

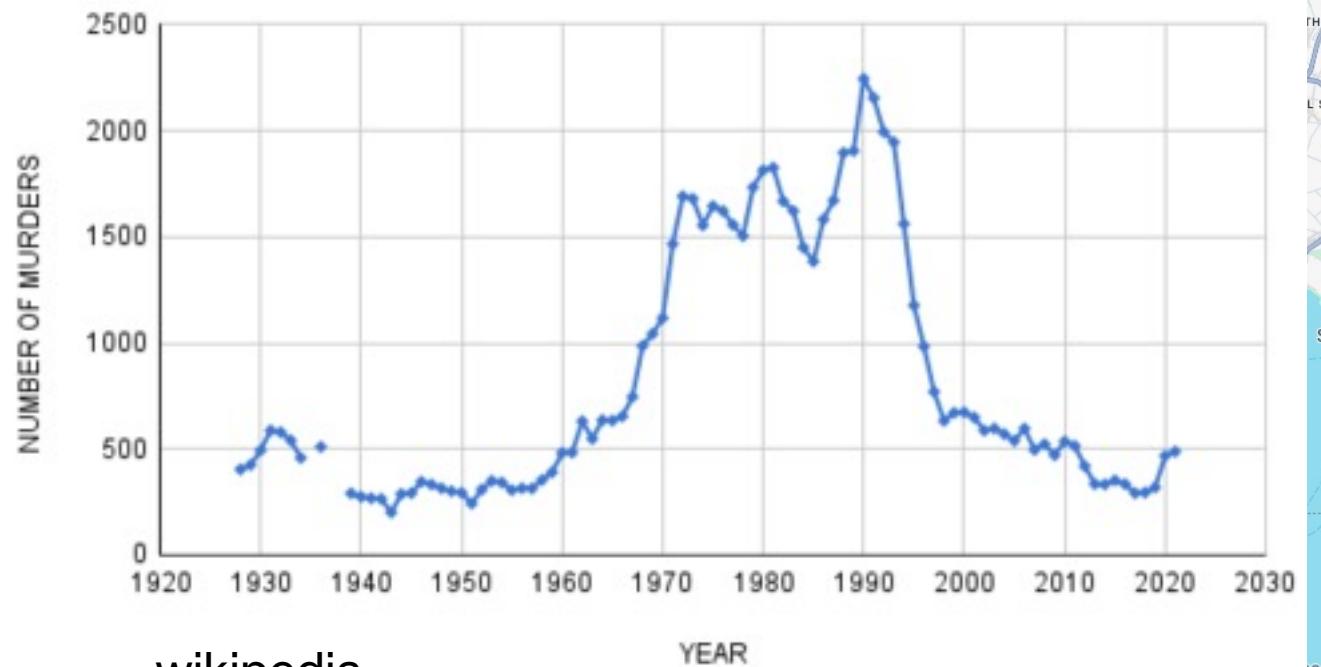
A large, abstract network graph composed of numerous small, semi-transparent blue triangles forming a larger, more complex polygonal shape. The vertices are small dark blue dots, and the edges are thin, dark blue lines connecting them. The overall effect is a sense of depth and connectivity.

Computing, Science, Personal History

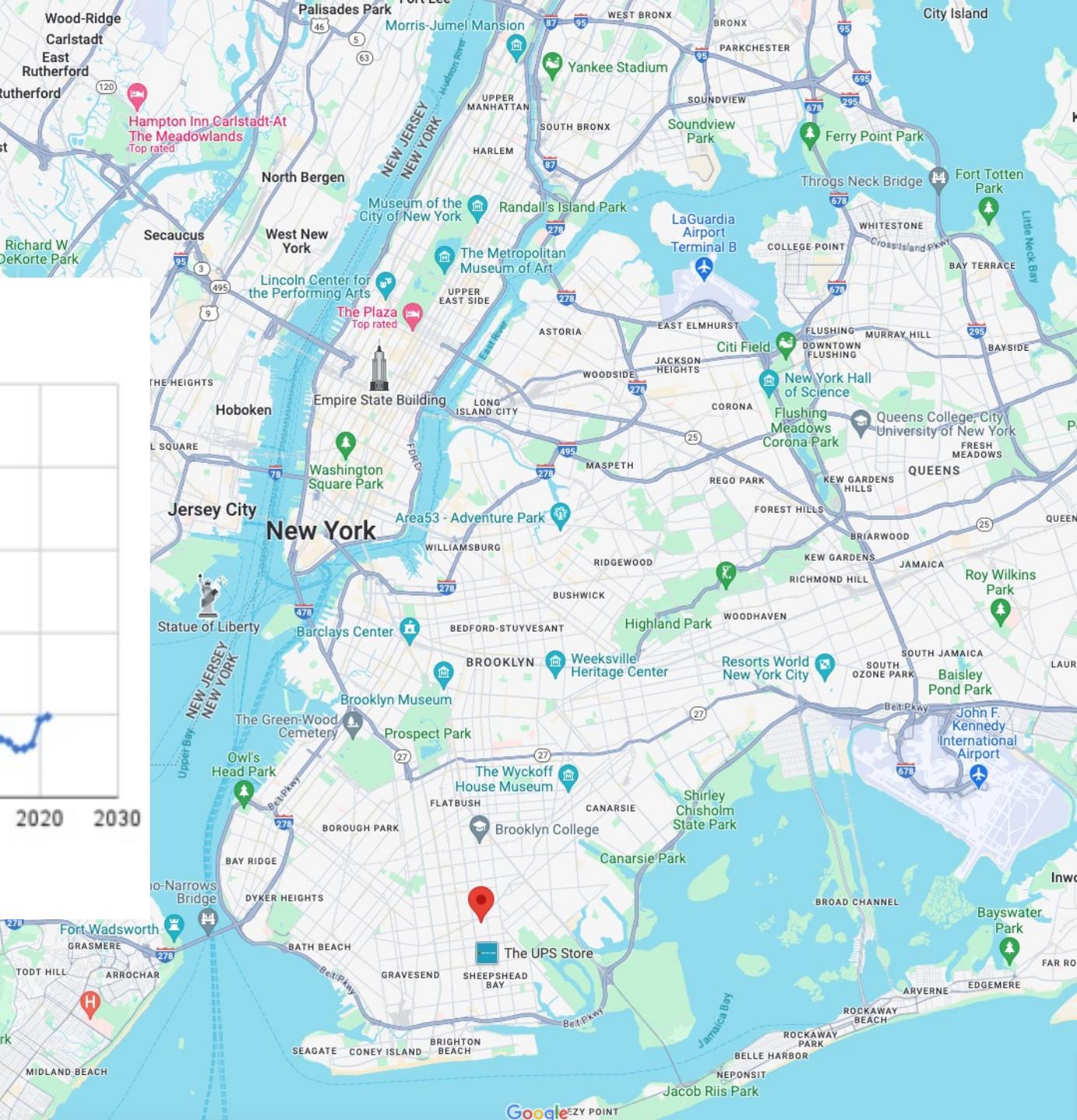
- Dan Zuckerman
 - Professor, Department of Biomedical Engineering, OHSU
-

Personal history

MURDERS IN NEW YORK CITY BY YEAR



wikipedia



Personal history



AtomicSpaceJunk.

Personal history

it's a loop!



Personal history

- NYC
- Boston
- Los Angeles
- Baltimore
- Pittsburgh
- Portland



Personal history

- 1989 Graduated college (major: comparative study of religion)
- 1989-1992 Worked, took math/science classes
- 1992-1998 Graduate school
- 1998-2002 Postdoc
- 2002-now Professor

Theory for chemistry, etc.

ANALYSIS, IMPROVEMENT, AND EXTENSION OF
ELECTROLYTE THEORIES

by

Daniel Mark Zuckerman

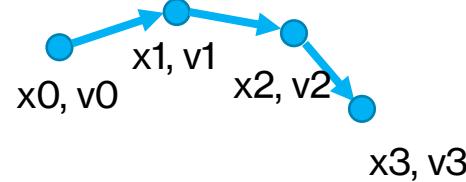
Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
1998

Advisory Committee:

Professor Michael E. Fisher, Chair/Advisor
Professor Theodore L. Einstein
Professor Theodore R. Kirkpatrick
Professor Athanassios Z. Panagiotopoulos
Professor Johanna M. H. Levelt Sengers

Molecular dynamics (how molecules behave)

$$\text{Newton: } f = m \cdot a \quad \text{or} \quad a = f/m$$



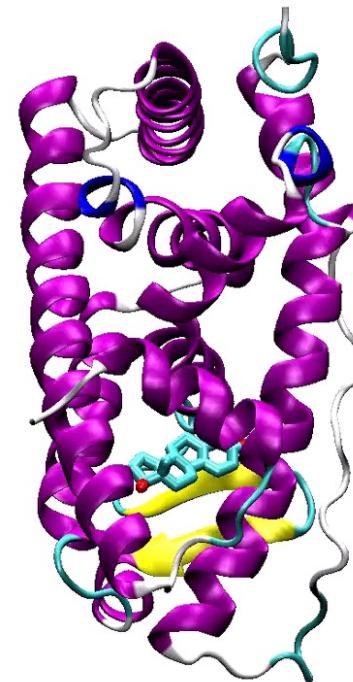
Trajectory Algorithm

$$x_{\text{new}} = x_{\text{old}} + v_{\text{old}} * \Delta t$$

$$v_{\text{new}} = v_{\text{old}} + (f_{\text{old}}/m) * \Delta t$$

Key application – Drug design
on/off rates

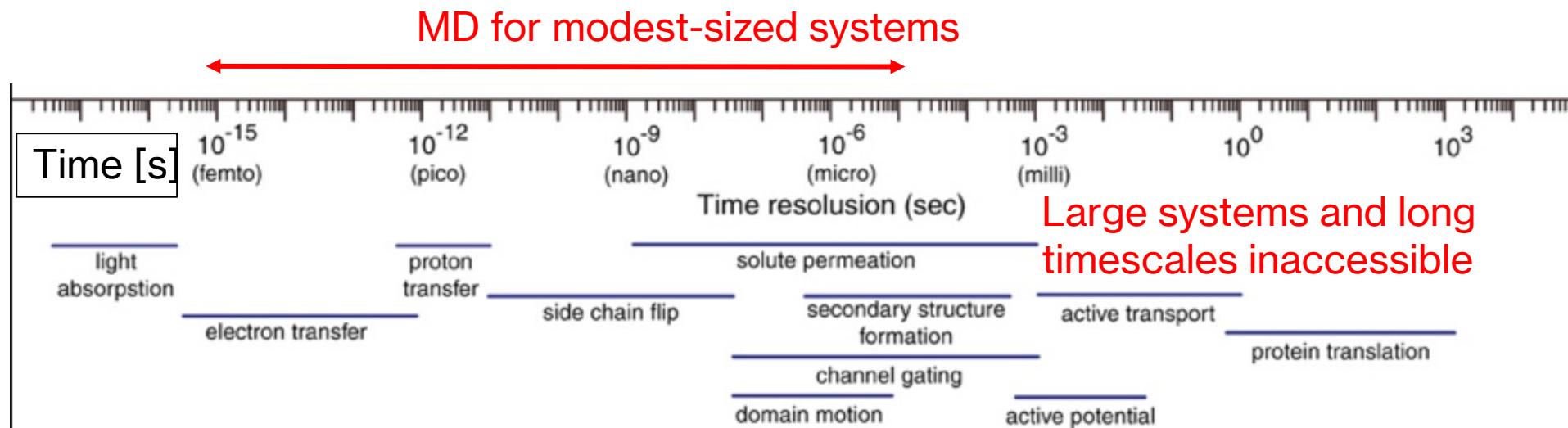
it's a loop!



Estrogen Receptor LBD with estradiol

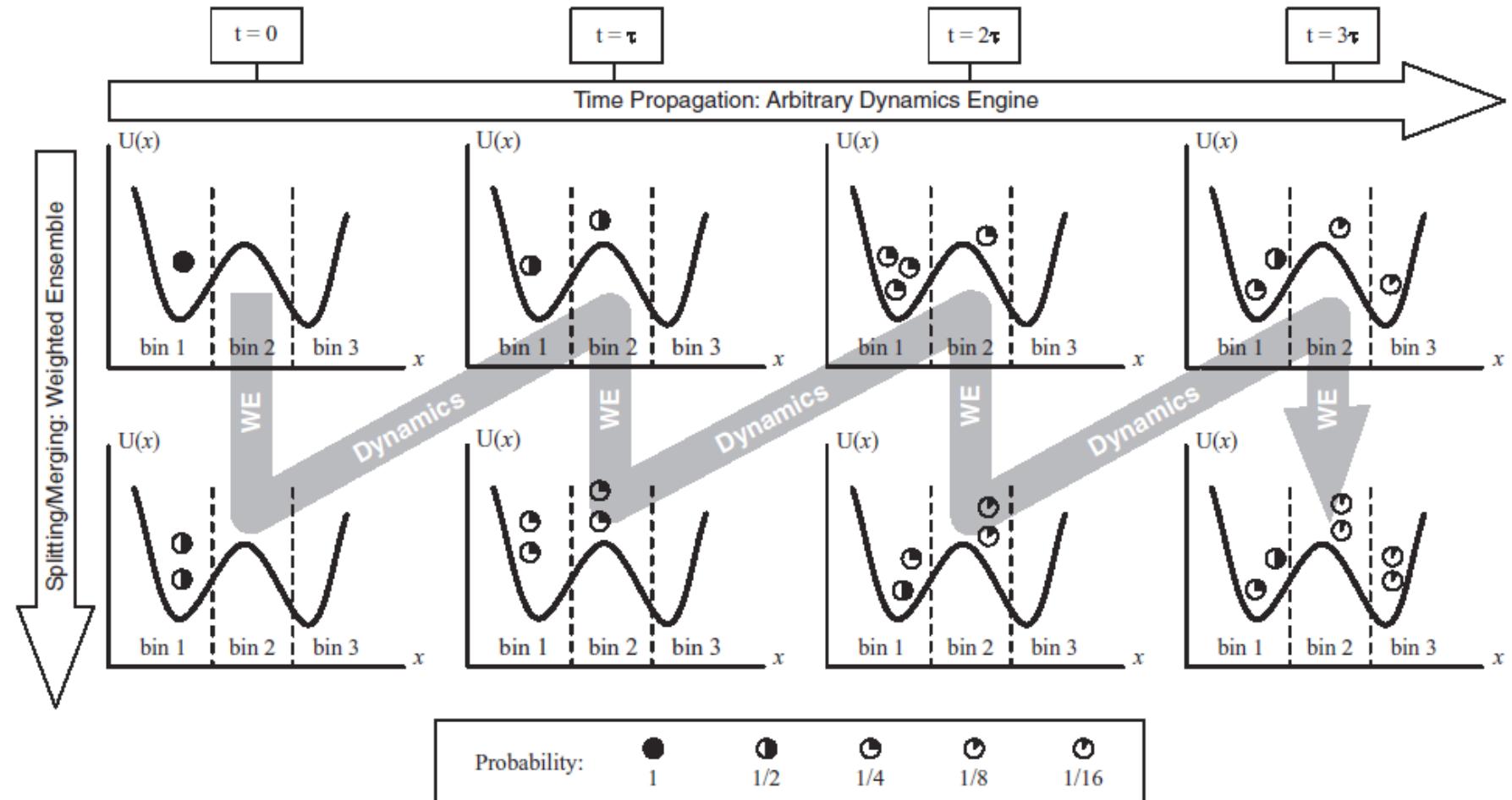
The problem with too-short movies

- Data is not reliable if timescales are inadequate



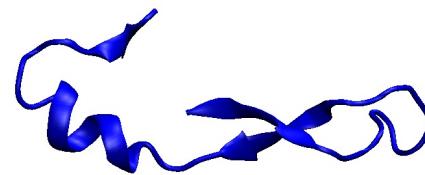
Can we rescue MD with a better algorithm?

The “weighted ensemble” (WE) method



[Original Weighted Ensemble: Huber & Kim, *Biophys J.* 1996;
Figure from Donovan et al., *J Chem Phys* 2013]

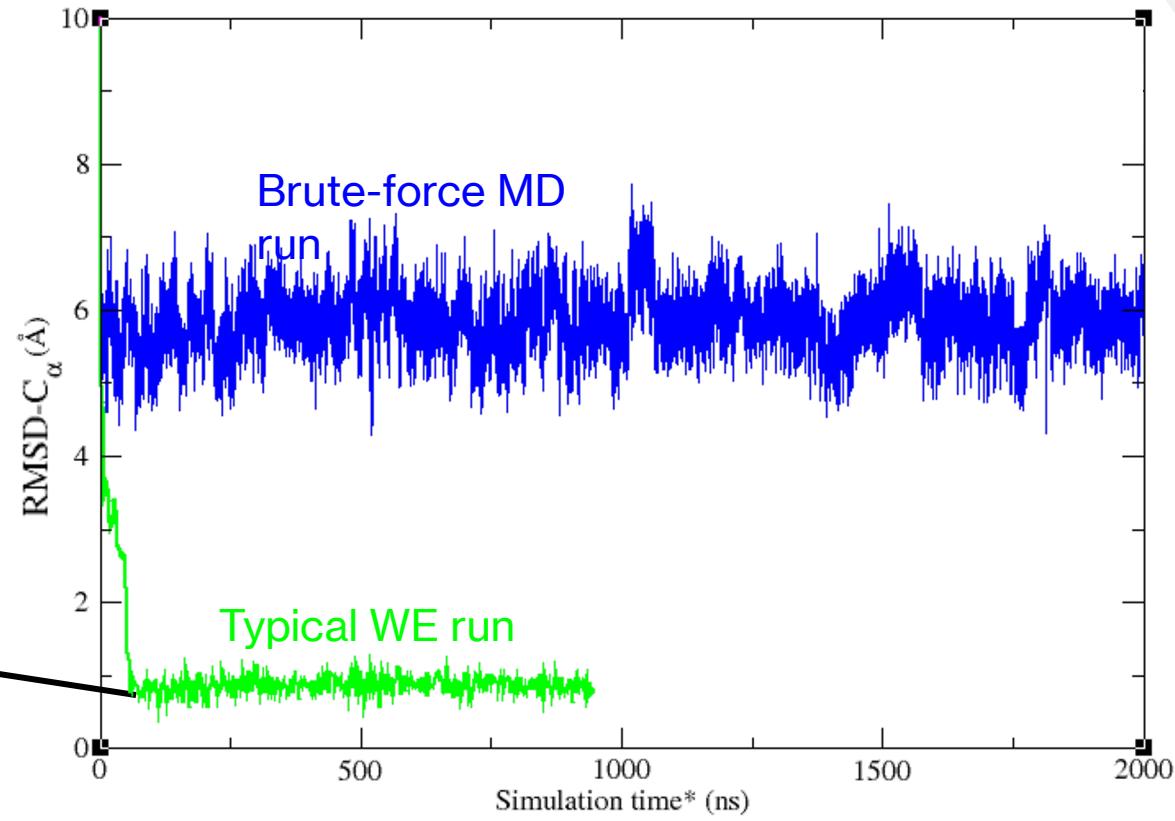
Protein folding by WE



Starting structure
(RMSD- C_α ~ 10.0 Å)



Folded structure
(RMSD- C_α ~ 1.0 Å)



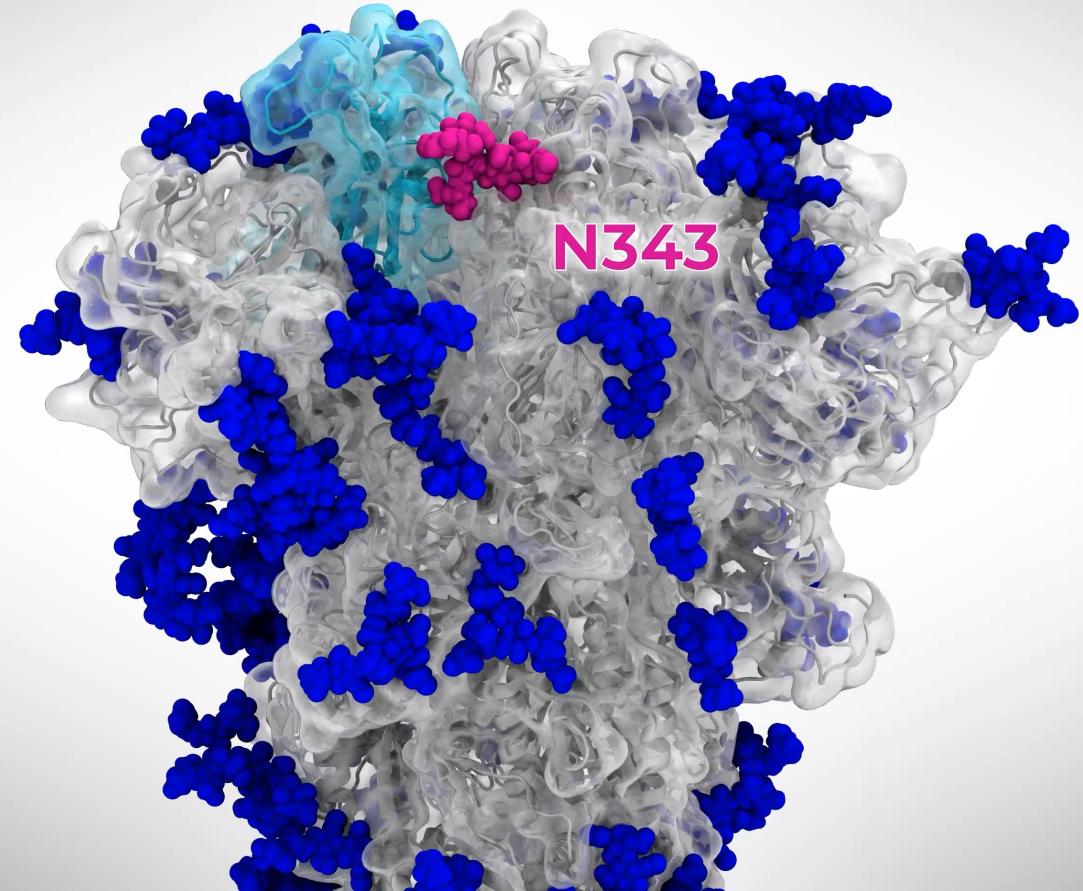
*WE aggregate time

[Adhikari et al., *Journal of the American Chemical Society*, 2019]

A glycan gate at N343 controls opening of the spike

Closed Spike
Side view

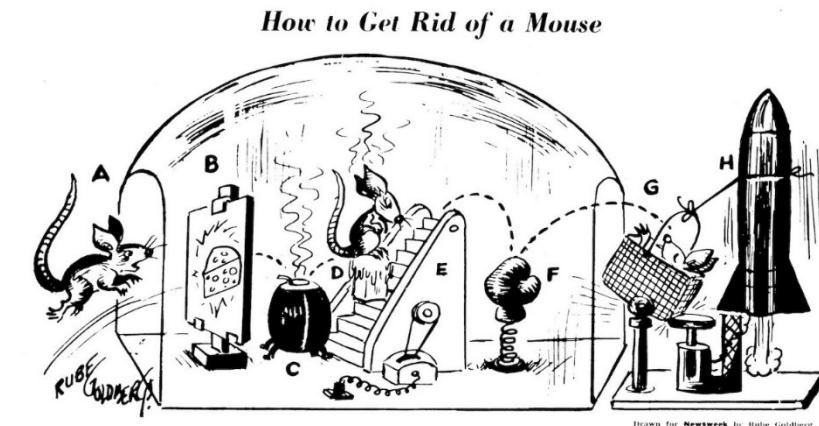
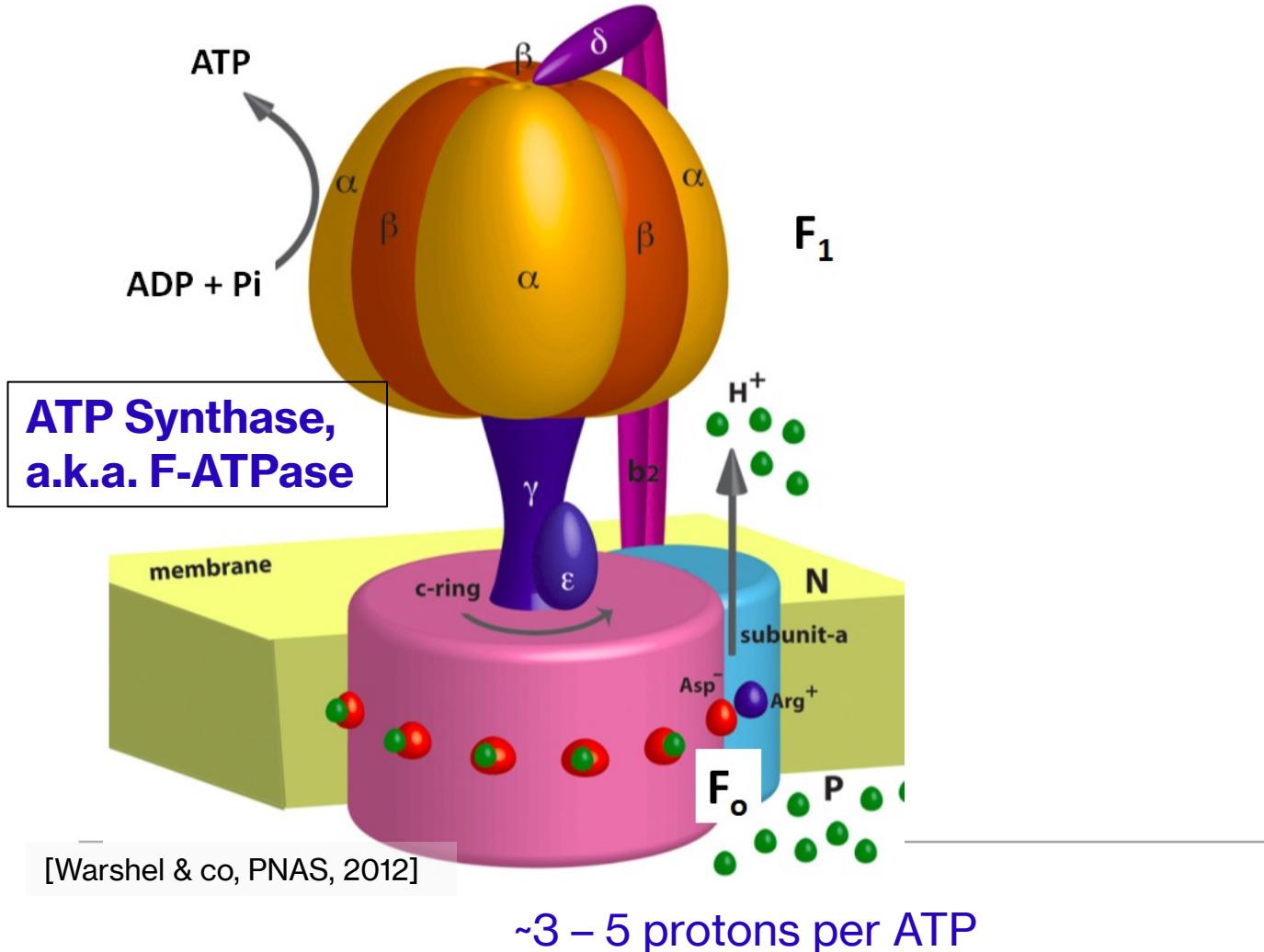
RBD “down”



T. SZTAIN, S.-H. AHN et al.
AMARO LAB (UCSD)
CHONG LAB (PITT)

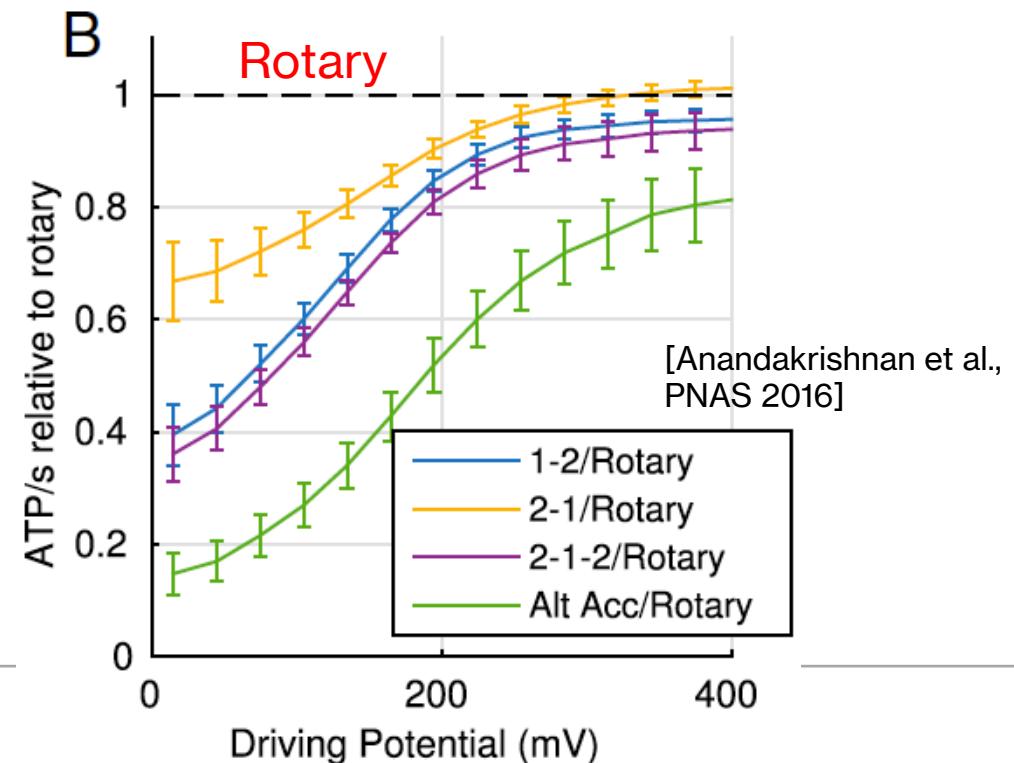
[Amaro, Chong & co, *Nature Chemistry*, 2021; Delta variant:
<https://www.nytimes.com/interactive/2021/12/01/science/coronavirus-aerosol-simulation.html>]

Did Rube Goldberg engineer nature's most important machine?



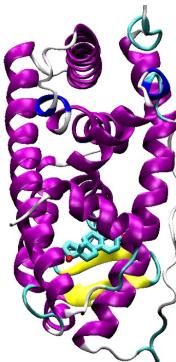
The best mousetrap by Rube Goldberg: Mouse (A) dives for painting of cheese (B), goes through canvas and lands on hot stove (C). He jumps on cake of ice (D) to cool off. Moving escalator (E) drops him on boxing glove (F) which knocks him into basket (G) setting off miniature rocket (H) which takes him to the moon.

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From proteins to cells

Both proteins and cells move and change with time. They can be analyzed with [trajectories](#).

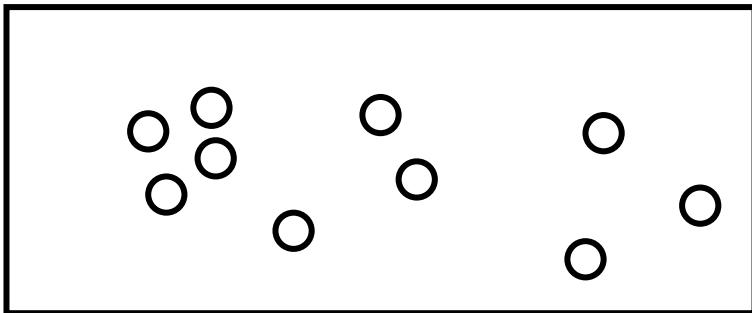


- MCF10A cells in EGF treatment (Heiser group)
- Phase contrast only.
- Automated segmentation shown.

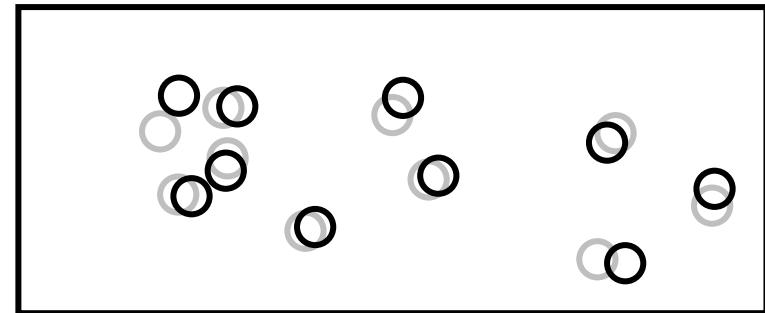
From trajectories to insight? Name the sport



- Top view of 5 v 5 pickup game



time = t



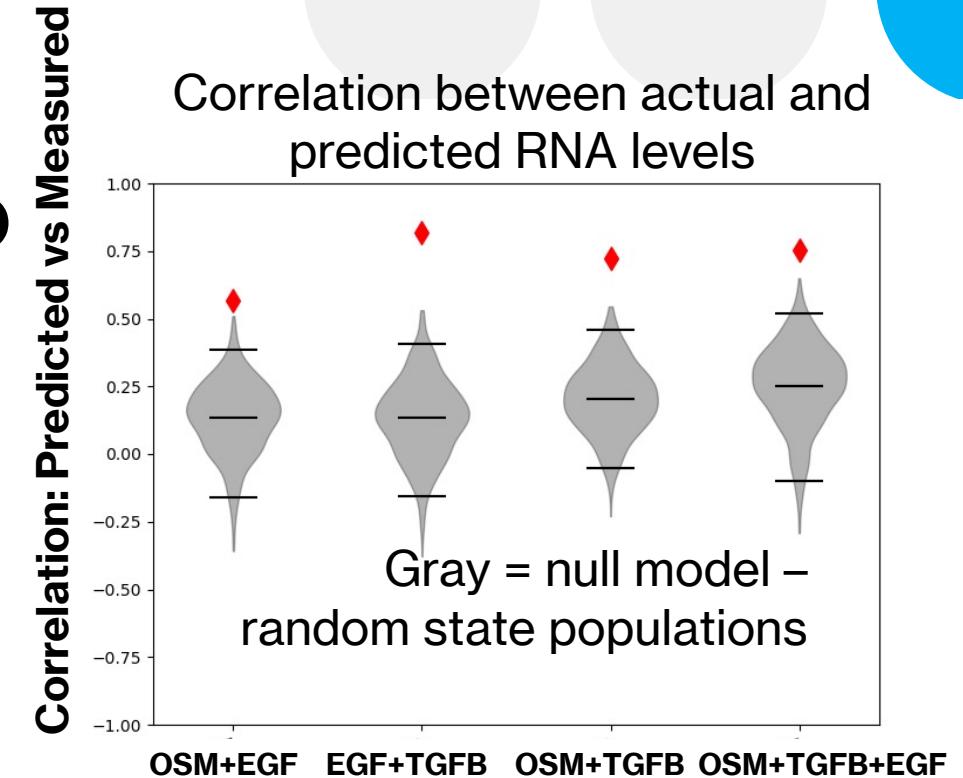
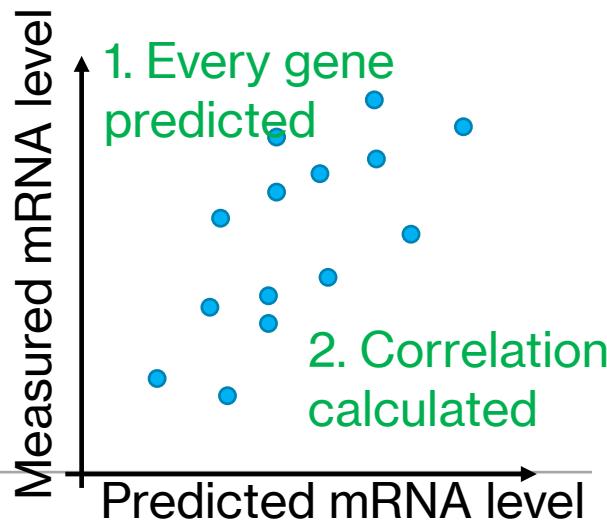
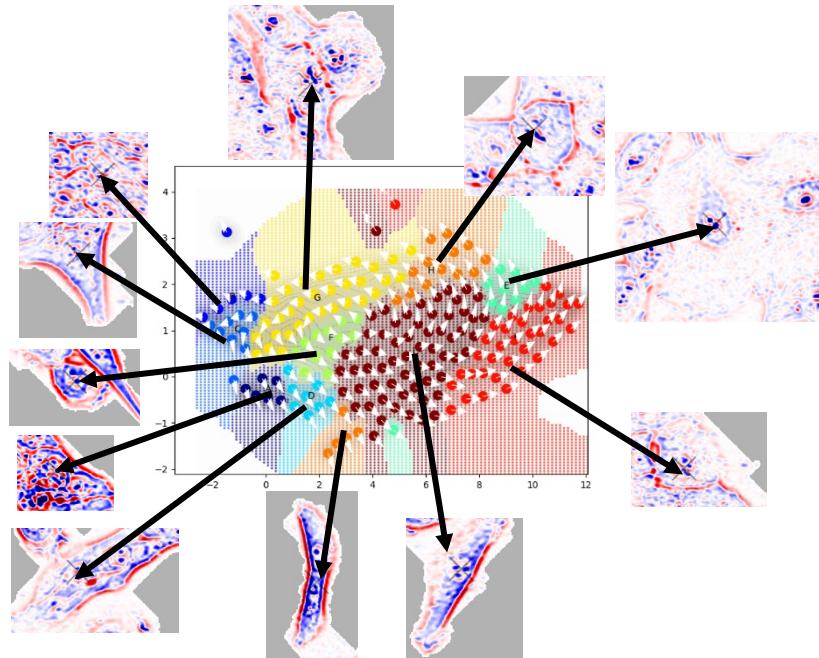
time = $t + \Delta t$

<https://hockey-graphs.com/2017/02/23/mikael-granlund-playing-behind-the-net-predicting-goals/>

<https://news.wisc.edu/west-campus-playfield-construction-to-increase-traffic/>

<https://www.dreamstime.com/editorial-photography-basketball-game-action-sport-player-isolated-overhead-view-image82255672>

Cell trajectories can be used to predict mRNA levels



up/down-regulated genes prediction

ligand	DICE_up	DICE_down
EGF+OSM	0.72	0.81
EGF+TGFB	0.72	0.84
EGF+OSM+TGFB	0.85	0.81

Is science great?

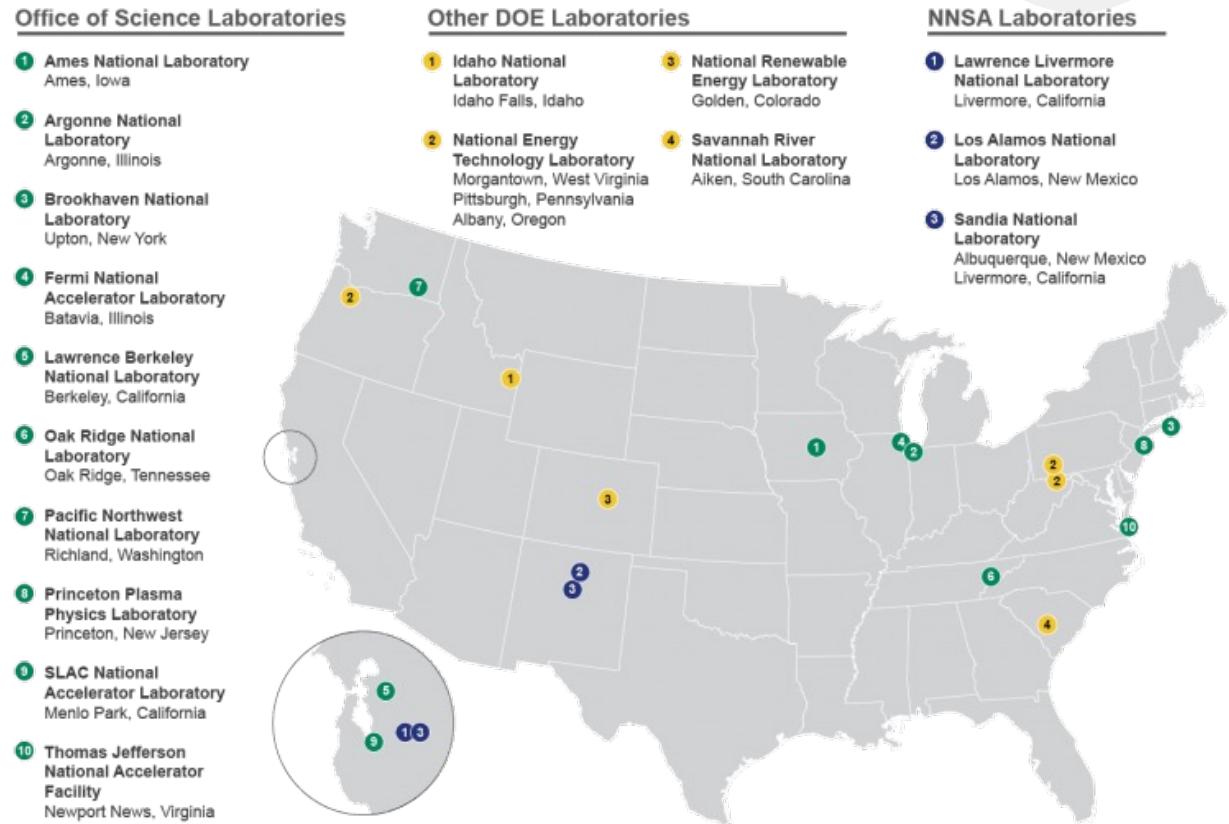
- The job is to discover things that no one else knew
 - Solve problems in creative ways
 - Build technologies that do new things (enable discoveries or health outcomes)
 - Software: Make something from nothing
-

How to become a Scientist

- Figure out what you like
 - Classes: Seek best teachers
 - Research: Seek best mentors – ask other group members
- Do research in college
 - Paid programs available
 - Get to know multiple professors
 - [Full disclosure: I didn't major in science or do any of this!]
- Apply to graduate school
 - Seek the best mentor!
 - Best = ? Most accomplished, best connected, healthiest group environment, best research topic
 - Do something you love to do well
 - Get to know multiple professors
- How to 'do good' as a scientist
 - Be a great teacher
 - Be a great mentor (even working for industry)
 - Solve an important problem (even working for industry)

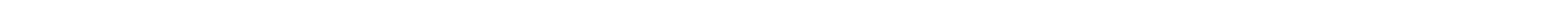
What if I don't want to be a professor?

- Government labs
- Industry
- School teacher
- Policy development
- Patent law



Can I learn to code?

- Do I need to be a math whiz?
- Did I need to start when I was in kindergarten?
- Do I need to have a fancy computer?
- Will I be taught to code in school?



Two flavors of modern coding

- Do what you know and can understand
- Copy (and check) what you can't understand

Why I love to teach introductory coding

- I understand it
 - You can understand it
-

Questions (asked) are golden



Introductions, and ... let's code!

