Introduction: Markov state models for molecular dynamics simulations

CS/CME/Biophys/BMI 371

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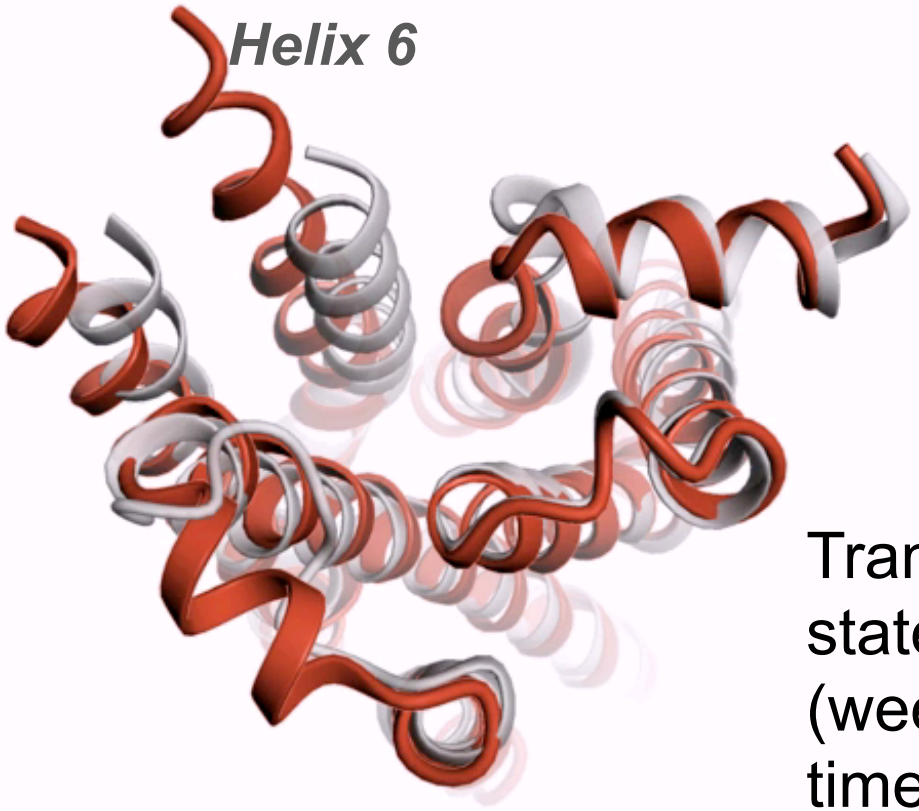
Many biochemical events we'd like to capture by molecular dynamics (MD) simulations take place on timescales longer than we can simulate



Simulation vs.
Inactive crystal structure

Transition to inactive state occurs after 11 μs (weeks of simulation time)

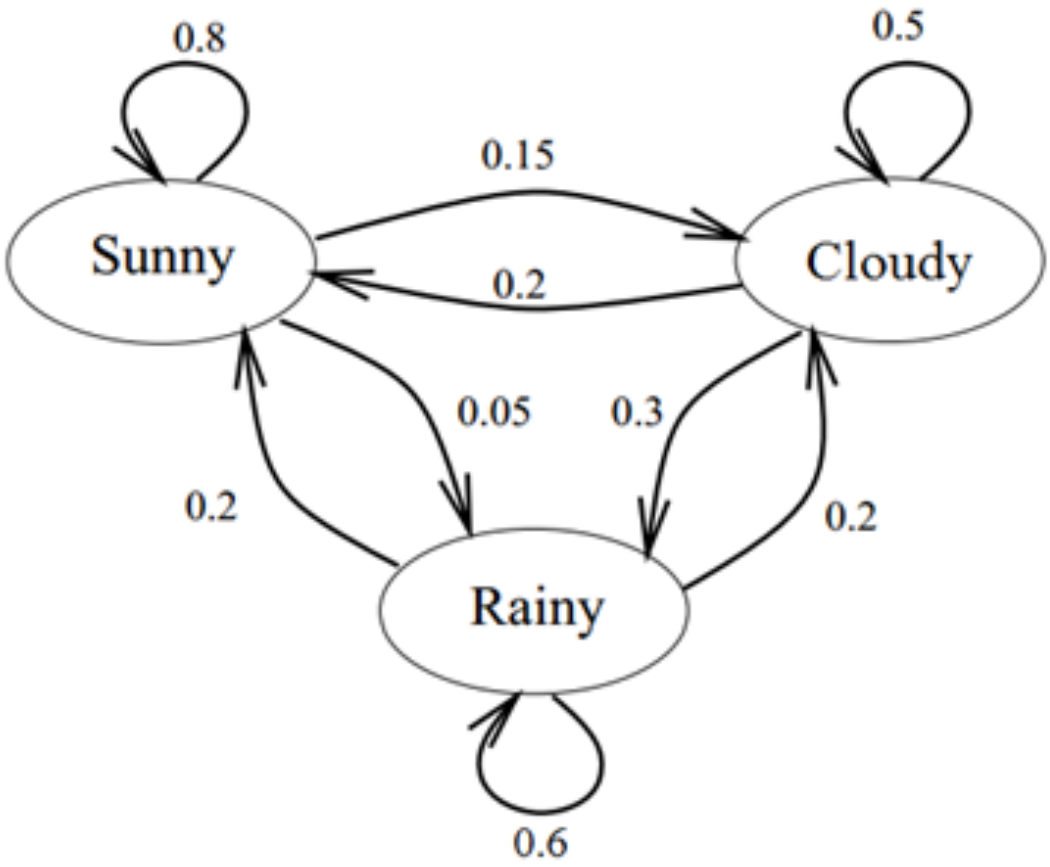
Simulation of β_2-adrenergic receptor transitioning spontaneously from its active state to its inactive state

Rosenbaum et al., *Nature* 2010; Dror et al., *PNAS* 2011

What if instead of running one long simulation, we run many short simulations?

- Can we use many short simulations to predict what would have happened in a longer simulation?
- We need a way to summarize the information from many short simulations
- One way to do this involves *Markov State Models*

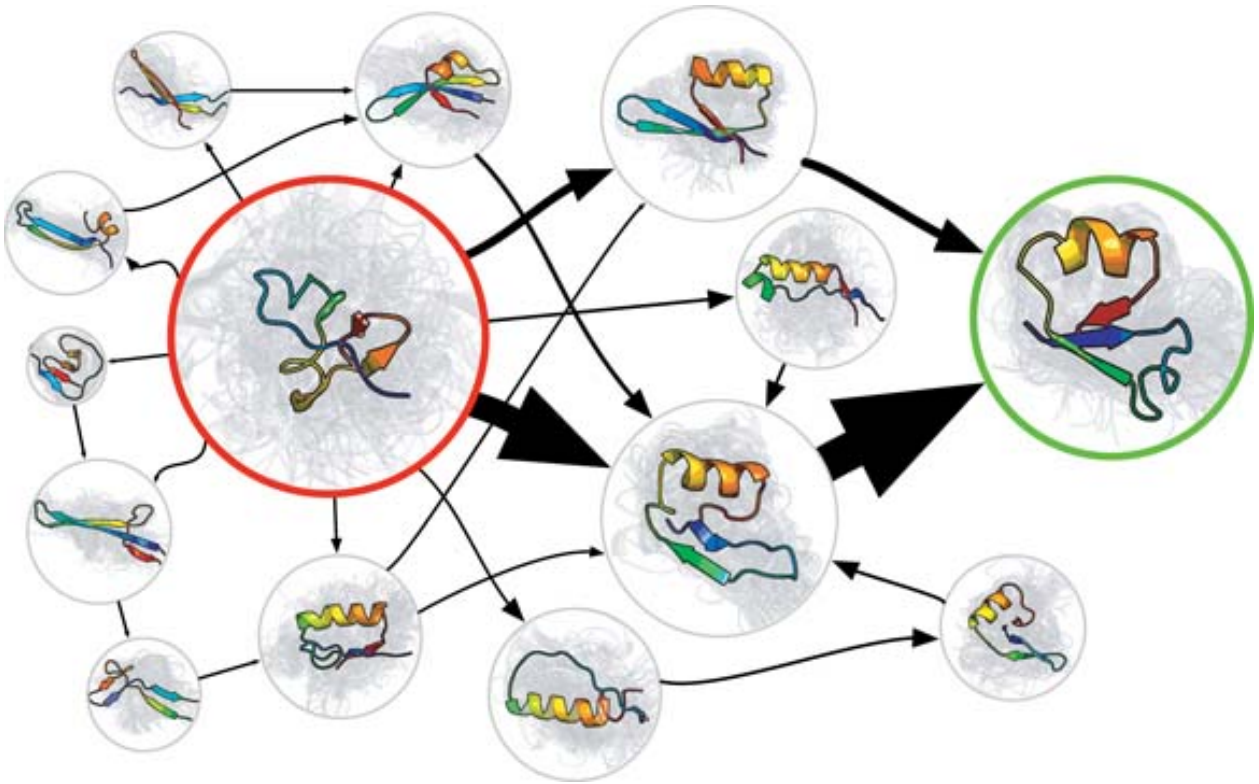
A Markov (state) model



A Markov model for predicting tomorrow's weather given today's weather

https://dzone.com/articles/markov-models-and-hidden

Markov state models for MD simulations



V.A. Voelz et al., *J. Am. Chem. Soc.* 132 (5) (2010) 1526–1528.

- Each node represents a conformational state (that is, a group of similar conformations)
- Each edge represents a transition from one state to another and has an associated probability

How can these Markov State Models be useful?

- Running many short simulations instead of one long simulation
  - E.g., Folding@Home
  - Need to decide initial conditions for each short simulation
- Potentially: reduce total amount of simulation time necessary
- Human interpretation/summarization of simulation data

Background material

- A basic introduction to Markov models
  - https://dzone.com/articles/markov-models-and-hidden
- Molecular dynamics slides from CS/CME/BioE/ Biophys/BMI 279:
  - http://web.stanford.edu/class/cs279/lectures/ lecture4.pdf

- Question: how is this connected to PageRank?