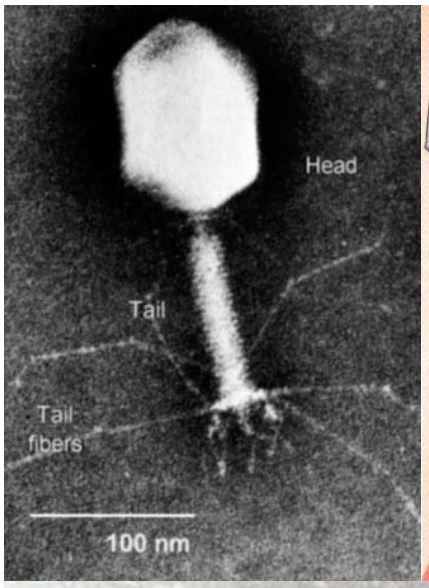
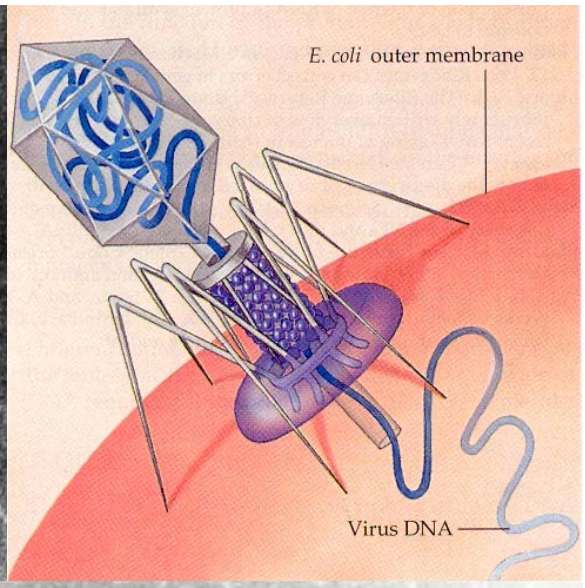
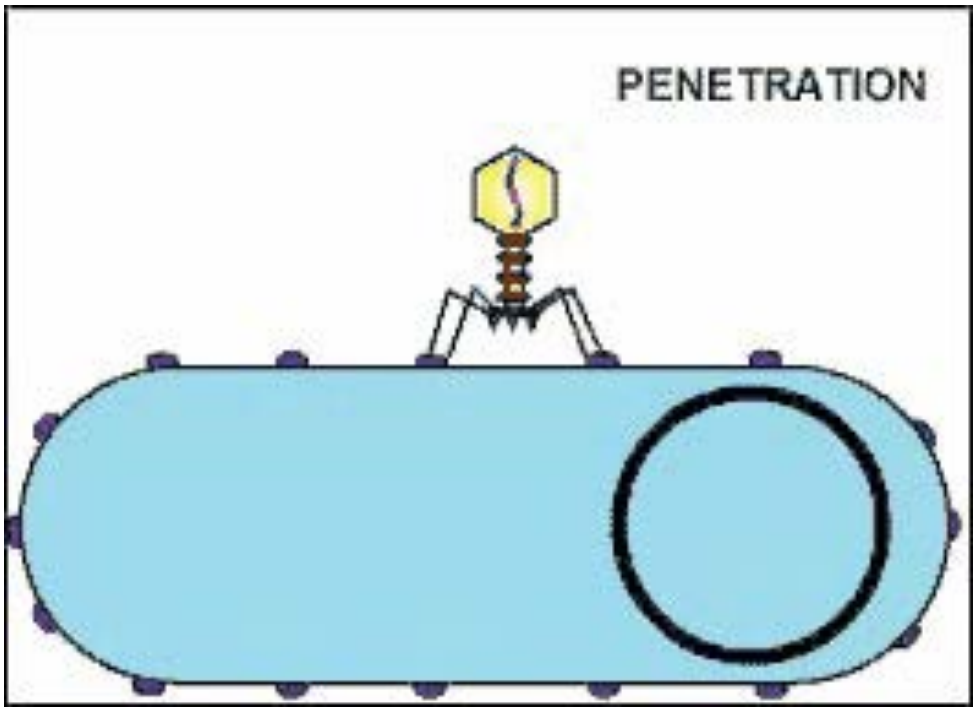
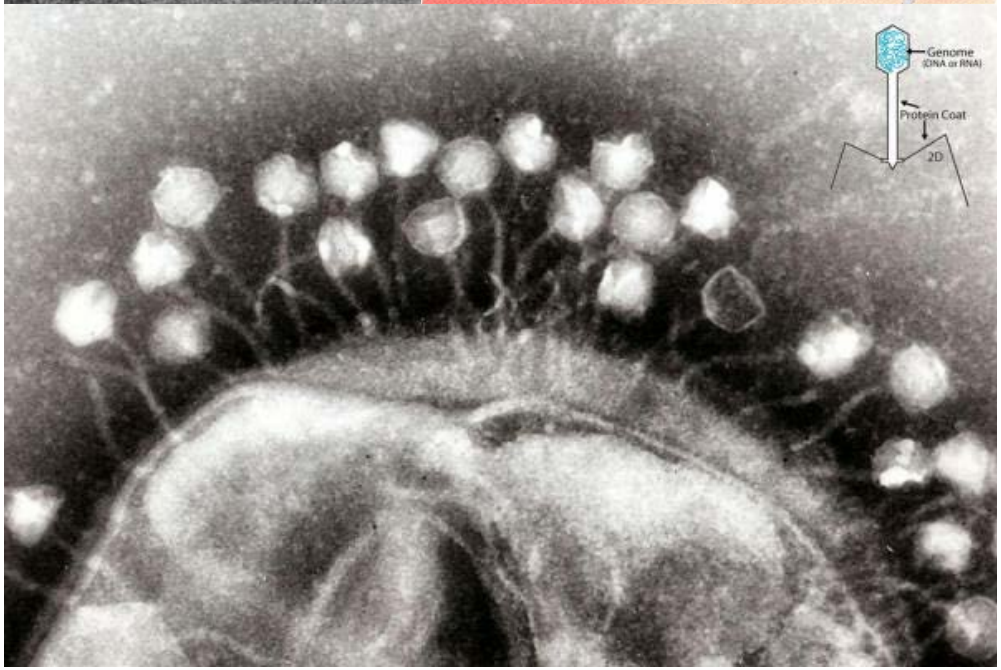
Motivation: Bacteriophage







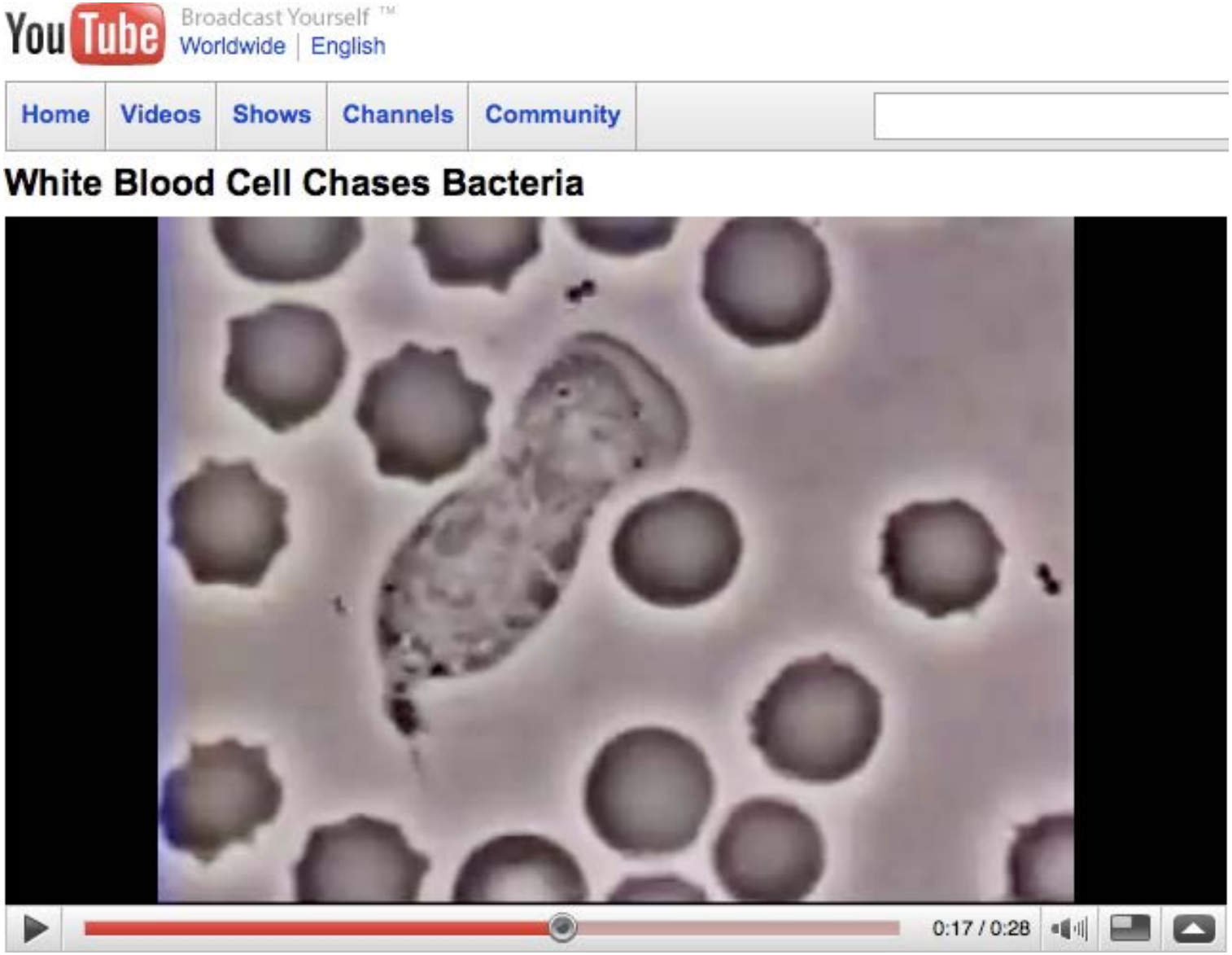


100-parts autonomous machine to search for, recognize & land on a target cell, drill a hole & inject DNA, which is self-assembled!

See How coronavirus works

None of the methods we have learned can simulate this

White Blood Cell Chases Bacteria



http://www.youtube.com/watch?v=JnlULOjUhSQ&eurl=http://video.google.com/videosearch?q=White%20Blood%20Cell%20Chases%20Bacteria&oe=utf-8&rls=org.mozilla:&feature=player_embedded

Transfer RNA in Ribosome

Supplementary Movie 1:
Simulating movement of transfer RNA into the ribosome during decoding

Sanbonmatsu*, K.Y., Joseph, S. and C.S. Tung
Los Alamos National Laboratory

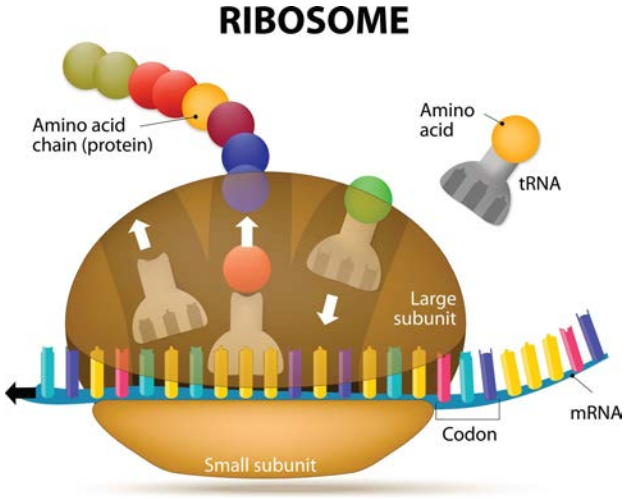
Explicit Solvent Targeted Molecular Dynamics

$N_{atoms} = 2.64 \times 10^6$

ASCI Q Machine (LANL)

*corresponding author: kys@lanl.gov

www.t10.lanl.gov/kys



Ribosome synthesizes proteins by binding messenger RNA & transfer RNA

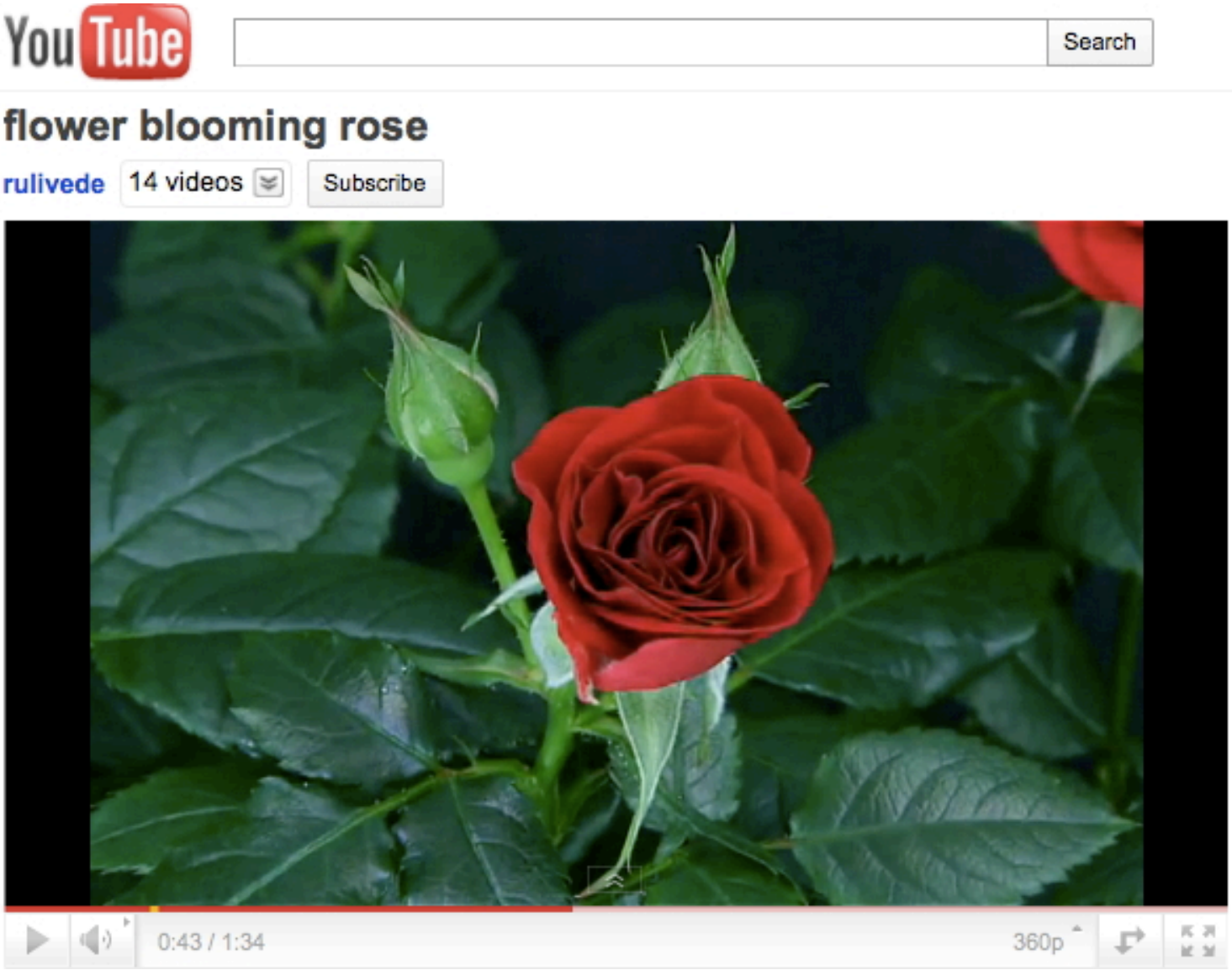
https://www.lanl.gov/projects/karissa/images/03456Movie1.mov

Long-time dynamics *via* a series of rare events!

Time Lapse Simulation?

Yes, it's called accelerated dynamics

D. Perez *et al.*, *Ann. Rep. Comput. Chem.* **5**, 79 ('09)



http://www.youtube.com/watch?v=HnbMYzdjuBs&feature=related

Accelerated Molecular Dynamics Methods: Introduction and Recent Developments

Danny Perez[1], Blas P. Uberuaga[2], Yunsic Shim[3], Jacques G. Amar[3] and Arthur F. Voter[1]

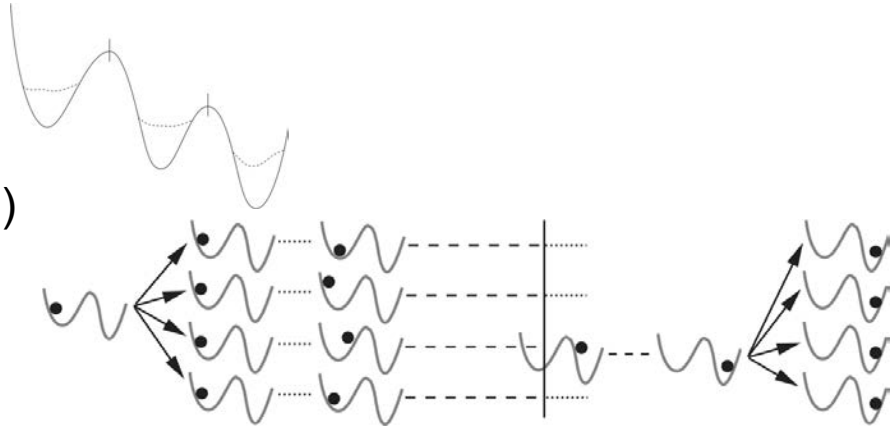
Accelerating atomic orbital-based electronic structure calculation via pole expansion and selected inversion

Lin Lin[1], Mohan Chen[2], Chao Yang[1] and Lixin He[2]

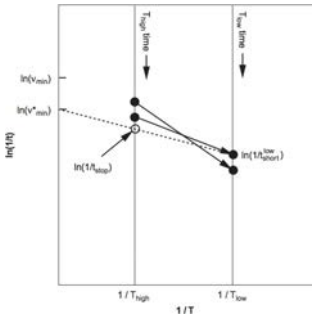
Decaheme Cytochrome MtrF Adsorption and Electron Transfer on Gold Surface

Tao Wei,*,† Heng Ma,† and Aiichiro Nakano*,‡,§,∥,⊥

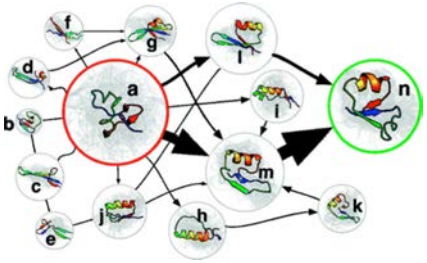
Accelerated Molecular Dynamics



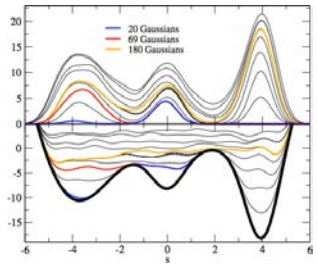
- **Hyperdynamics**
  A. F. Voter, *J. Chem. Phys*. **106**, 4665 ('97)
- **Parallel replica dynamics**
  A. F. Voter, *Phys. Rev. B* **57**, R13985 ('98)
- **Temperature accelerated dynamics**
  M. R. Sorensen & A. F. Voter, *J. Chem. Phys*. **112**, 9599 ('00)



- **Markov state model**
  V. Pande, *et al*., *Methods* **52**, 99 ('10)

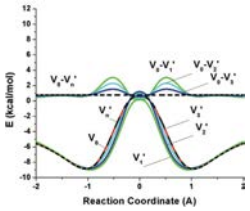


- **Metadynamics**
  A. Laio & M. Parrinello, *Proc. Nat'l Acad. Sci*. **99**, 12562 ('02)

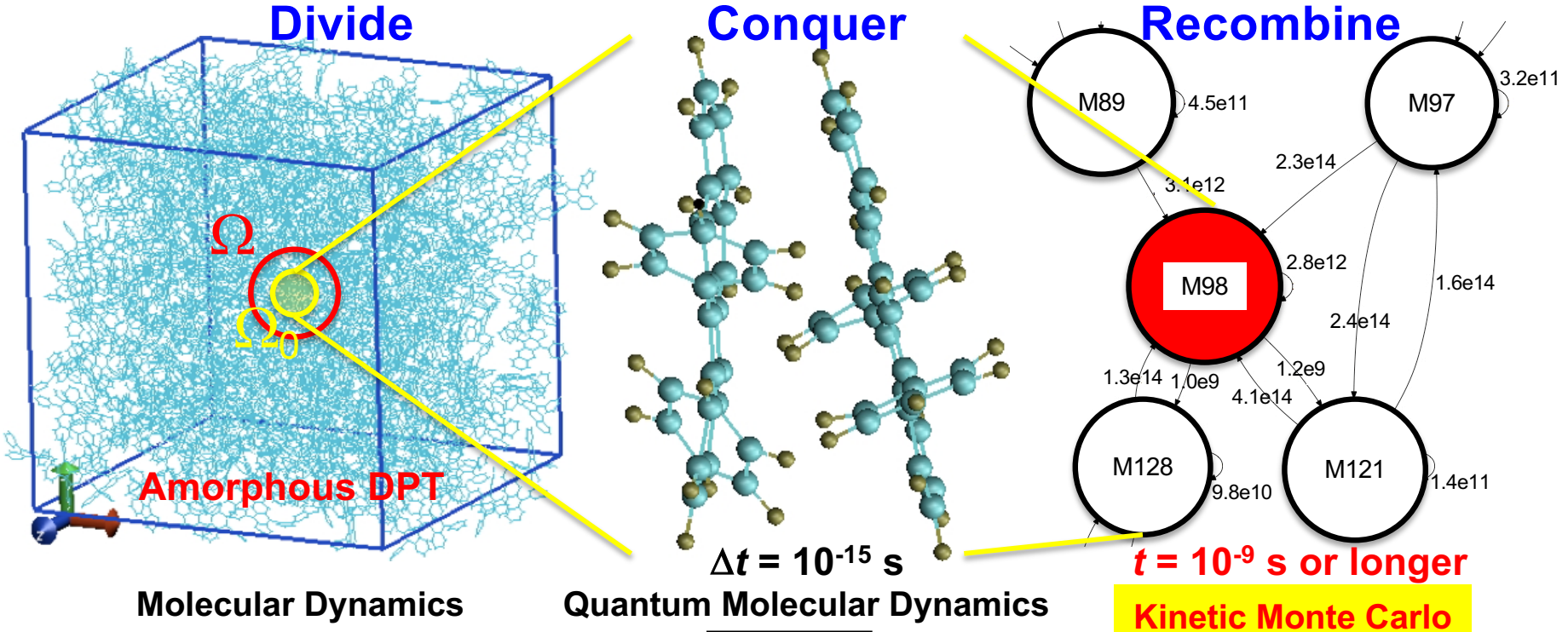


- **Paradynamics**
  N. V. Plotnikov, S. C. L. Kamerlin & A. Warshel, *J. Phys. Chem. B* **115**, 7950 ('11)

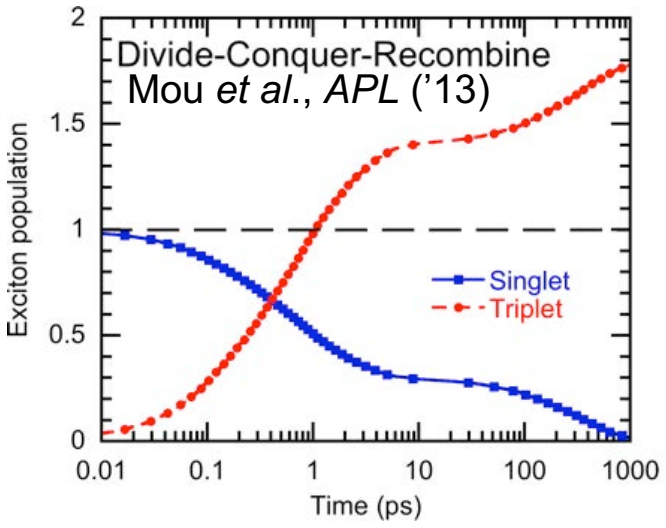
...

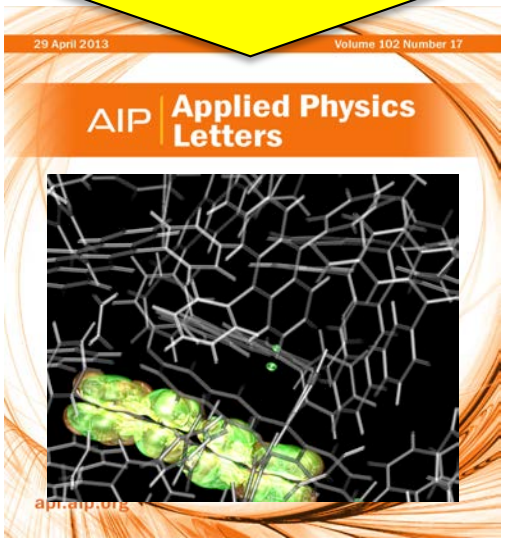


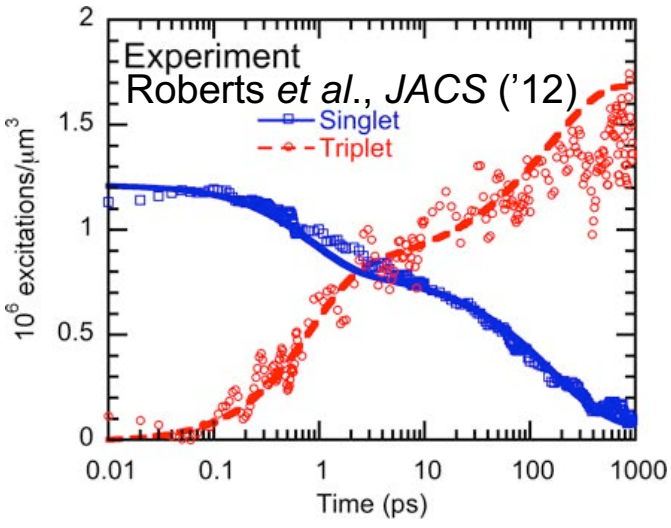
Divide-Conquer-Recombine KMC



Experimental Length & Time Scales



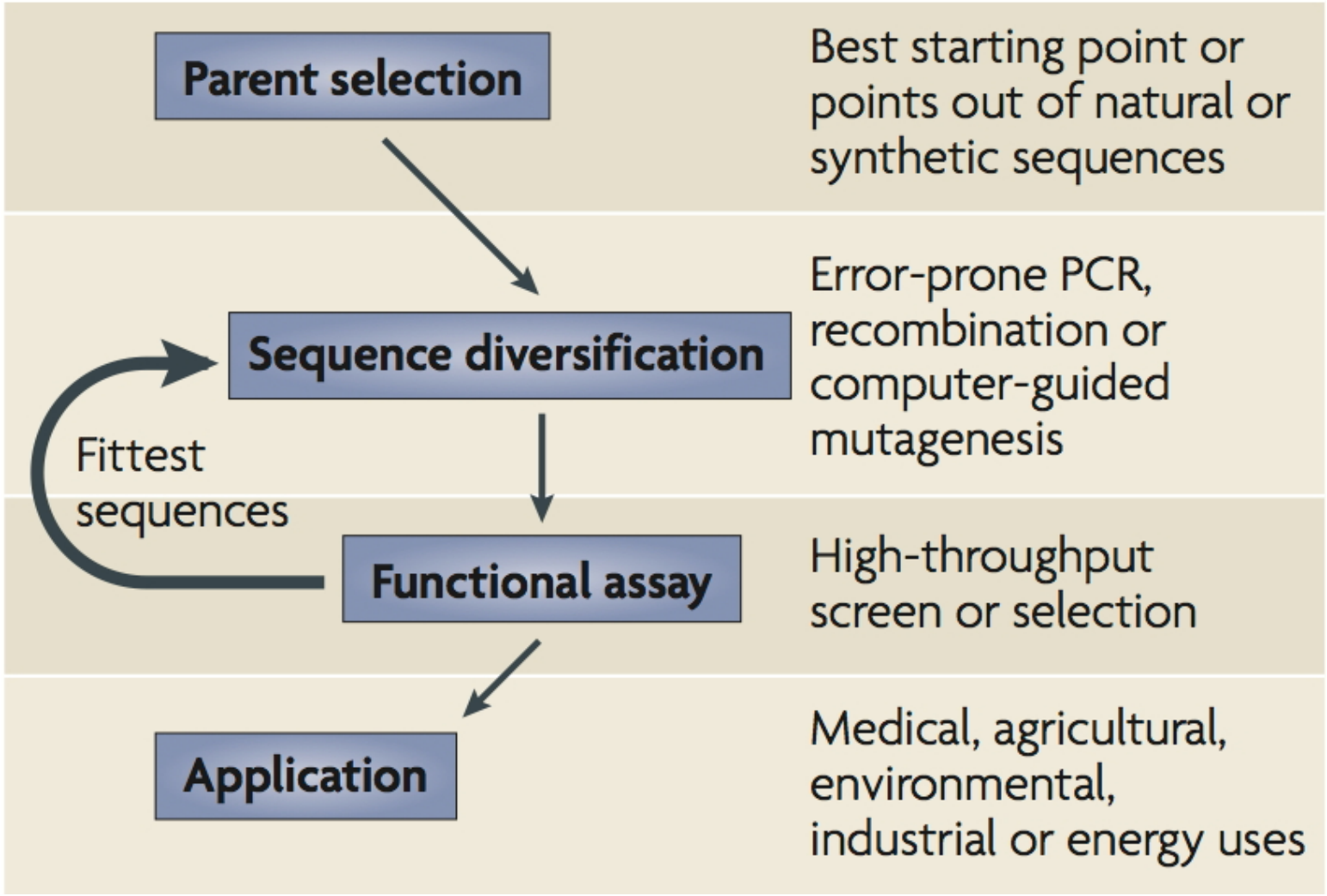




Accelerated Evolution?

Directed evolution

P. A. Romero & F. H. Arnold, *Nature Rev. Mol. Cell Biol*. **10**, 867 ('09)



Accelerating directed evolution to design new materials *in silico*?

Nobel Chemistry Prize in 2018

© Nobel Media AB. Photo: A. Mahmoud

Frances H. Arnold

Prize share: 1/2

© Nobel Media AB. Photo: A. Mahmoud

George P. Smith

Prize share: 1/4

© Nobel Media AB. Photo: A. Mahmoud

Sir Gregory P. Winter

Prize share: 1/4

The Nobel Prize in Chemistry 2018 was divided, one half awarded to Frances H. Arnold "for the directed evolution of enzymes", the other half jointly to George P. Smith and Sir Gregory P. Winter "for the phage display of peptides and antibodies."

Evolbability?

Abstract. Living organisms function in accordance with complex mechanisms that operate in different ways depending on conditions. Darwin's theory of evolution suggests that such mechanisms evolved through variation guided by natural selection. However, there has existed no theory that would explain quantitatively which mechanisms can so evolve in realistic population sizes within realistic time periods, and which are too complex. In this article, we suggest such a theory. We treat Darwinian evolution as a form of computational learning from examples in which the course of learning is influenced only by the aggregate fitness of the hypotheses on the examples, and not otherwise by specific examples. We formulate a notion of evolvability that distinguishes function classes that are evolvable with polynomially bounded resources from those that are not. We show that in a single stage of evolution monotone Boolean conjunctions and disjunctions are evolvable over the uniform distribution, while Boolean parity functions are not. We suggest that the mechanism that underlies biological evolution overall is "evolvable target pursuit", which consists of a series of evolutionary stages, each one inexorably pursuing an evolvable target in the technical sense suggested above, each such target being rendered evolvable by the serendipitous combination of the environment and the outcomes of previous evolutionary stages.

L. G. Valiant, *J. ACM* **56(1)**, 3 ('09)