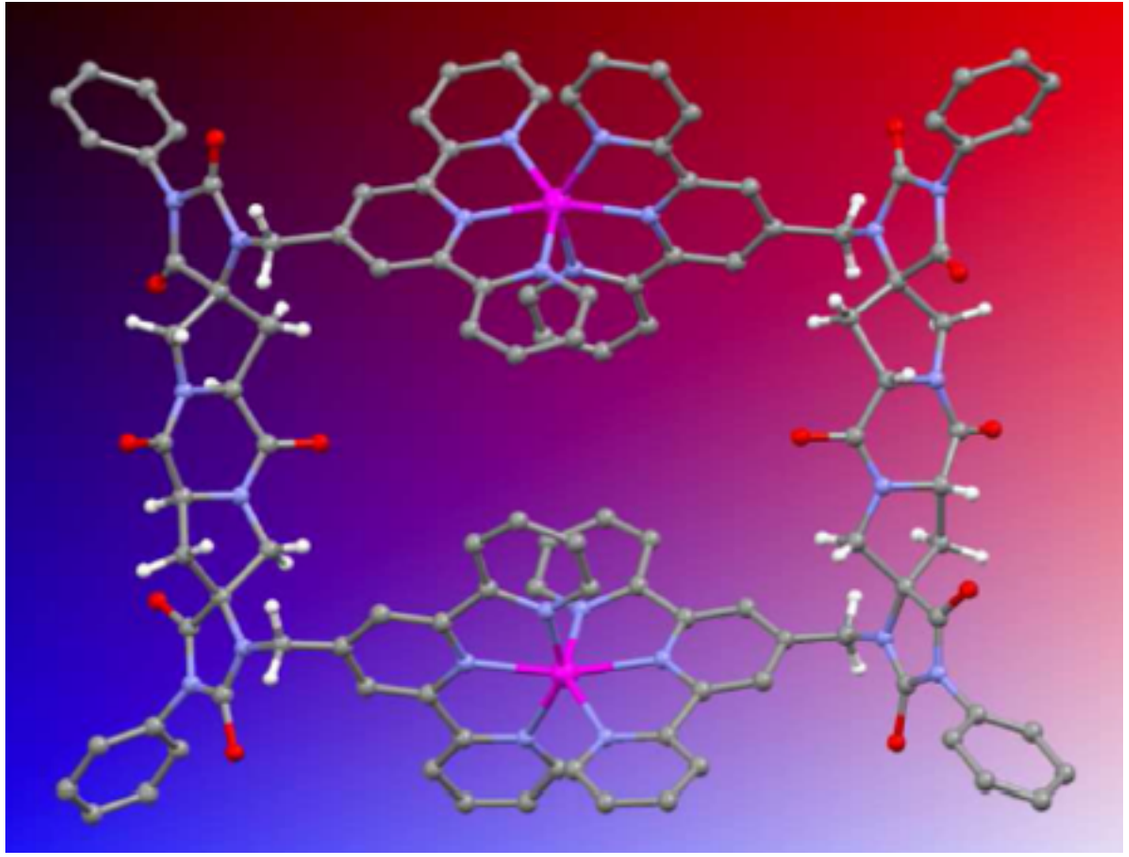
Selective ion and water channels

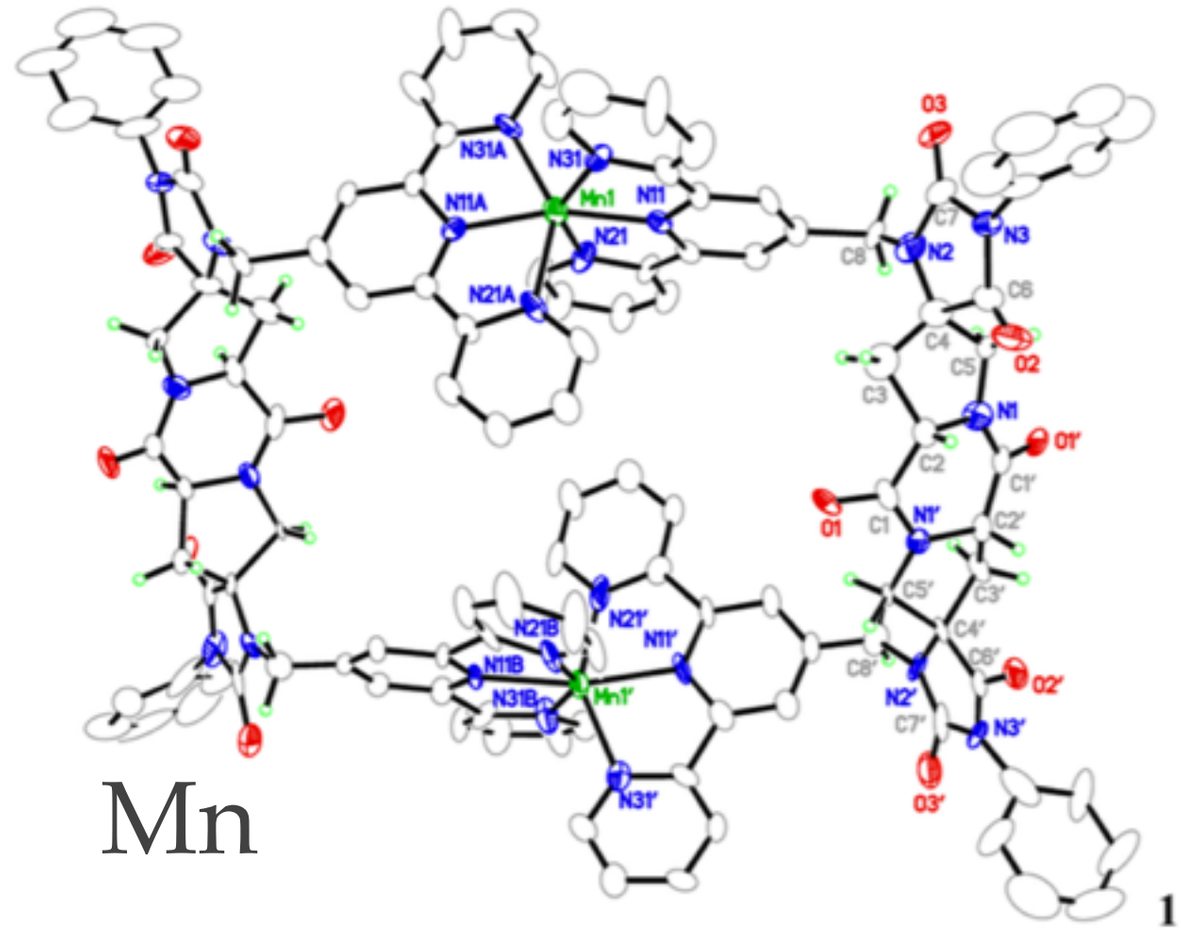


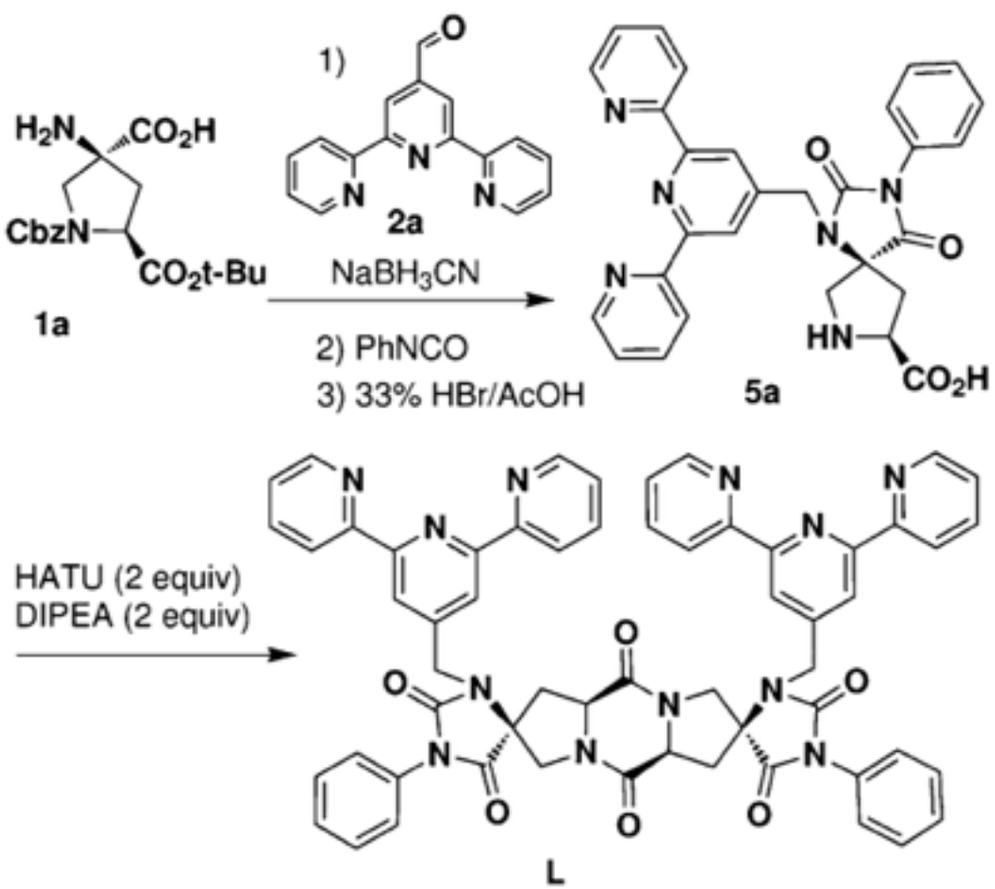


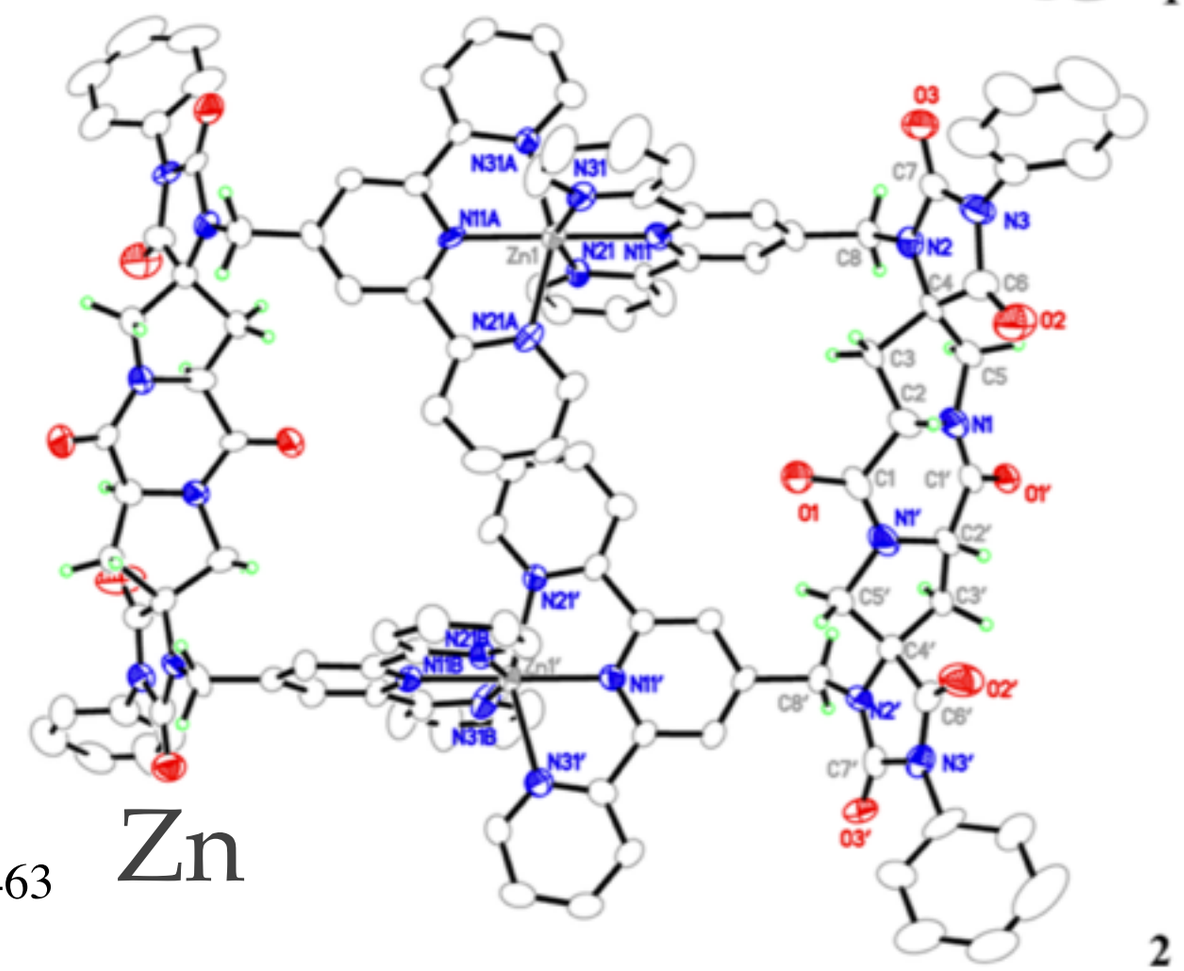
(3) 3D Printing of Atomically Precise Nanostructures





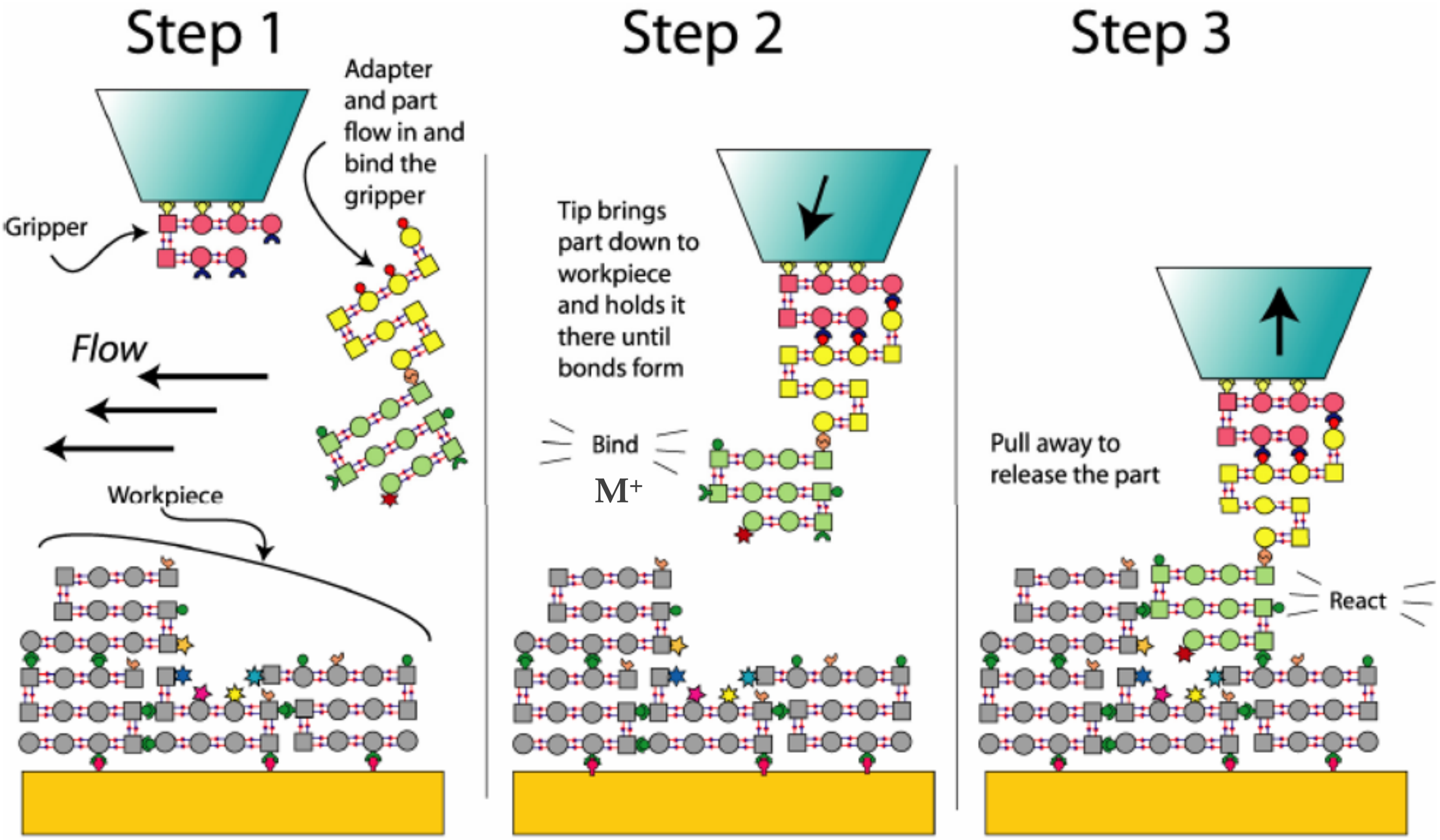




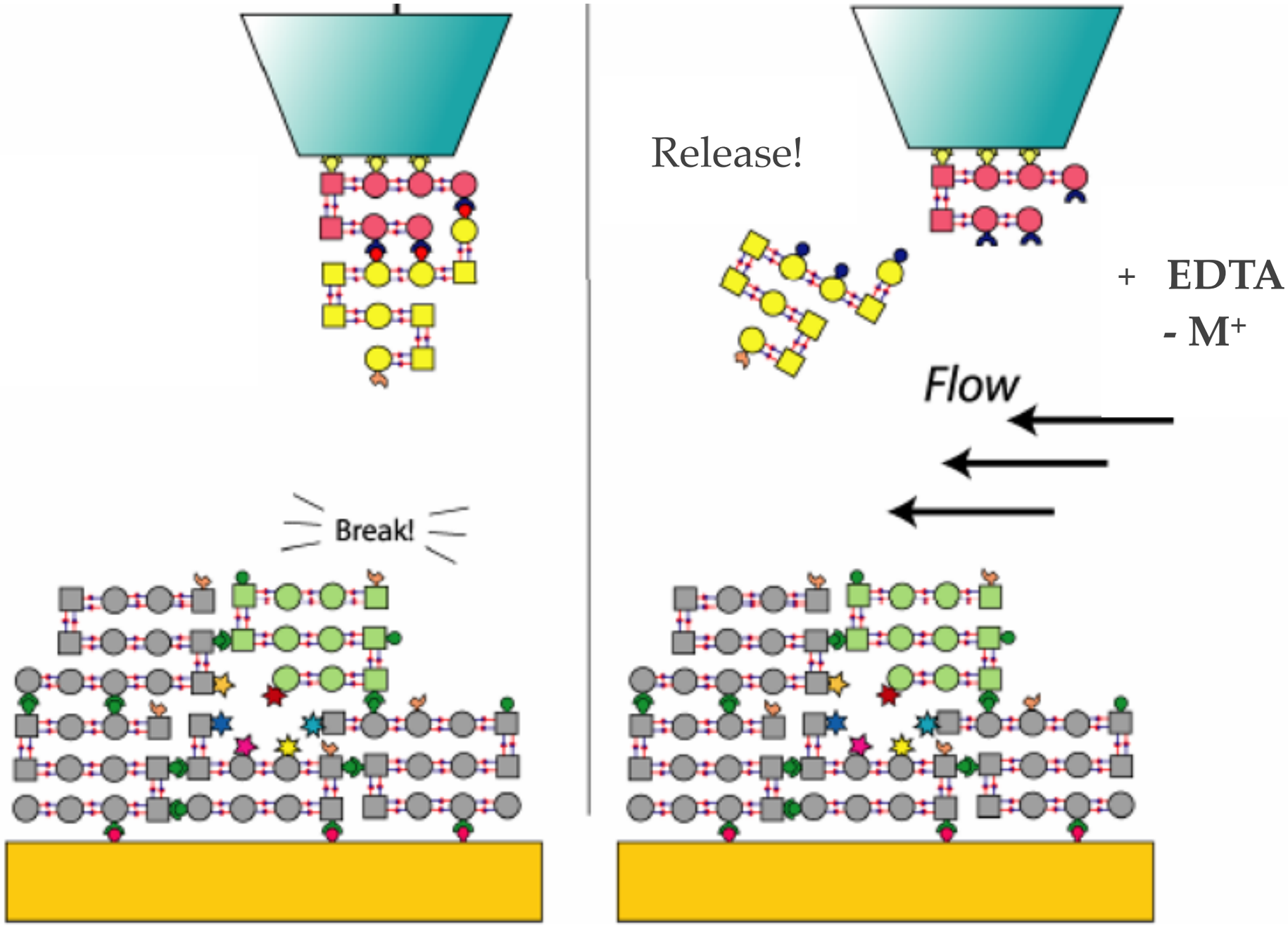


dx.doi.org/10.1021/ic4003498 | Inorg. Chem. 2013, 52, 6457–6463

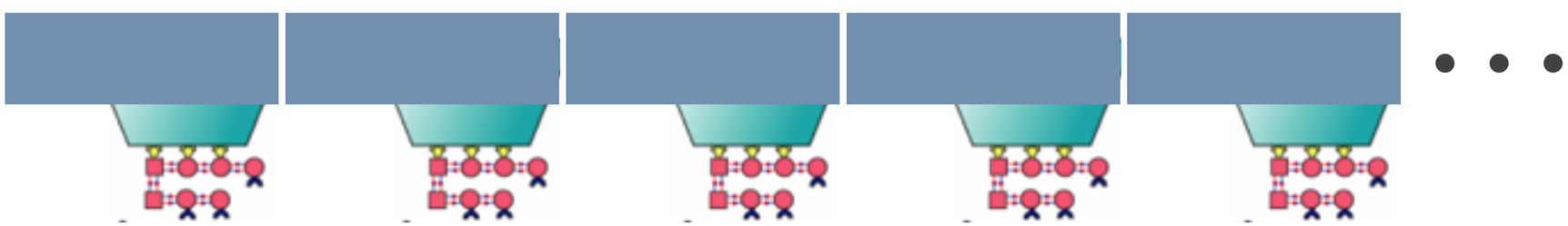
3D Printing of Atomically Precise Nanostructures



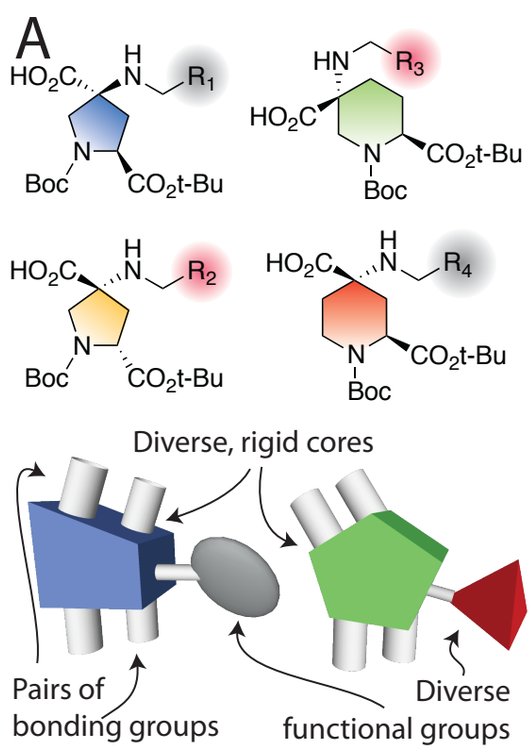
3D Printing of Atomically Precise Nanostructures

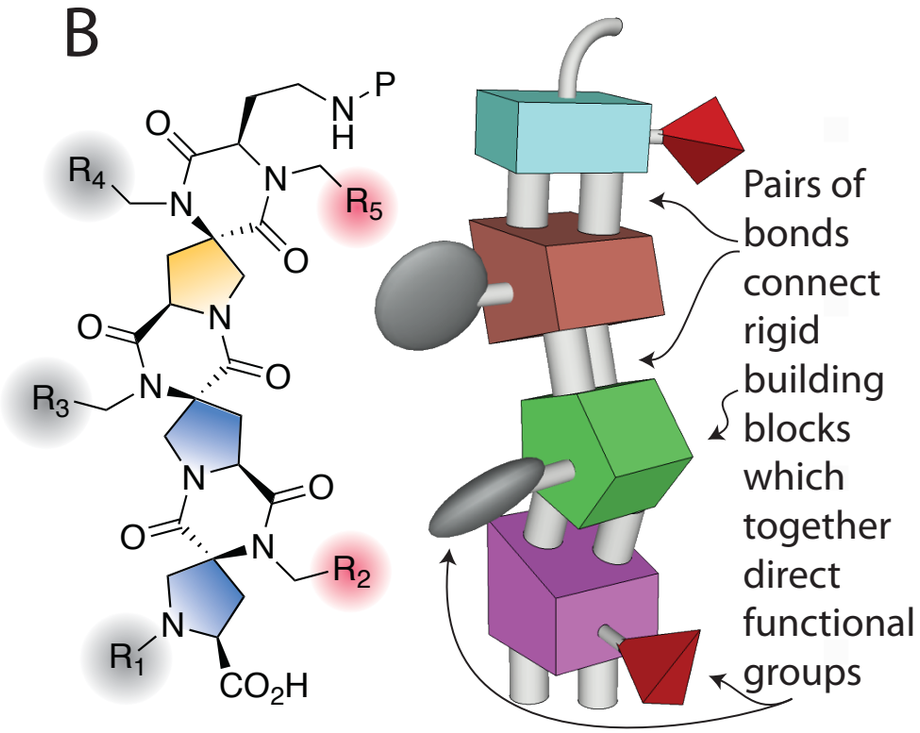


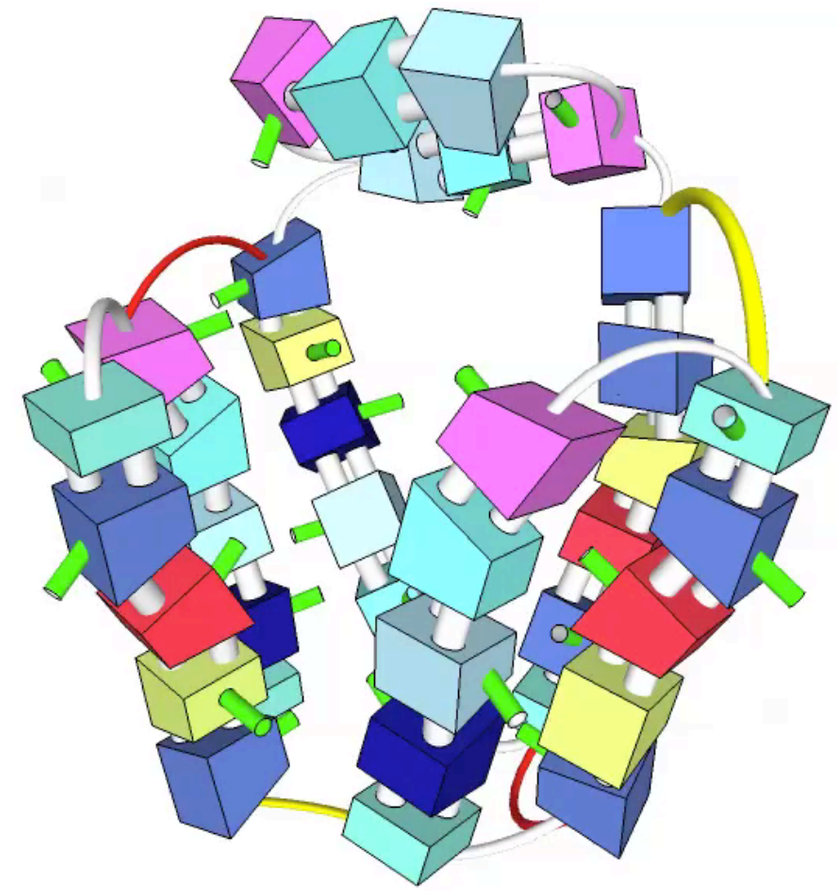
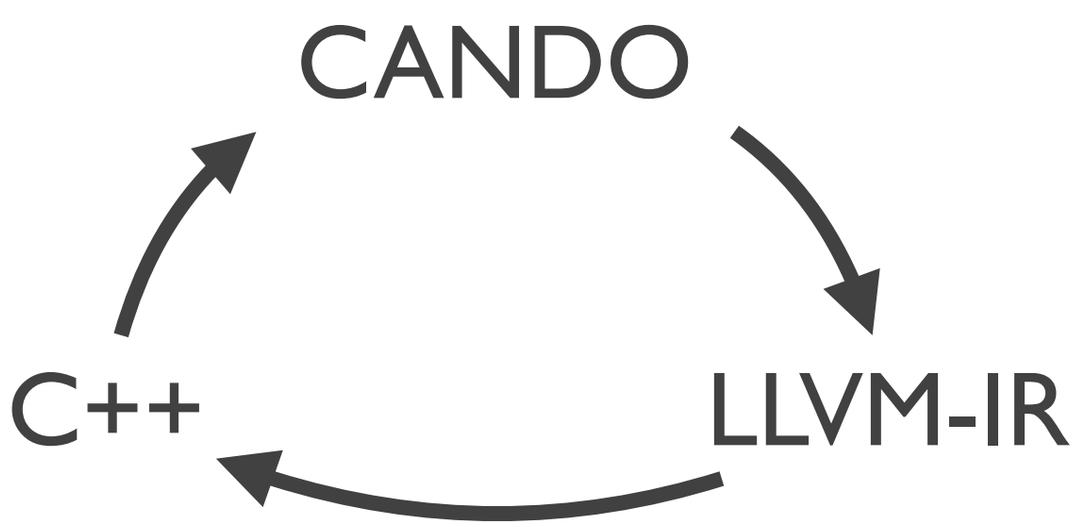
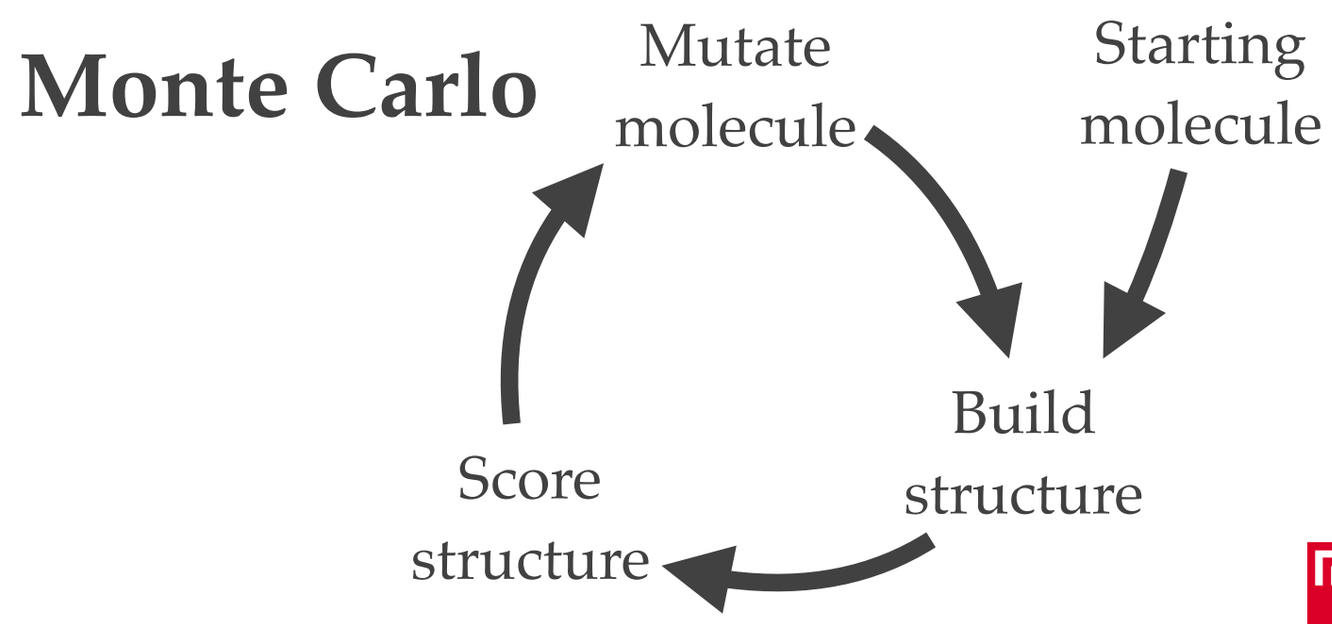
Could be parallelized using (2) LB 2D array



Hardware: Spiroligomers







Design Software: CANDO