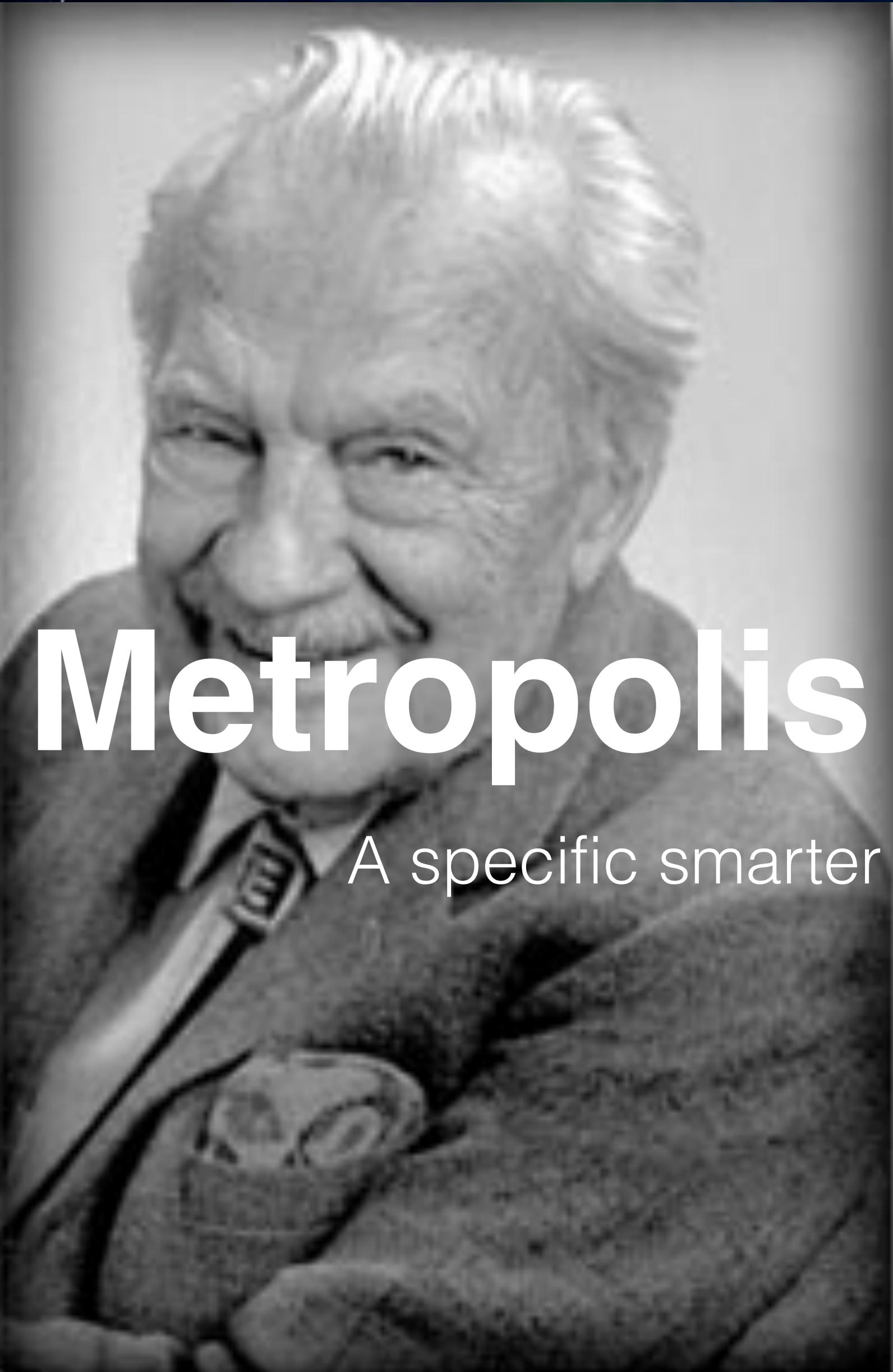


# 10/30/2024 Molecular Simulation

- Today's lecture and exercise are intended to help you achieve the following learning objectives: recall the purpose of key algorithms in molecular dynamics
- Revision of Exercise 6
- Molecular simulation methods
  - Metropolis Monte Carlo
  - Molecular Dynamics
  - Compare/contrast and combine
- Exercise 8: Performing a Molecular Simulation with OpenMM



# Metropolis Monte Carlo

A specific smarter way to sample the Nile



Metropolis, N.; Rosenbluth, A. W.; Rosenbluth, M. N.; Teller, A.; Teller, E. Equation of State Calculations by Fast Computing Machines. *Journal of Chemical Physics* 1953, 21 (6), 1087–1092.

# About Metropolis Monte Carlo

- First Markov chain Monte Carlo algorithm
- Used throughout scientific computing
- “Metropolis et al. introduced the sampling method and periodic boundary conditions that remain at the heart of Monte Carlo statistical mechanics simulations of fluids. This was one of the major contributions to theoretical chemistry of the twentieth century.” - William Jorgensen, 2011
- “Hastings generalized the Metropolis algorithm into the well-known Metropolis–Hastings algorithm (MH) … “the celebrated Metropolis–Hastings algorithm has the highest acceptance probability of all Hastings algorithms” - Minh & Minh, 2015



Nicholas Metropolis -  
provided computing time,  
gets most credit!



Arianna Rosenbluth -  
final implementation  
of code



Marshall Rosenbluth -  
"[We] did all the work"

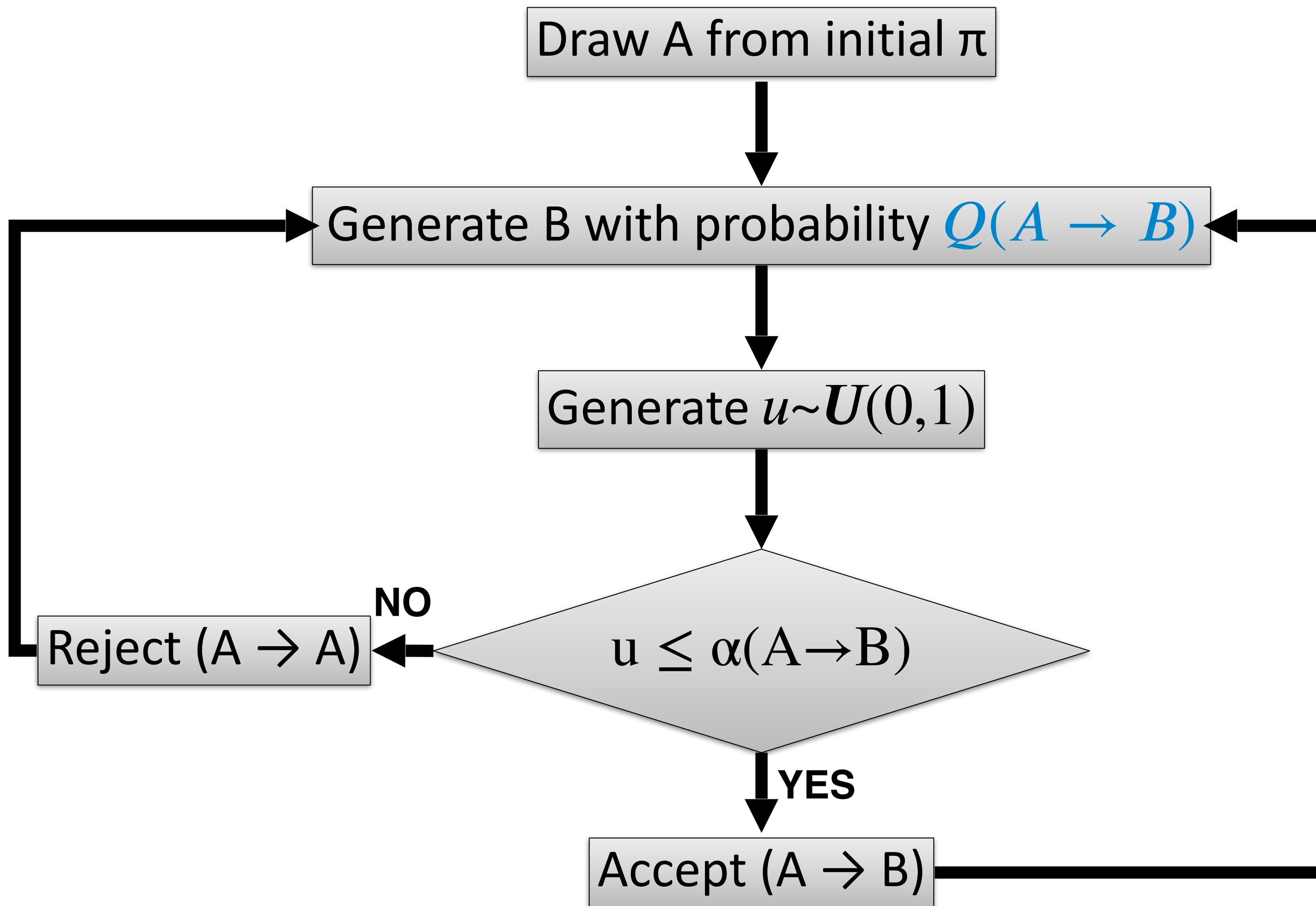


Edward Teller,  
"Father of H bomb" -  
key suggestion

Augusta Teller -  
wrote draft  
of code

Gubernatis, J. E. Marshall Rosenbluth and the Metropolis Algorithm. Physics of Plasmas 2005, 12 (5), 057303.  
<https://doi.org/10.1063/1.1887186>

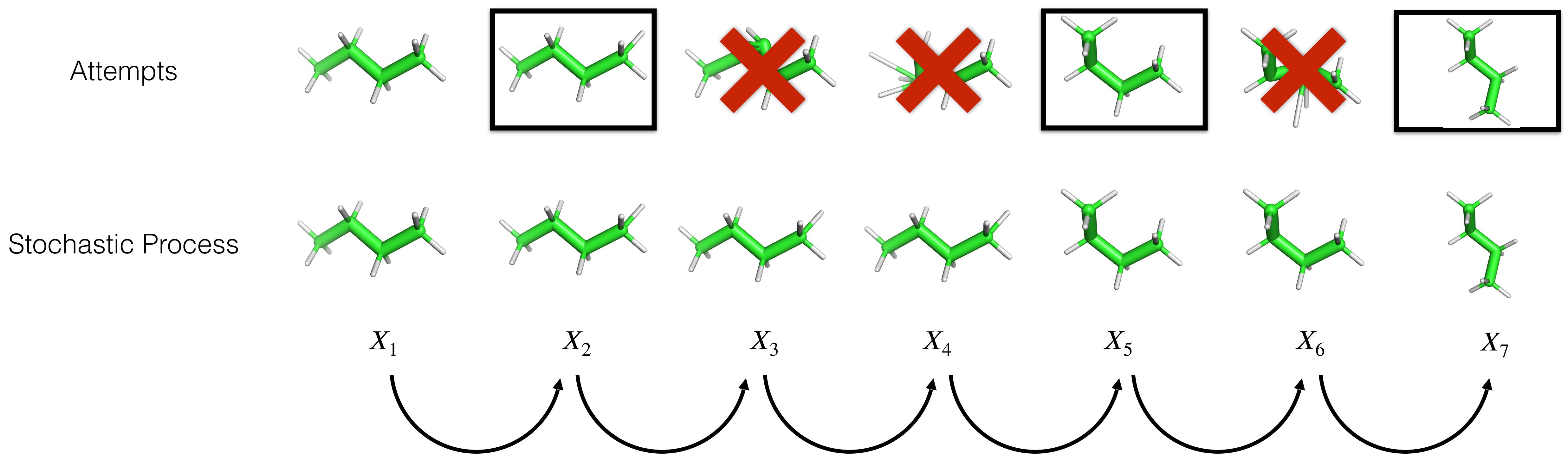
# The Metropolis Algorithm



$$\alpha(A \rightarrow B) = \min\left(1, \frac{\pi(B)Q(B \rightarrow A)}{\pi(A)Q(A \rightarrow B)}\right)$$



# Schematic Markov chain for Molecules



# The Metropolis–Hastings Acceptance Criterion

- Enforces detailed balance, causing stationary distribution to match target distribution

detailed balance

$$\pi(A)P(A \rightarrow B) = \pi(B)P(B \rightarrow A)$$

proposal  
distribution

$$\pi(A)Q(A \rightarrow B) \neq \pi(B)Q(B \rightarrow A)$$

correcting term

$$\pi(A)Q(A \rightarrow B)\alpha(A \rightarrow B) = \pi(B)Q(B \rightarrow A)\alpha(B \rightarrow A) \Leftrightarrow \frac{\alpha(A \rightarrow B)}{\alpha(B \rightarrow A)} = \frac{\pi(B)Q(B \rightarrow A)}{\pi(A)Q(A \rightarrow B)}$$

Metropolis-  
Hastings

$$\alpha(A \rightarrow B) = \min\left(1, \frac{\pi(B)Q(B \rightarrow A)}{\pi(A)Q(A \rightarrow B)}\right)$$

- With equal transition probabilities,
  - moves to higher probability (lower energy) are always accepted
  - moves to lower probability (higher energy) are sometimes accepted, depending on this ratio

# **Molecular Dynamics**

# What is Molecular Dynamics?

- Add energy to a system modeled by molecular mechanics and simulate its progress with time using Newton's second law of motion  $\vec{F} = ma$
- See 0:45 to 2:20 of “An Introduction to Molecular Dynamics” (<https://www.youtube.com/watch?v=ILFEqKI3sm4>)
- See a separation of alkane and water: <https://www.youtube.com/watch?v=xcMSHy3CqXA>

# Why do biological molecular dynamics?

- “everything that living things do can be understood in terms of the jigglings and wiggles of atoms” - Richard Feynman
- Check out David’s molecular dynamics YouTube playlist: [https://www.youtube.com/playlist?list=PLYEyeVFrqfAu0ft6sF4vVe5FOEbJYyi\\_L](https://www.youtube.com/playlist?list=PLYEyeVFrqfAu0ft6sF4vVe5FOEbJYyi_L)

# General MD Algorithm

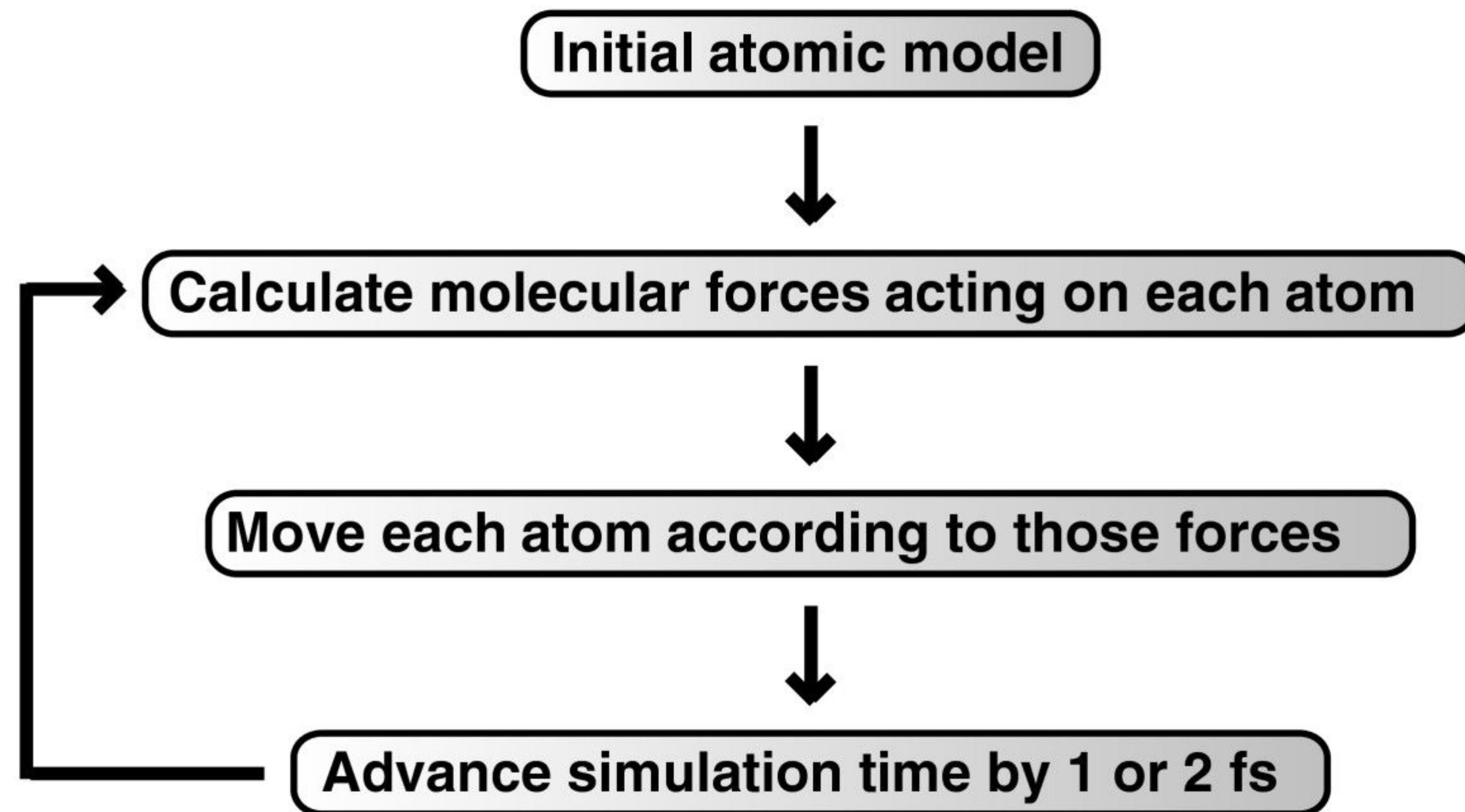


Figure 2 of Durrant & McCammon, 2011

# Some more MD details

- Integrator
  - Algorithm for moving atoms according to forces
  - Can be deterministic (e.g. velocity Verlet) or stochastic (e.g. Langevin)
  - Choice can affect numerical stability and time step
- Constraints
  - Degrees of freedom fixed to specific values
    - Lengths of bonds involving H
    - Rigid water
    - Torsional dynamics
  - Can allow for a larger time step [Spiridon & Minh, 2017]

# Fixing thermodynamic variables

- Thermostat
  - Maintains temperature
  - Part of integrator, e.g. Langevin dynamics, or separate Monte Carlo move
  - Andersen thermostat - periodically reinitialized velocity according to the Maxwell-Boltzmann distribution
- Barostat
  - Maintains pressure
  - Monte Carlo move that changes system volume

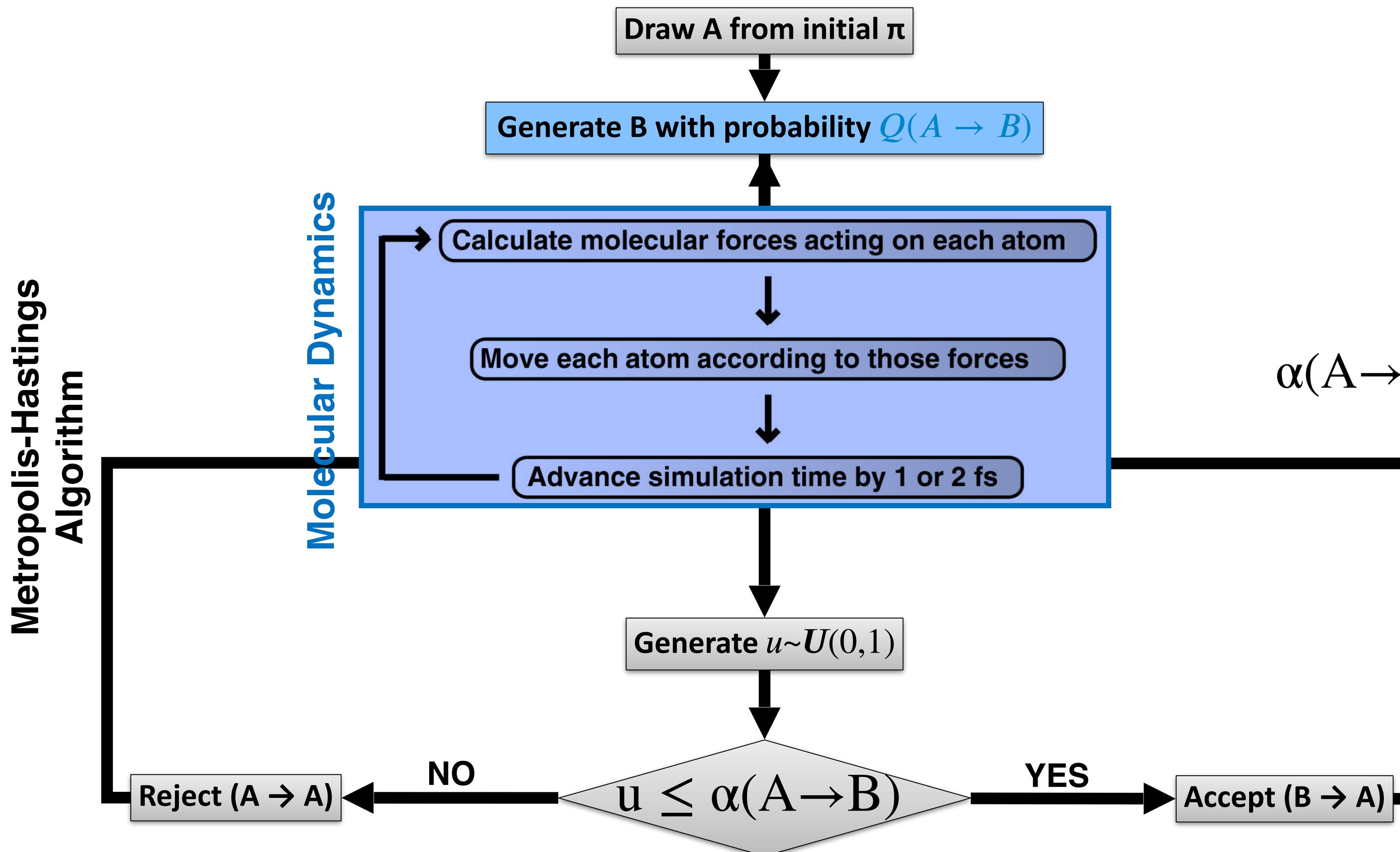
# **Molecular Dynamics and Markov Chain Monte Carlo**

Compare/contrast and combine

# Compare/Contrast

	MCMC	MD
Uses random numbers as its main tool	X	
Particles have velocity		X
Includes the Metropolis algorithm	X	
Allows the calculation of averages	X	X
In principle, has memory of its past		X

# Hybrid Monte Carlo



$$\alpha(A \rightarrow B) = \min \left( 1, \frac{\pi(B)Q(B \rightarrow A)}{\pi(A)Q(A \rightarrow B)} \right)$$

Duane, S.; Kennedy, A. D.; Pendleton, B. J.; Roweth, D. Hybrid Monte Carlo. Physics Letters B 1987, 195 (2), 216–222.

# Some specific types of HMC

- Nonequilibrium candidate Monte Carlo - use driven process, changing potential energy with time, to generate candidate configuration
- Constrained dynamics, e.g. torsional dynamics

Nilmeier, J. P.; Crooks, G. E.; Minh, D. D. L.; Chodera, J. D. PNAS Plus: Nonequilibrium Candidate Monte Carlo Is an Efficient Tool for Equilibrium Simulation. *Proceedings of the National Academy of Sciences of the United States of America* 2011, 108 (45), E1009–E1018. <https://doi.org/10.1073/pnas.1106094108>.

Spiridon, L.; Minh, D. D. L. Hamiltonian Monte Carlo with Constrained Molecular Dynamics as Gibbs Sampling. *Journal of Chemical Theory and Computation* 2017, 13 (10), 4649–4659. <https://doi.org/10.1021/acs.jctc.7b00570>.

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# **Exercise 8: Performing a Molecular Simulation with OpenMM**

<https://colab.research.google.com/github/daveminh/Chem456-2024F/blob/main/exercises/08-OpenMM.ipynb>