Simulations with MM Force Fields

Monte Carlo (MC)
and
Molecular Dynamics (MD)
Video II.vi

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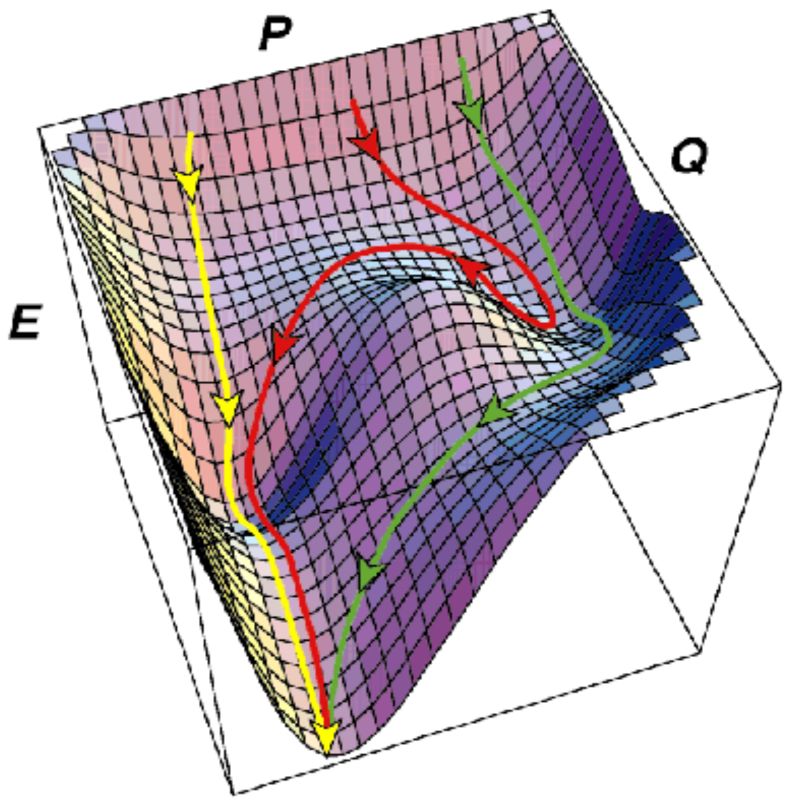
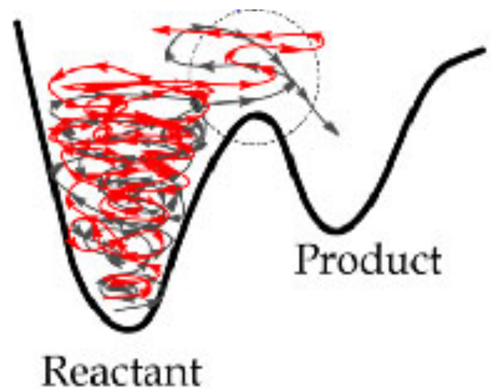
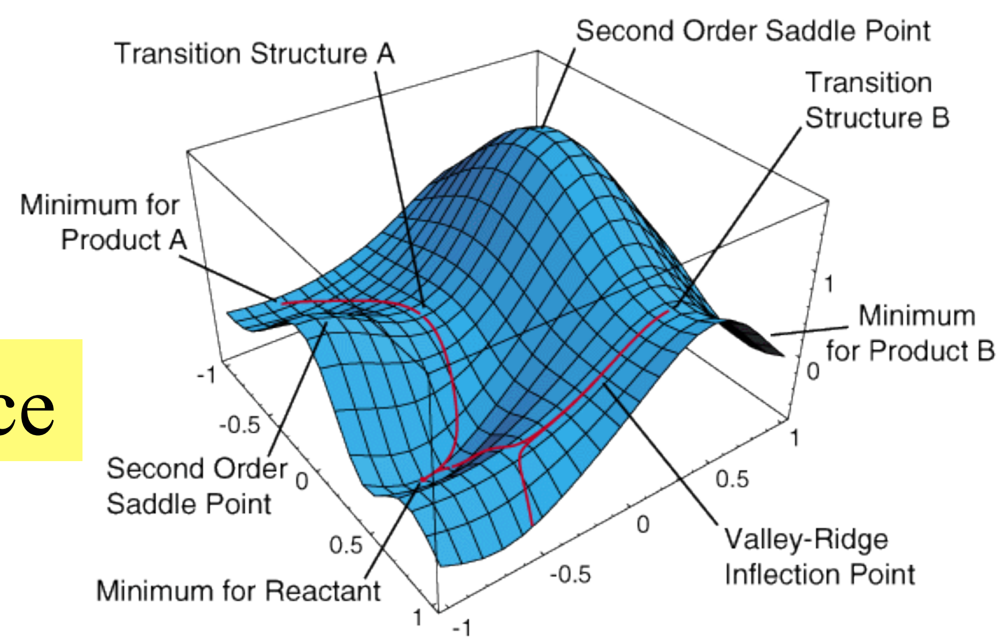
Walking on the Surface

We often draw in 1D, but we're hiding a lot.

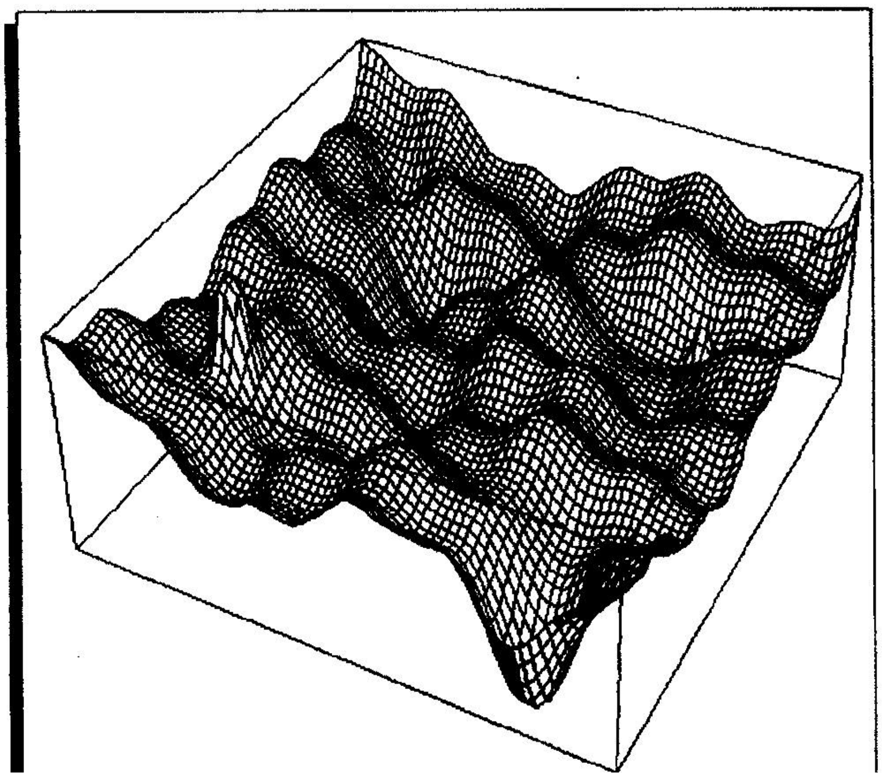






“Finding a Needle in a Haystack”

The lowest point on
The Energy Landscape
is the most stable point
(Global Minimum)



At Absolute Zero
a system in thermal equilibrium
must be at its global minimum

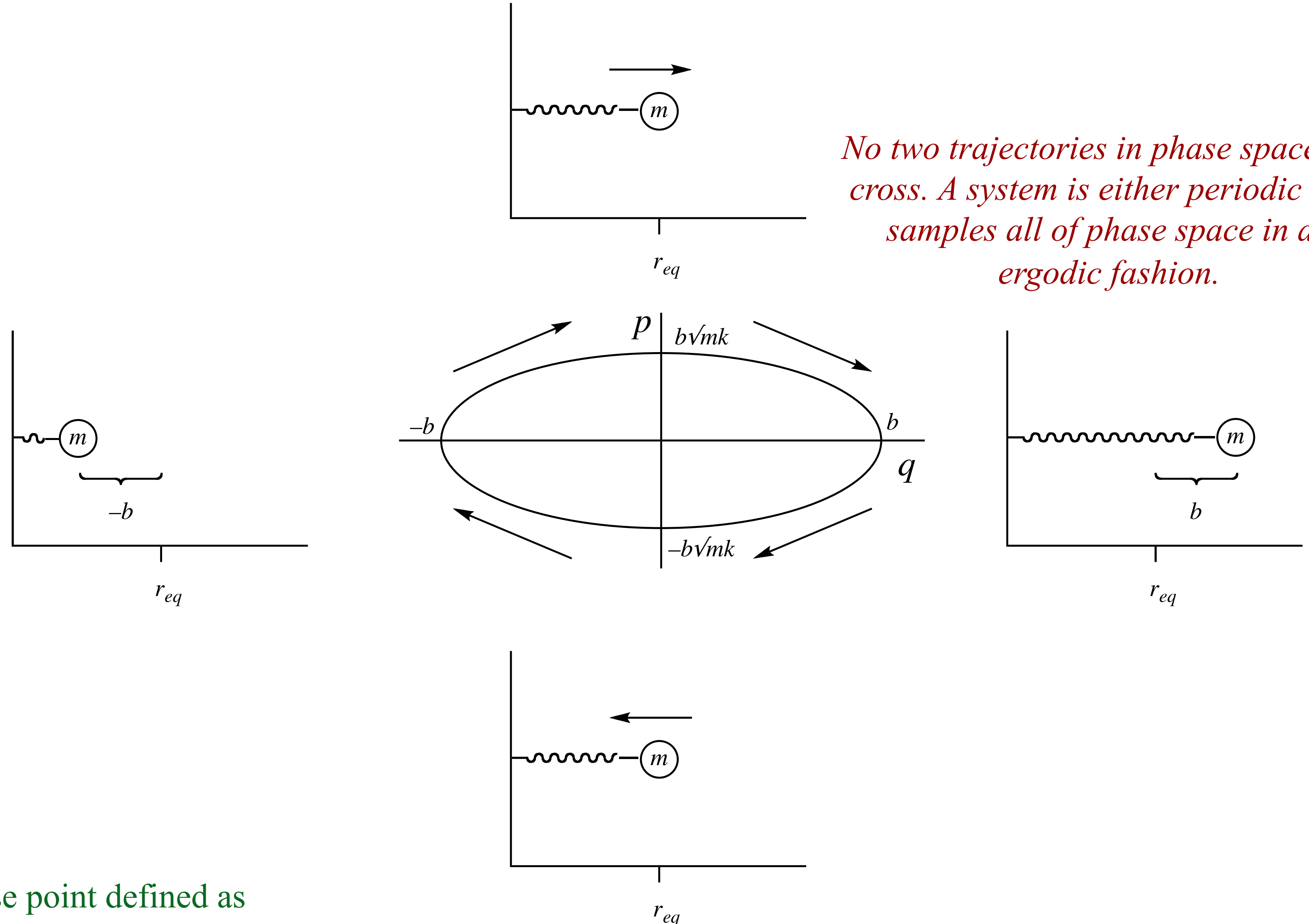
Increasing the efficiency of searching for the global minimum is an active area of research

Some Common Search Strategies
(Optimization Techniques)

1. **Systematically search all coordinates.**
   IMPOSSIBLE! ~ N^{100} (or so).
2. **Dynamics + "Quench"**
   Roam over the surface, occasionally sliding down to the nearest local minimum.
3. **Simulated Annealing**
   Heat the system up, and cool very slowly.
4. **Evolutionary/Genetic Algorithms**
   Allow "good" geometries to survive and to share properties, but "bad" ones to die.

#2 and **#3** require a discussion of Molecular Dynamics and Metropolis Monte Carlo Techniques

Phase Space — 1D Harmonic Oscillator



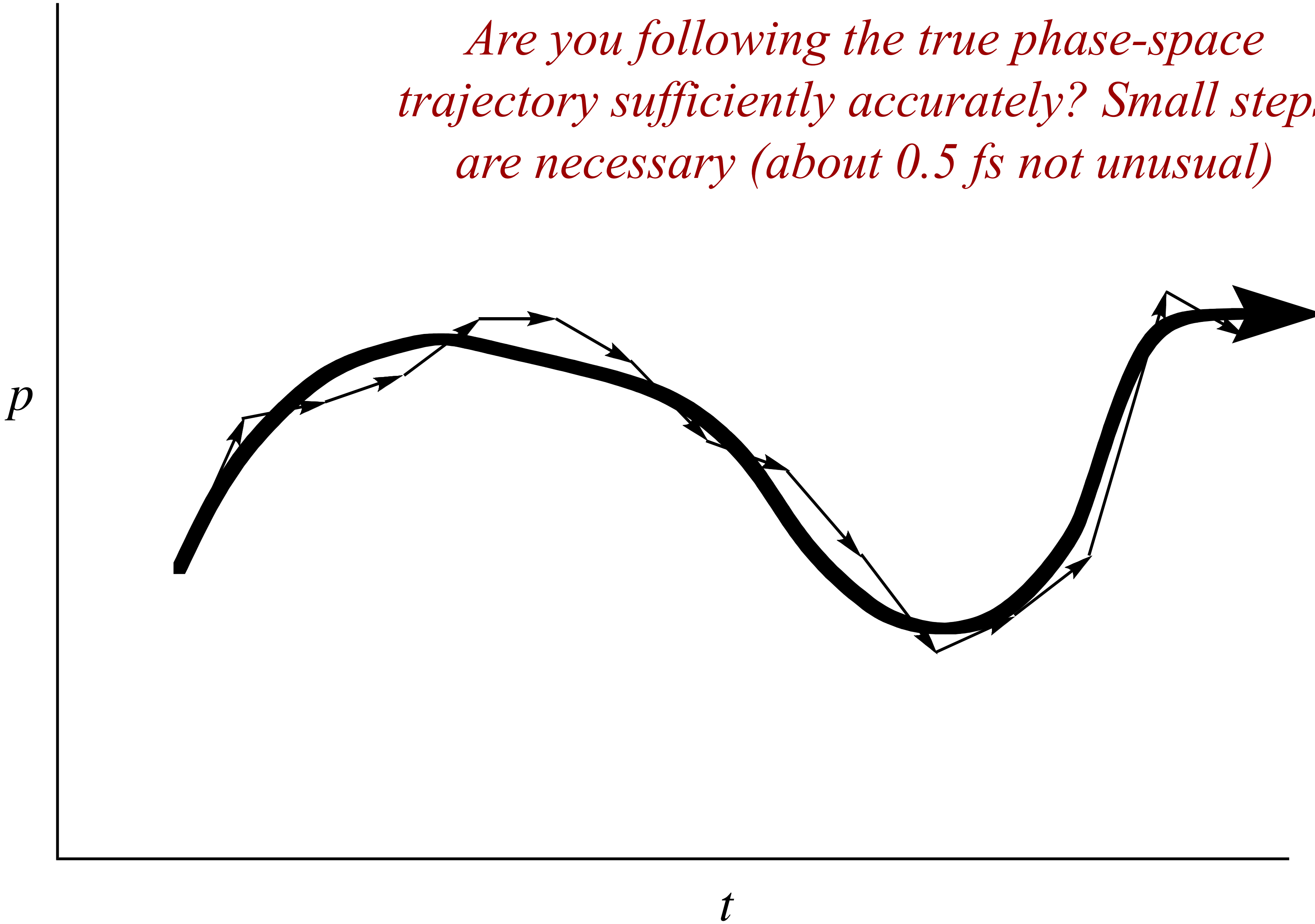
No two trajectories in phase space can cross. A system is either periodic or it samples all of phase space in an ergodic fashion.

Phase point defined as

$\mathbf{r} = (q,p)$ generalized for N particles as

$\mathbf{r} = (q_{1x}, q_{1y}, q_{1z}, p_{1x}, p_{1y}, p_{1z}, \ldots, q_{Nx}, q_{Ny}, q_{Nz}, p_{Nx}, p_{Ny}, p_{Nz})$

Are you following the true phase-space trajectory sufficiently accurately? Small steps are necessary (about 0.5 fs not unusual)



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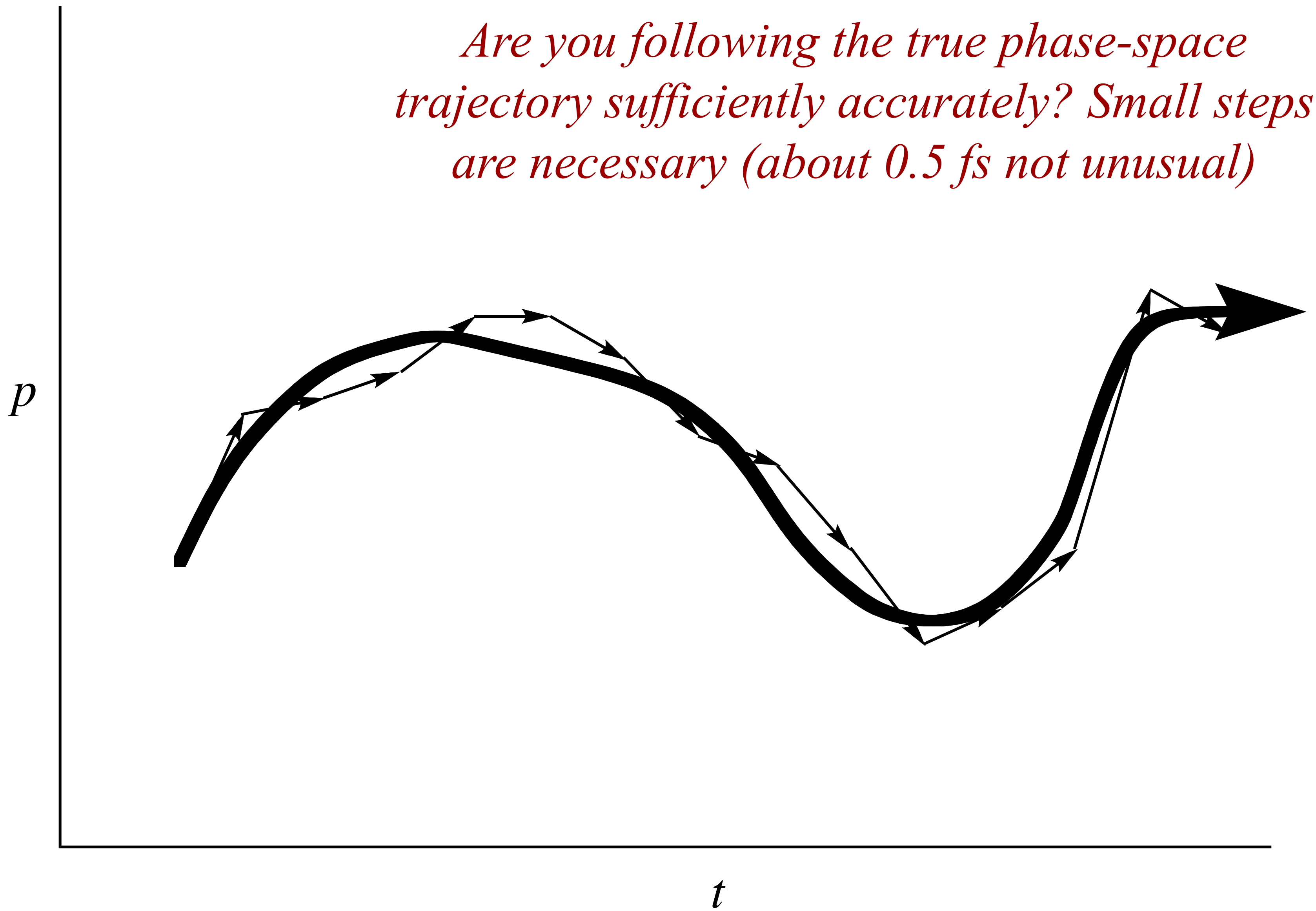


Integrating over Phase Space

$$\langle \Xi \rangle = \frac{\int_{\mathrm{PS}} \Xi(\mathbf{r}) P(\mathbf{r}) \mathrm{d}\mathbf{r}}{\int_{\mathrm{PS}} P(\mathbf{r}) \mathrm{d}\mathbf{r}}$$

Expectation values are dictated by the relative probabilities of being in different regions of phase space

$$P(\mathbf{r}) = e^{-E(\mathbf{q},\mathbf{p})/k_{\mathrm{B}}T} \qquad Q = \int_{\mathrm{PS}} P(\mathbf{r}) \mathrm{d}\mathbf{r}$$

Key point: Don't waste time evaluating Ξ(r) if *P*(r) is zero.

Difficulty: Phase space is 6*N*-dimensional. If you only want to sample all possible combinations of either positive or negative values for each coordinate (i.e., hit every "hyperoctant" in phase space *once*), you need 2^{6N} points!

Metropolis Monte Carlo:

For simplicity we work here with a property independent of momentum, thereby reducing the computational overhead by a factor of 2

Generates a thermal population of geometries

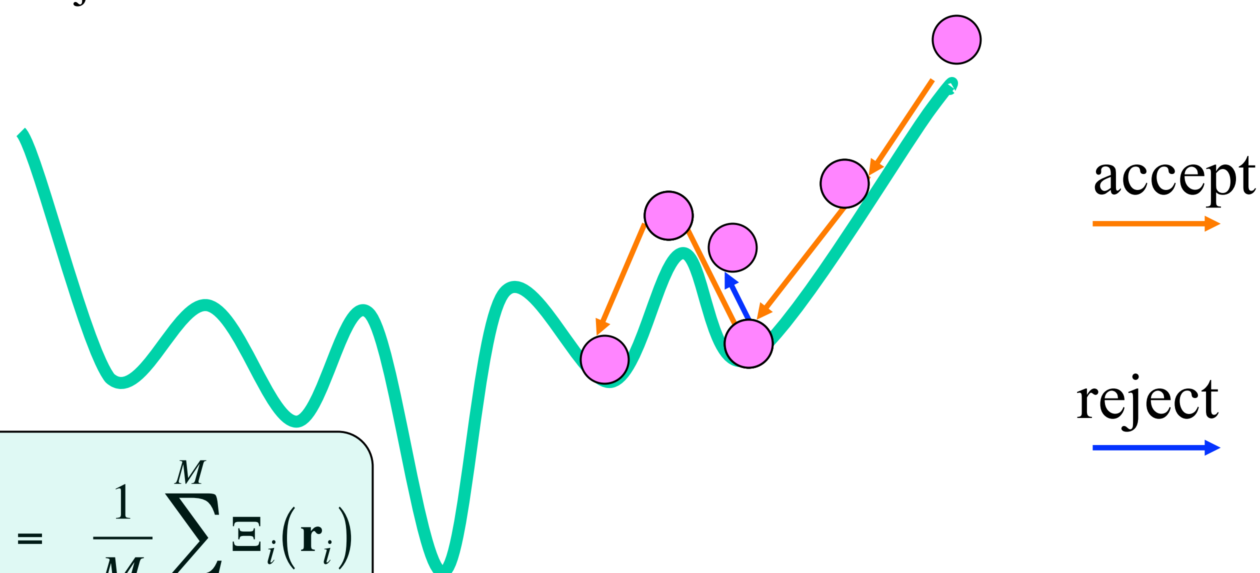
such that $n(\mathbf{r_1})/n(\mathbf{r_2}) = \exp(-[U(\mathbf{r_1})-U(\mathbf{r_2})]/k_BT)$

Boltzmann Distribution

Method.

1. Propose "move" $\mathbf{r_1} \rightarrow \mathbf{r_2}$
2. "Accept" move if (i) $U(\mathbf{r_1})<U(\mathbf{r_2})$

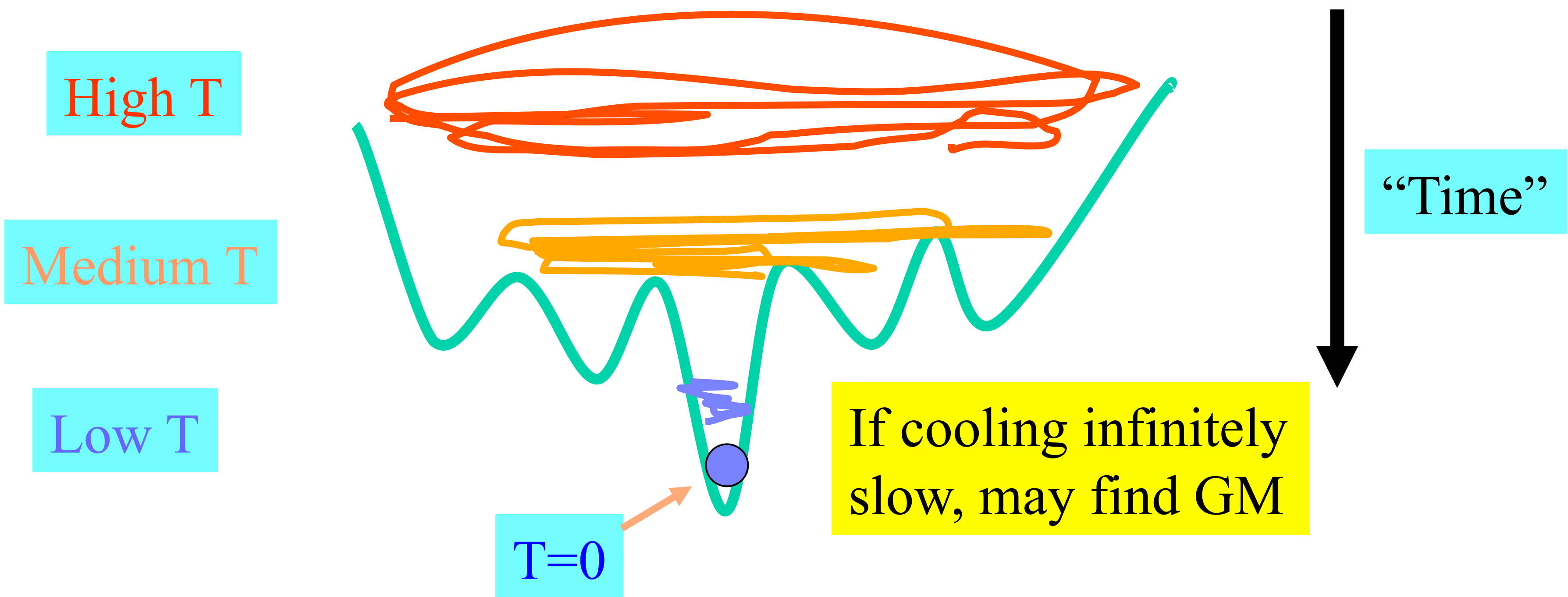
   (ii) $\exp[-(U(\mathbf{r_1})-U(\mathbf{r_2}))/k_BT]$ > random # ε[0,1]
3. Else "reject"



So, now $\langle \Xi \rangle = \frac{1}{M}\sum_{i=1}^{M} \Xi_i(\mathbf{r}_i)$

Simulated Annealing

Start at high temperature, then decrease temperature slowly with time.



Molecular Dynamics (MD)

Solve classical equations of motion from

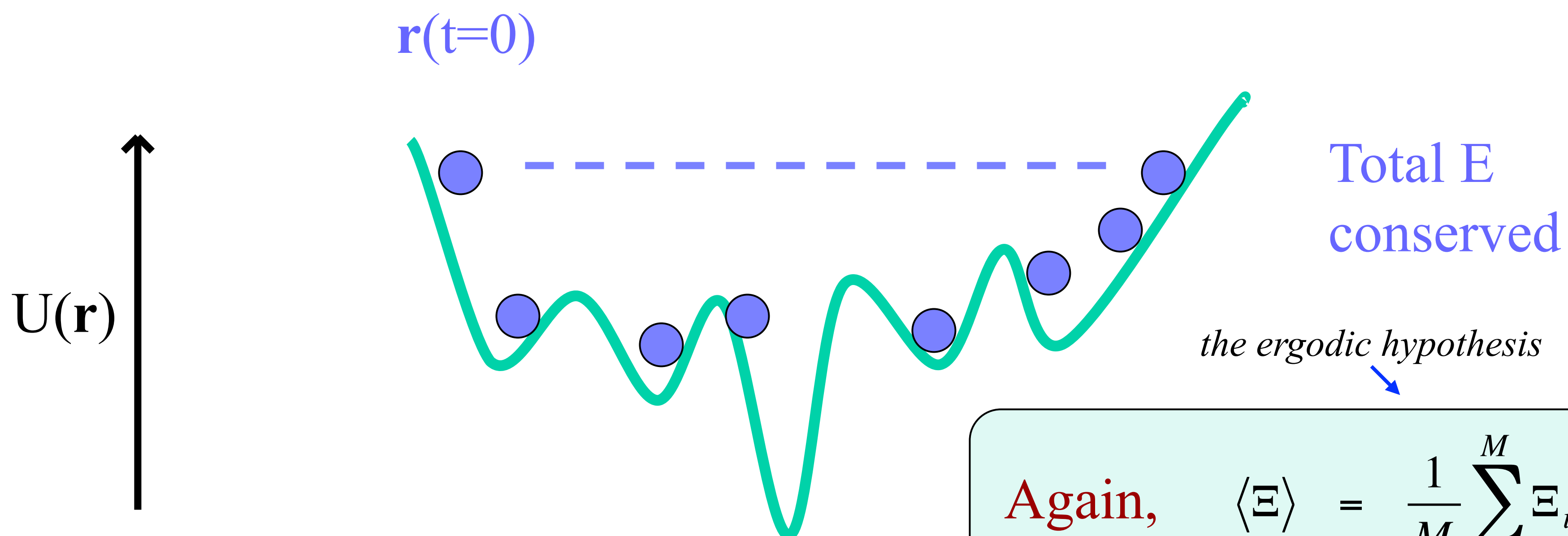
some initial geometry and velocity

r(0) → **r**(t) ; **v**(0) → **v** (t)

Newton's Law **F** = m**a** = -dU(**r**)/d**r**

Need **r**(0) ,**v**(0), U(**r**), dU/d**r**

v(0) from temperature (randomly distributed)

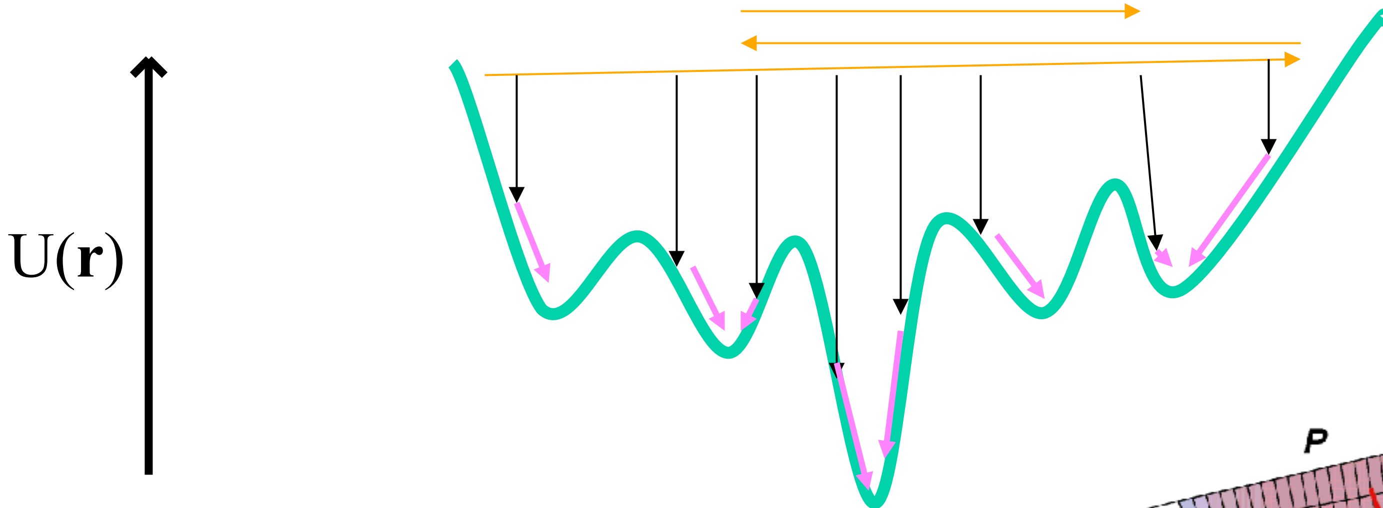


the ergodic hypothesis

Again, $$\langle \Xi \rangle = \frac{1}{M}\sum_{i=1}^{M} \Xi_i(\mathbf{r}_i)$$

High Energy Dynamics

to cross barriers freely

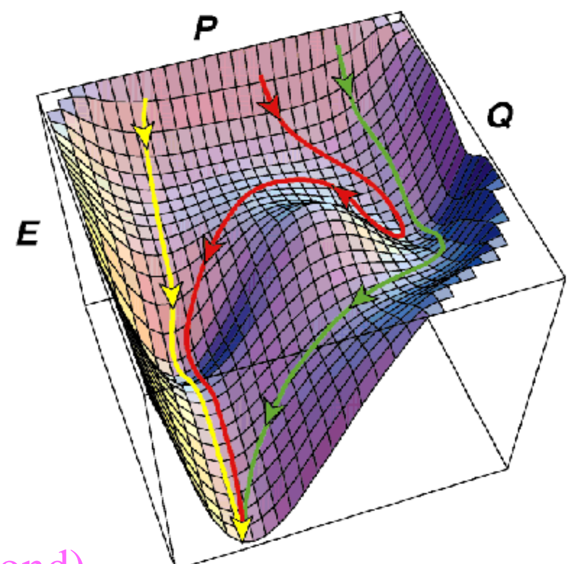


Occasional Quenches

Remove kinetic energy.

Slide from the current geometry down the steepest slope

(better, conjugate gradient)



Requires first (often second) derivatives.

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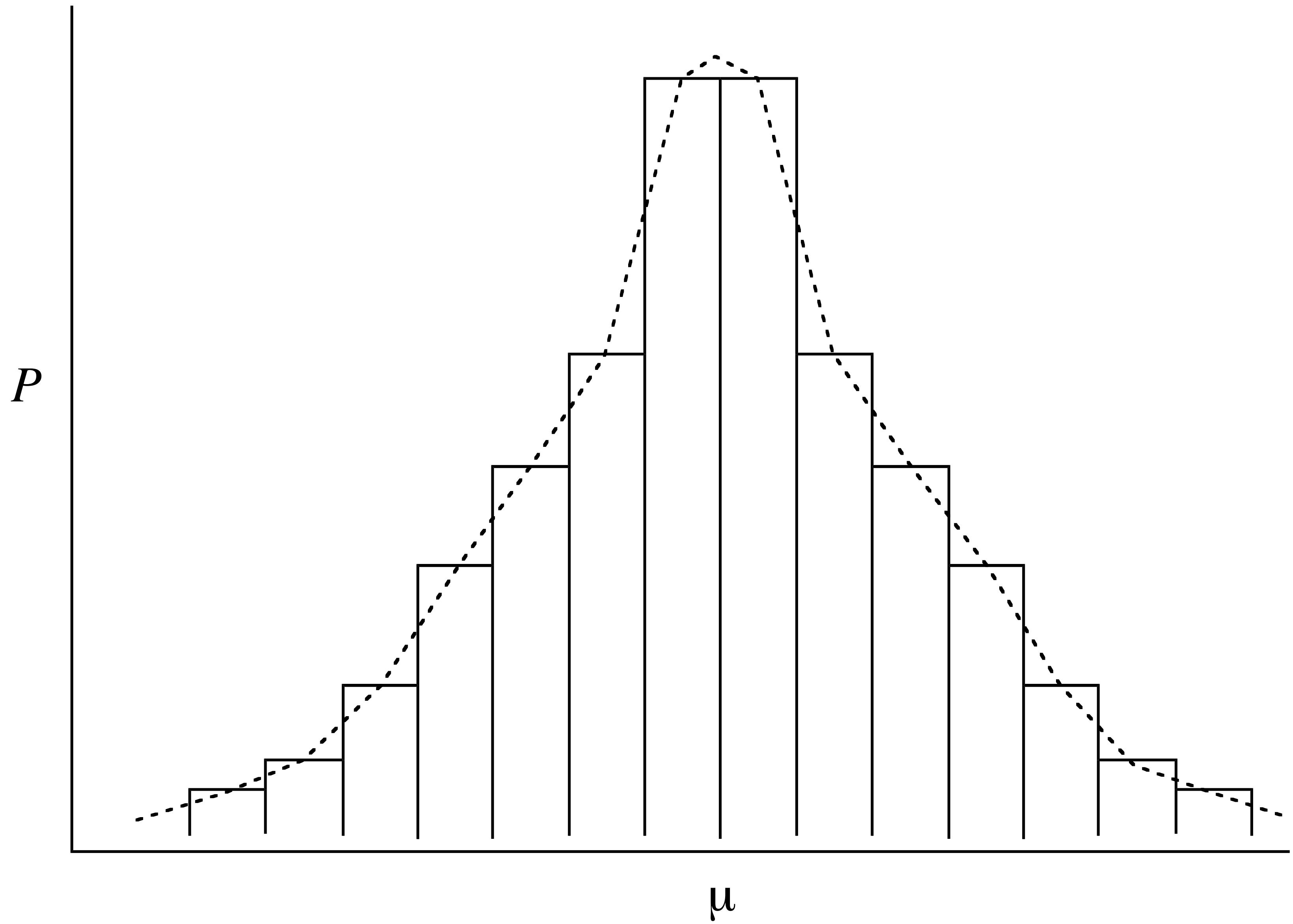
Nota bene: the standard deviation in an expectation value is not (necessarily) an error, but may instead be a manifestation of dynamical variation



Molecular Dynamics

Simulation yields **r**(t), **v**(t), U(**r**(t)),
correlation functions

➔ Dynamic structure (e.g. does reaction happen?)

➔ Transport properties (D, viscosity, etc)

Molecular Dynamics

Using “tricks” can be made to run at:

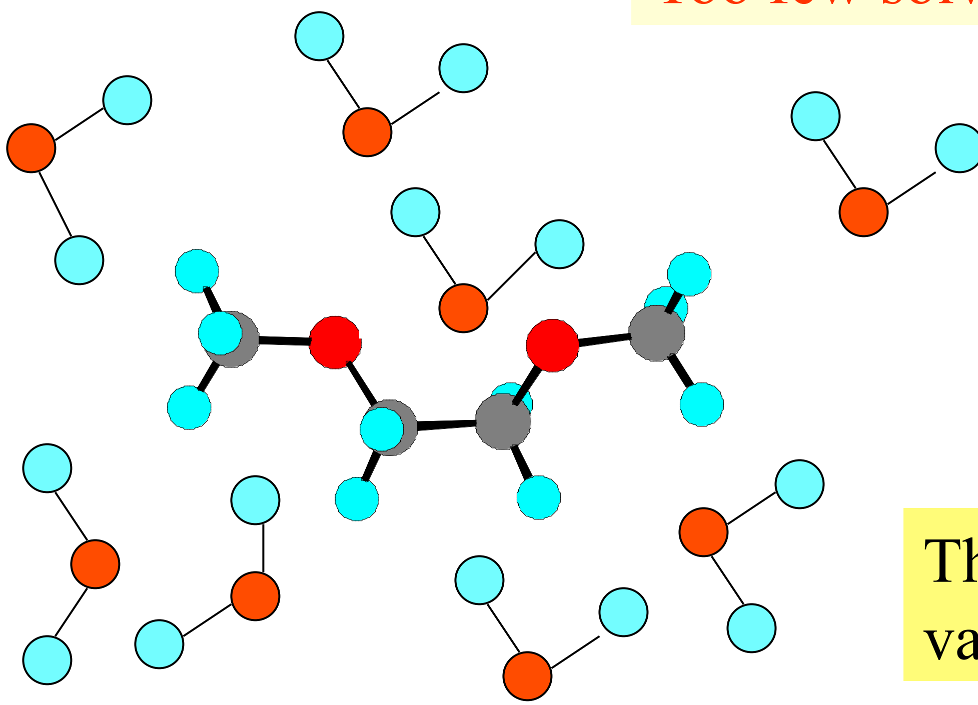
- constant T,
- constant P,

or combinations thereof.

(Keywords: Statistical mechanical ensemble;
heat bath; thermostats; pistons)

"Tricks" in Simulations, continued…

Problem!
Too few solvent molecules!

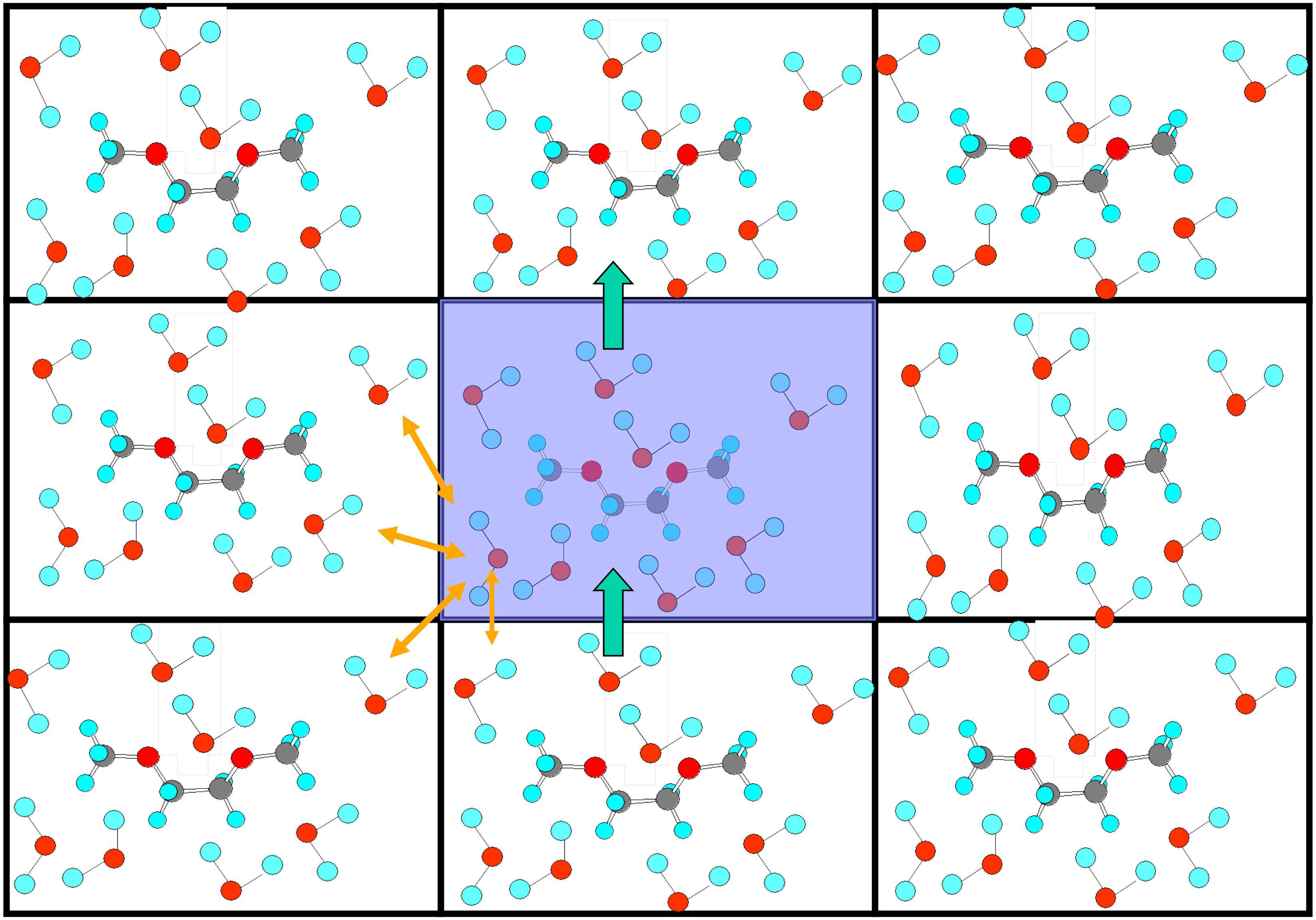


The solvent sees vacuum, not bulk.

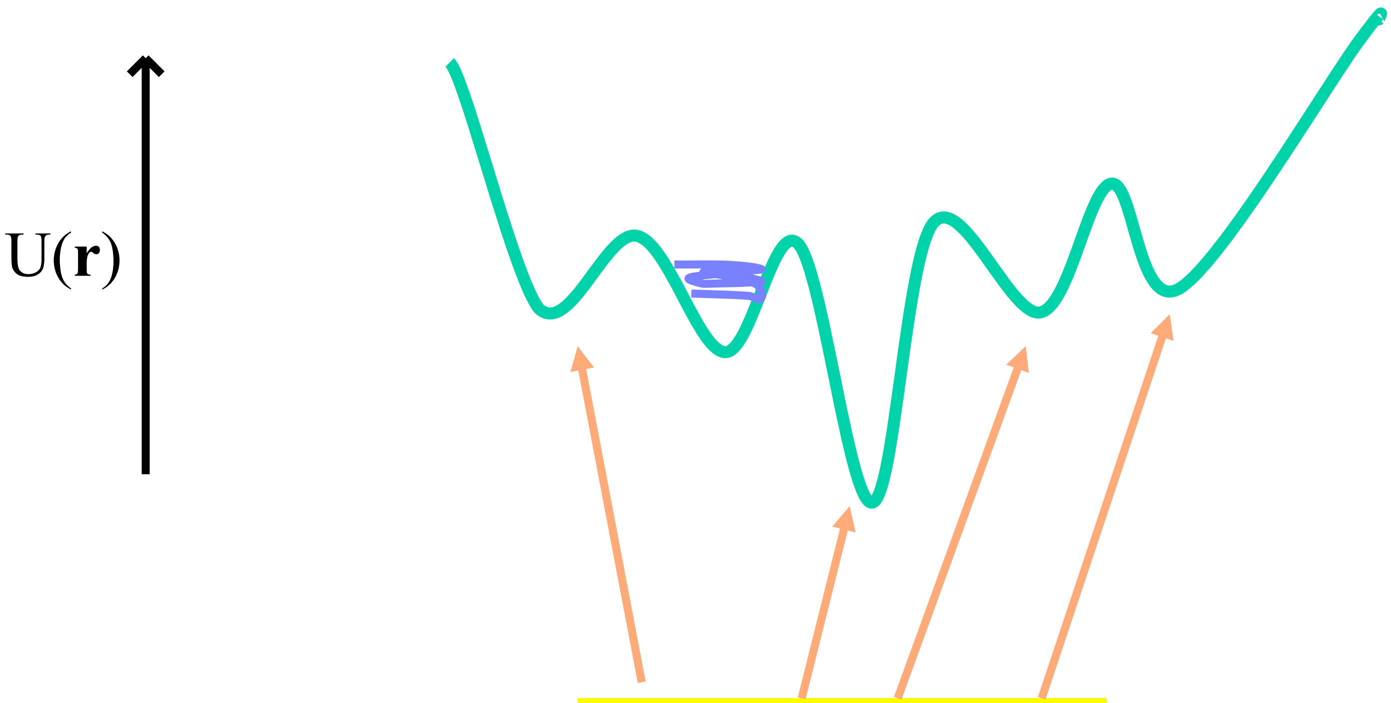
Adding more solvent molecules increases computational effort!

Periodic Boundary Conditions

Make the system thinks it's larger than it really is.



Problem with MD and Monte Carlo
"Quasi-Ergodic" Sampling Problem



Low T
Trapped by barriers in finite runs

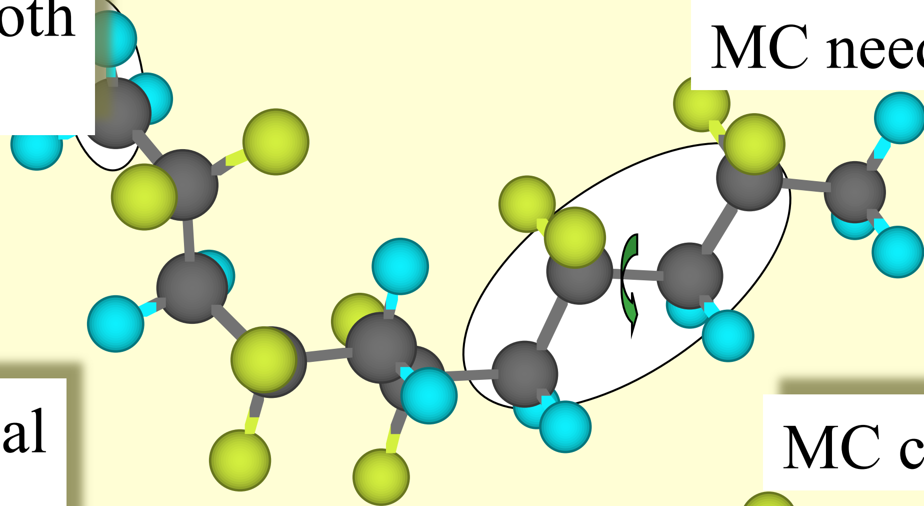
However, all these wells are thermally accessible

Solution 1
Nature's Solution
Run $t \rightarrow \infty$

What method to use?

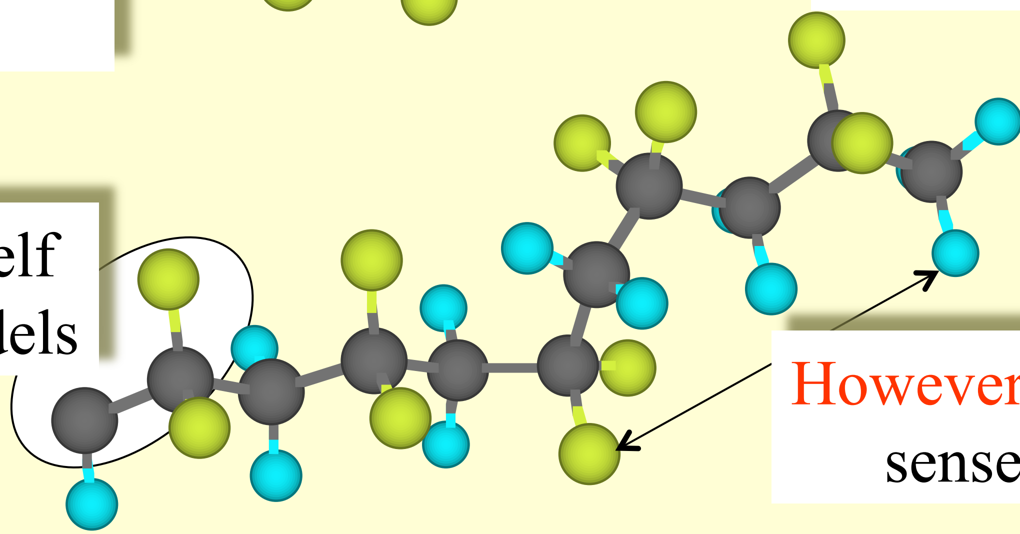
MD needs smooth derivatives

MC needs no derivatives



MD needs global updates

MC can use local updates

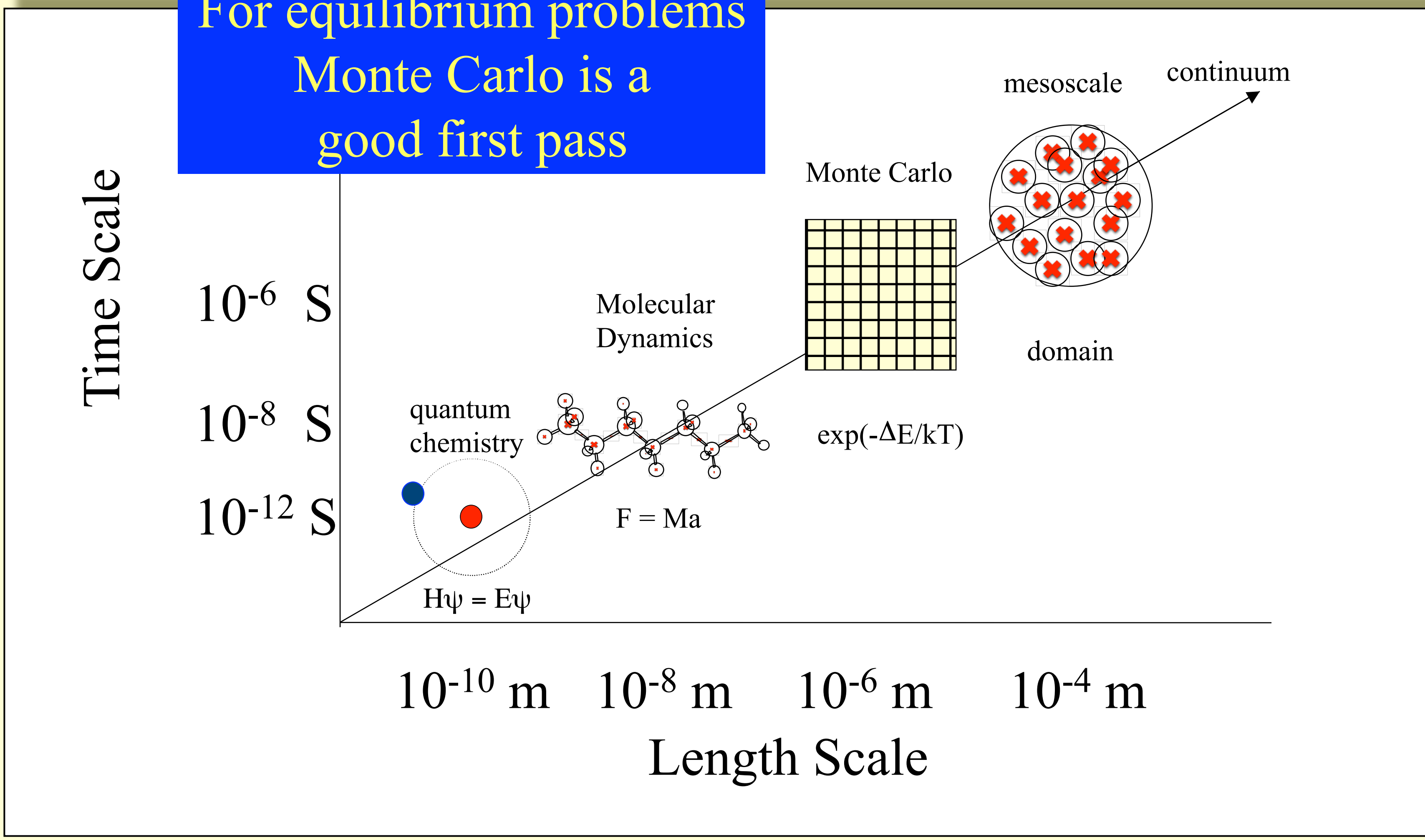


MC lends itself to simple models

However, MC has no sense of time!

So, What Method To Use?

For equilibrium problems
Monte Carlo is a
good first pass



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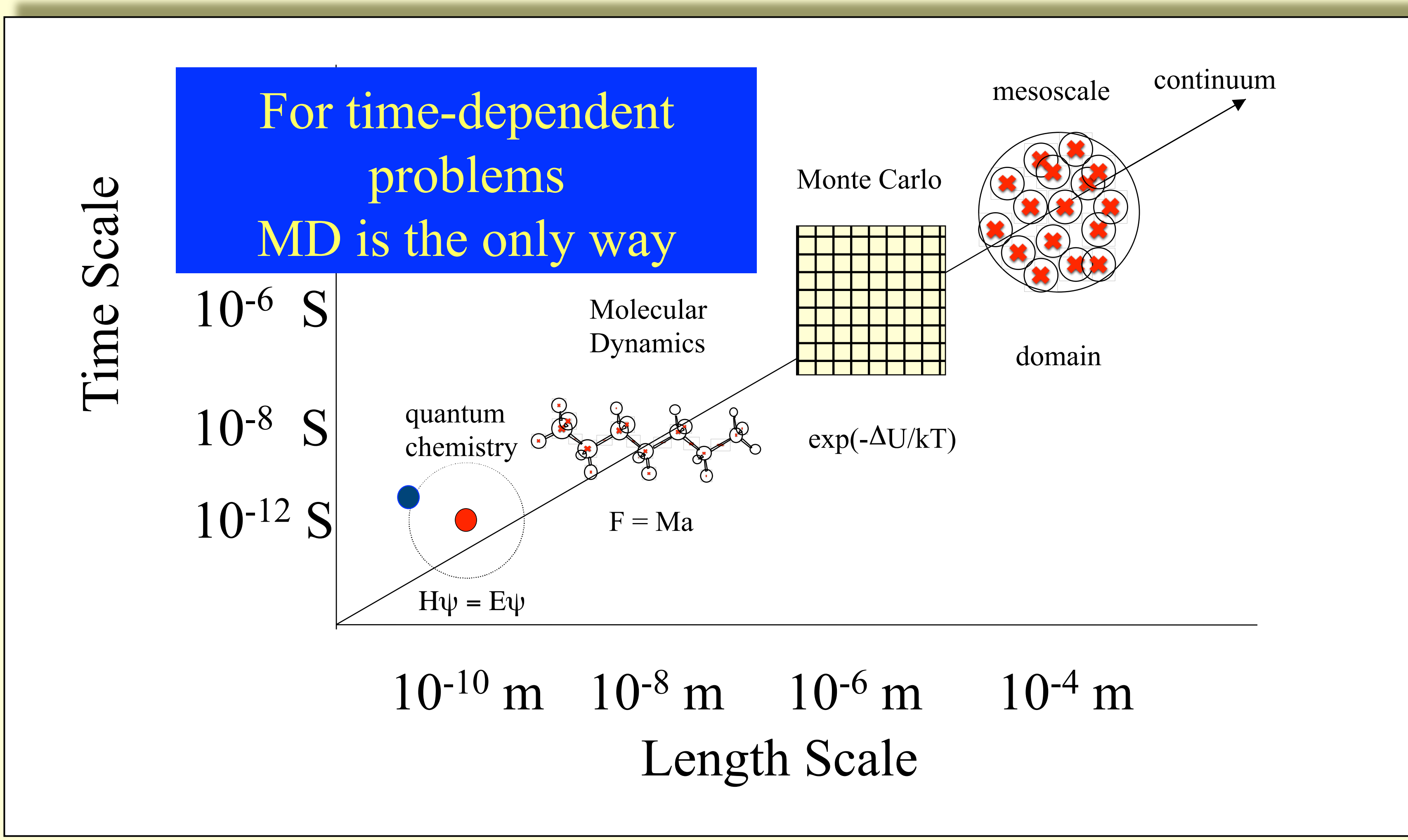

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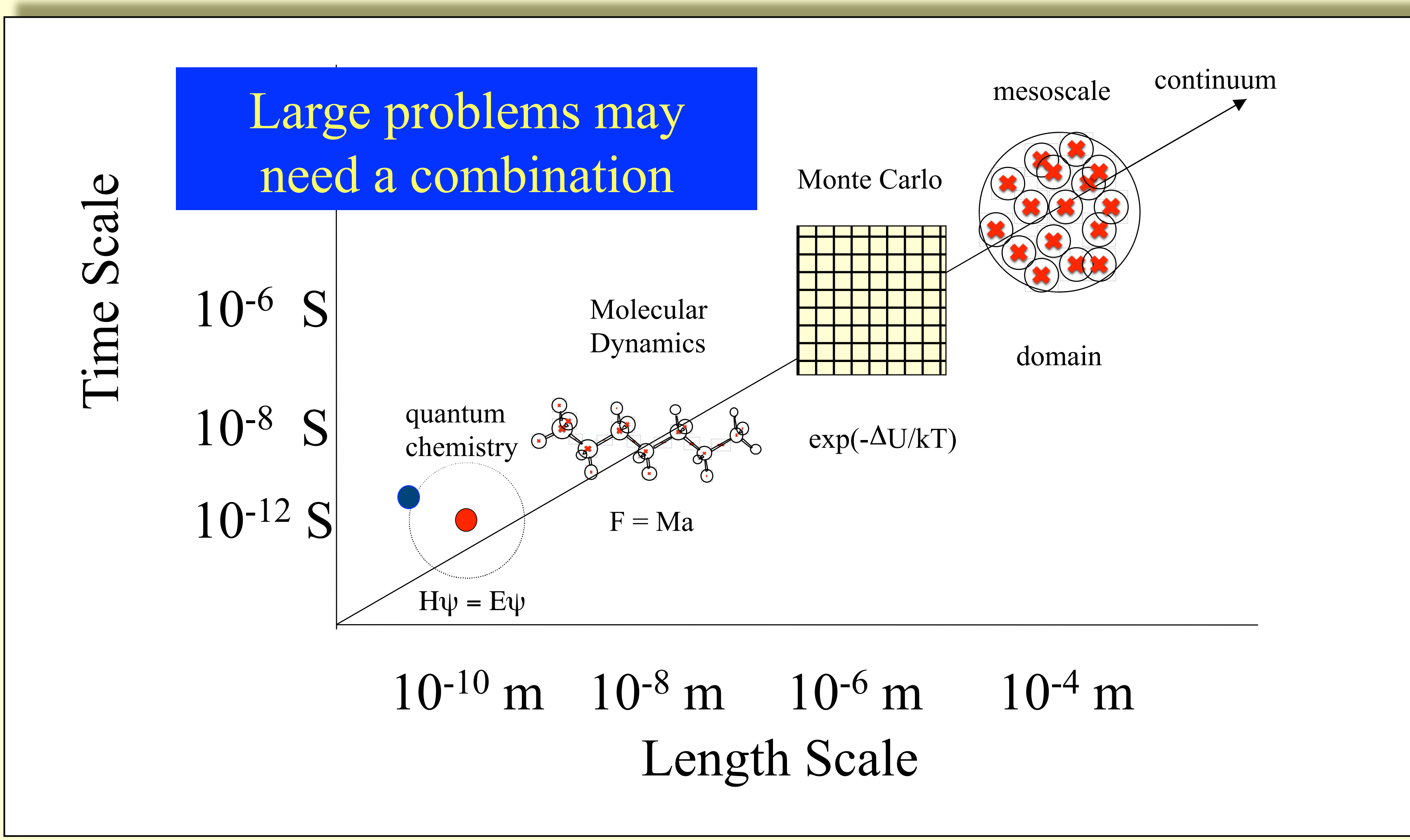

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