Transition Paths for Molecular Motion: What are the Characteristics of the Most Probable Paths (MPPs)?

And how (un)physical are these MPPs?

Frank J. Pinski

Department of Physics, University of Cincinnati

Andrew Stuart

Mathematics Institute, University of Warwick

Abstract

- We explore transition paths of particles moving across energy barriers.
- The underlying motion is described by Brownian Dynamics, the overdamped limit of Langevin's equations.
- The density of paths is governed by a well-known probability measure.
- For a variety of models, we use gradient descent to find the Most Probable Paths (MPPs), paths that exist at a probability maximum.
- In the talk, we will describe characteristics of such paths. Some are unexpected; others can be anticipated.
- Many of the features of paths in Lennard-Jones Clusters are also seen in simple one- and two-dimensional models, giving a framework for a discussion of our findings.

Outline

- **Introduction**
- **Brownian dynamics**
- **Onsager-Machlup functional**
- **Continuum limit: path space**
- **Path sampling**
- **Steepest descent -- and the characteristics of MPPs**
- **Illustrative Models**
  - 1-d and 2-d, vacancy assisted diffusion, L-J Clusters
- **Summary**

Introduction

- Derive a mathematical framework for the sampling of path space, in which the Onsager-Machlup functional plays a central role.
- Other approaches: Transition Path Sampling, String Methods, etc. I will not try to review the long history.
- The approach taken here is to employ a Langevin equation in path space, based on Brownian Dynamics as a way to sample paths that are conditioned to cross a relevant free-energy barrier.
- Define the Most Probable Path (MPP) as the path that generates the maximum probability.
- This MPP does not have all the properties of an actual path - e.g. it is twice differentiable. But what do they look like?
- In some cases, these MPPs are simply strange.

SDE Langevin Equation

Newton's equations $$\frac{d\mathbf{r}_i}{dt} = \frac{\mathbf{p}_i}{m_i} \qquad \frac{d\mathbf{p}_i}{dt} = \mathbf{F_i} - \gamma\,\mathbf{p}_i + \mathbb{R}_i$$

where $\mathbb{R}_i$ is a random force and γ is the damping coefficient.

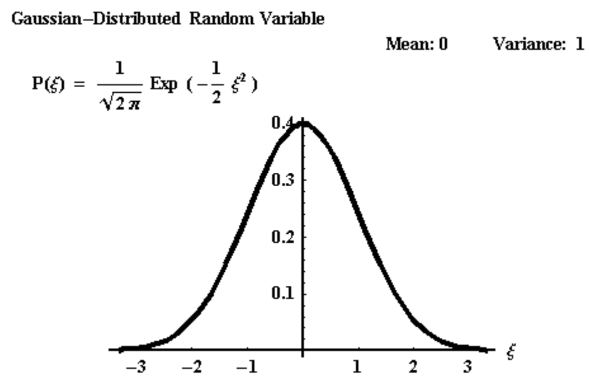
Over-damped case: $$\frac{d\mathbf{r}_i}{du} = \gamma\, m_i \frac{d\mathbf{r}_i}{dt} = \mathbf{F}_i + \mathbb{R}_i$$

Rescale time, use white noise and the fluctuation-dissipation theorem:

$$\frac{dr_{i\alpha}}{du} = F_{i\alpha} + \sqrt{2kT}\,\frac{dW}{du} = kT\,\frac{\partial \log P_B}{\partial r_{i\alpha}} + \sqrt{2kT}\,\frac{dW}{du}$$

Finite realization: $$r_{n+1\,i\alpha} = r_{n\,i\alpha} + \Delta u\; F_{n\,i\alpha} + \sqrt{2\Delta u\, kT}\;\; \xi_{in\alpha}$$

Gaussian Random Numbers GRN



Brownian Motion: $\mathbf{F}_{i\alpha} = 0$

Boltzmann factor

$$P_B(\{\mathbf{r}_i\}) = Z^{-1} e^{-E/kT}$$

SDE: Original application of the Langevin method

$$\frac{dr_{i\alpha}}{d\,u} = kT\,\frac{\partial \log P_B}{\partial r_{i\alpha}} + \sqrt{2\,kT}\,\frac{dW}{du}$$

$$r_{i\alpha}(u+\Delta u) = r_{i\alpha}(u) + \Delta u\,F_{i\alpha}(u) + \sqrt{2\,\Delta u\,kT}\;\xi_u$$

GRN $P_G(\xi_u) = \frac{1}{\sqrt{2\pi}}\,e^{-\frac{1}{2}\xi_u^2}$ $\xi_u^2 = \frac{\Delta u}{2\,kT}\left(\frac{\Delta r_{i\alpha}}{\Delta u} - F_{i\alpha}\right)^2$

Onsager-Machlup functional for the path probability

$$\log \Pi_p = C - \frac{\Delta u}{4kT}\sum\left(\frac{\Delta r_{i\alpha}}{\Delta u} - F_{i\alpha}\right)^2$$

Onsager-Machlup functional

$$\log \Pi_p = C - \frac{\Delta u}{4kT} \sum \left(\frac{\Delta r_{i\alpha}}{\Delta u} - F_{i\alpha} \right)^2$$

Continuum Limit - Stratonovich Integral

$$\Pi_p^c \approx \exp\left(- \frac{\Gamma}{2kT} \right) \qquad G = \sum_{i\alpha} \left\{ \frac{1}{2} F_{i\alpha}^2 + kT \frac{\partial F_{i\alpha}}{\partial r_{i\alpha}} \right\}$$

$$\Gamma = \int_0^U du \left\{ \frac{1}{2} \sum_{i\alpha} \left\{ \left(\frac{\partial r_{i\alpha}}{\partial u} \right)^2 - F_{i\alpha} \frac{\partial r_{i\alpha}}{\partial u} \right\} + G \right\}$$

Conservative Forces (informally) Measure - Girsanov Formula

$$\Gamma = \frac{1}{2} (V(U) - V(0)) + \int_0^U du \left\{ \frac{1}{2} \left(\sum_{i\alpha} \frac{\partial r_{i\alpha}}{\partial u} \right)^2 + G \right\}$$

$$G = \sum_{i\alpha} \frac{1}{2} \left(\frac{\partial V}{\partial r_{i\alpha}} \right)^2 - kT \frac{\partial^2 V}{\partial r_{i\alpha}^2}$$

Remember the Langevin equation (original SDE)

$$\frac{dr_{i\alpha}}{du} = kT\,\frac{\partial \log P_B}{\partial r_{i\alpha}} + \sqrt{2kT}\,\frac{dW}{du}$$

SPDE describes the sampling of paths

$$\Pi_p = C\exp\left(-\frac{\Gamma}{2kT}\right) \qquad \Gamma = \int_0^U du\left\{\frac{1}{2}\left(\sum_{i\alpha}\frac{\partial r_{i\alpha}}{\partial u}\right)^2 + G\right\}$$

$$\frac{\partial r_{i\alpha}}{\partial t} = 2kT\,\frac{\partial \log \Pi_p}{\partial r_{i\alpha}} + \sqrt{4kT}\,\frac{dw}{dt}$$

$$\frac{\partial r_{i\alpha}}{\partial t} = \frac{\partial^2 r_{i\alpha}}{\partial u^2} - \frac{\partial G}{\partial r_{i\alpha}} + \sqrt{4kT}\,\frac{dw}{dt}$$

SPDE Stuart, Voss, Wiberg

where

$$G = \sum_{i\alpha}\frac{1}{2}\left(\frac{\partial V}{\partial r_{i\alpha}}\right)^2 - kT\,\frac{\partial^2 V}{\partial r_{i\alpha}^2}$$

Advantage of the SPDE: every path can be conditioned to start in one Free Energy basin and end in another

Most Probable Paths MPPs

What Path Minimizes $\Gamma = \int_0^U du \left\{ \frac{1}{2} \left(\sum_{i\alpha} \frac{\partial r_{i\alpha}}{\partial u} \right)^2 + G \right\}$?

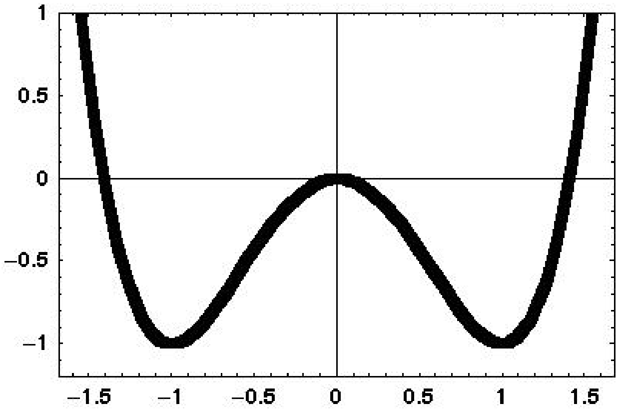
This is what we call the MPP (most probable path).
It is a path that is never realized; the MPP is twice differentiable. Actual paths are almost nowhere differentiable.

How do we find the MPP? We use gradient descent:

$$\frac{\partial r_{i\alpha}}{\partial t} = \frac{\partial^2 r_{i\alpha}}{\partial u^2} - \frac{\partial G}{\partial r_{i\alpha}}$$

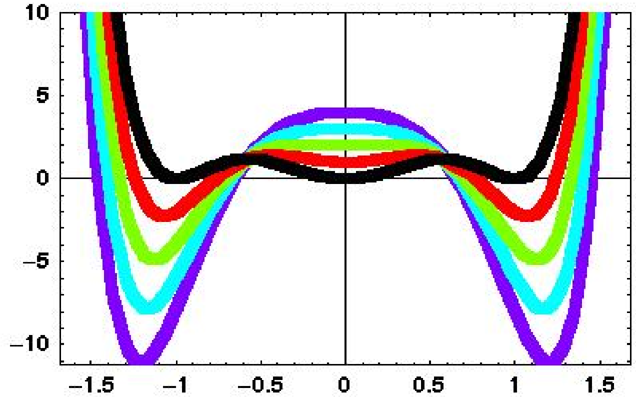
Using Crank-Nicolson, and other Numerical Techniques

1-d Double Well



V(x)

G(x)



Black: T=0 Purple: T=1
various Temperatures

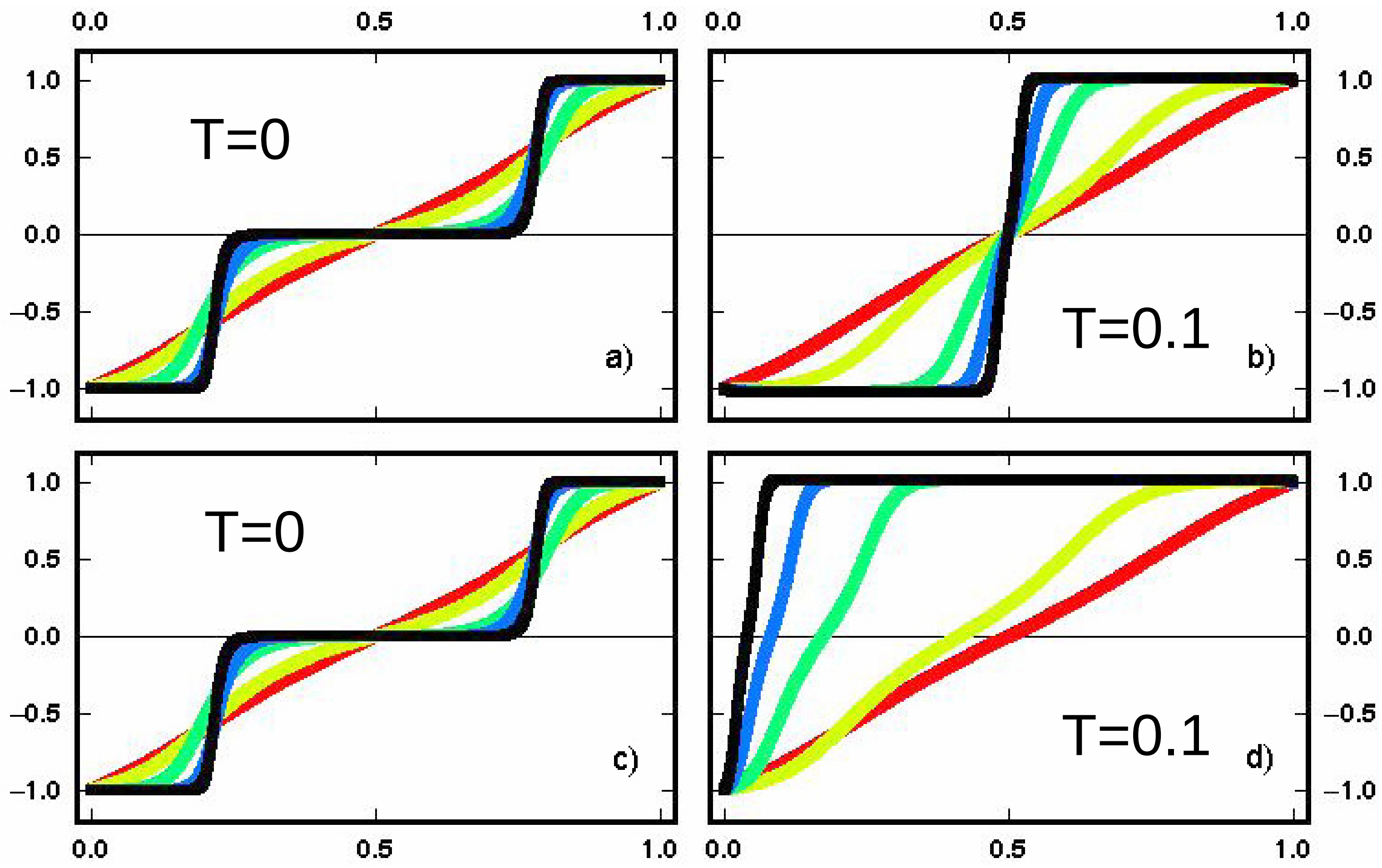
Paths x(u): Various Lengths (U) U = 20 (Black),10, 5, 2, 1 (Red)

T=0

T=0.1

QuickTime™ and a
TIFF (LZW) decompressor
are needed to see this picture.

Paths x(u)   Various Lengths (U)   U = 20,10, 5, 2, 1



1-d

Symmetric

Asymmetric
δV=0.01

Barrier energy E≈1

When T>0:

Small asymmetry in the potential - Large asymmetry in the Path

2-d Potential

y

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x

Path - diverging

y

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x

$$V(x, y) = \frac{1}{4}\left(1 - x^2\right)^2 + \frac{y^2}{2}\left(1 + x^2\right)$$

$$G(0, y) = -\left(T - \frac{1}{2}\right) y^2$$

Minimizing when T > 1/2

$$\Gamma = \int_0^U du \left\{ \frac{1}{2} \left(\sum_{i\alpha} \frac{\partial r_{i\alpha}}{\partial u} \right)^2 + G \right\}$$

The minimization emphasizes the places where G is “smallest” the most negative

2-d Potential

Minimize

$$\Gamma = \int_0^U du \left\{ \frac{1}{2} \left(\sum_{i\alpha} \frac{\partial r_{i\alpha}}{\partial u} \right)^2 + G \right\}$$

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The minimization emphasizes the places where G is “smallest” the most negative

Paths “Direct” “Circular”

T=0

T=0

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T=0.01

T=0.1

T=0.1

LJ_7 in 2 spatial dimensions

P. Bolhuis, C. Dellago and D. Chandler

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TIFF (LZW) decompressor
are needed to see this picture.

T=0.4

E

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are needed to see this picture.

T=0

u

Energy along the path

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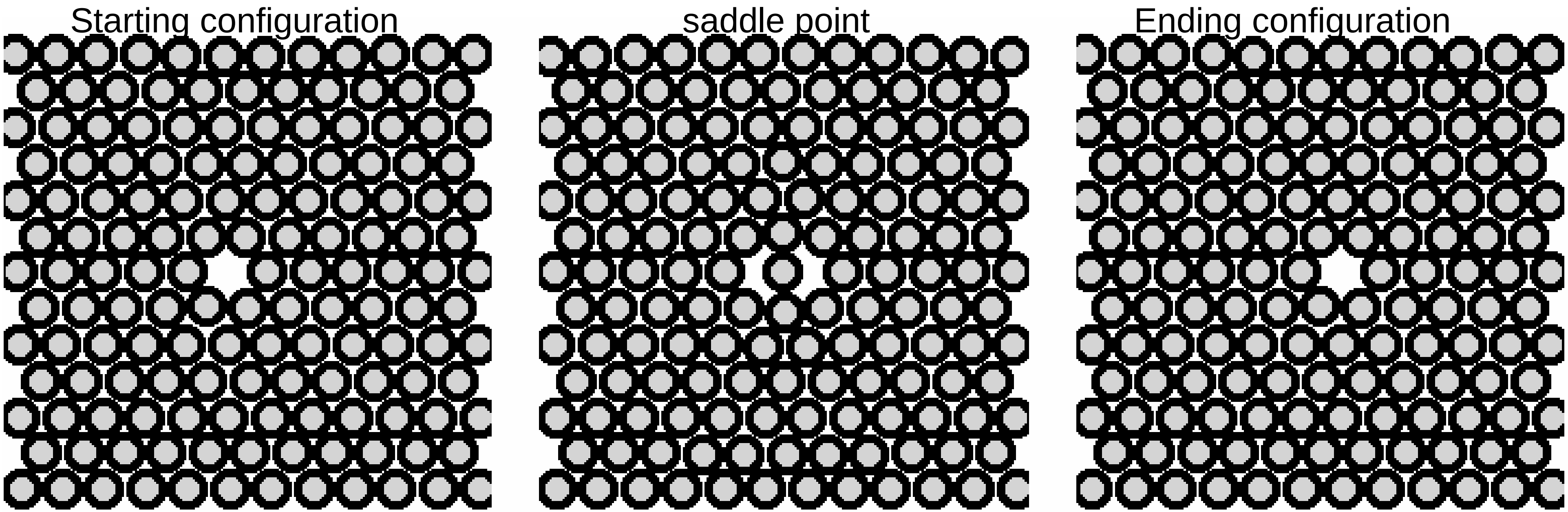
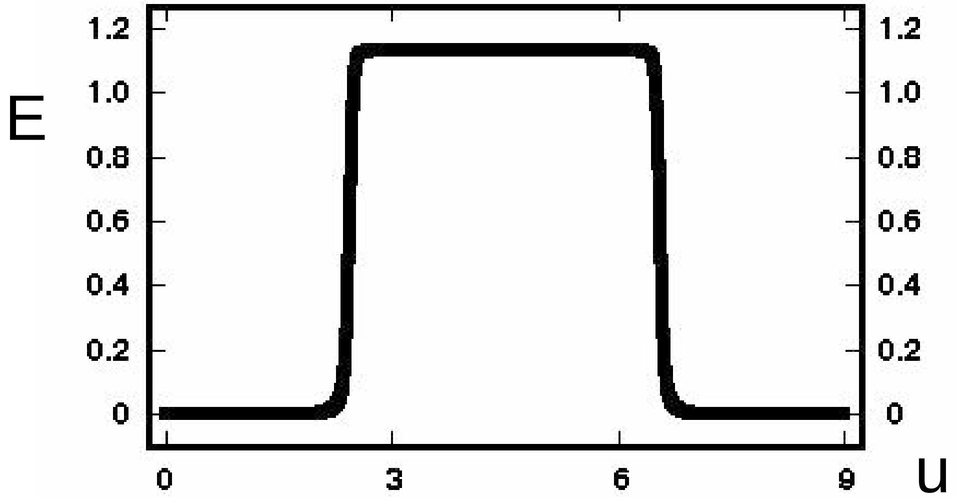
Segmenting

T-dependence of G suggest conformation change

Vacancy-assisted diffusion T=0
2 spatial dimension soft-core potential

$$V = \epsilon \sum_{i<j} \left(\frac{1}{r_{ij}} \right)^{12}$$





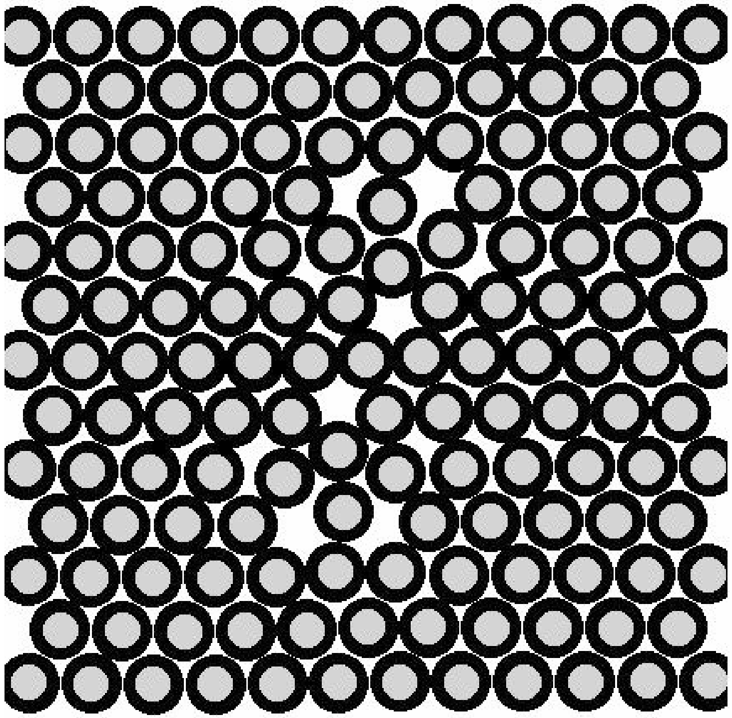
Energy along the path

Segmented

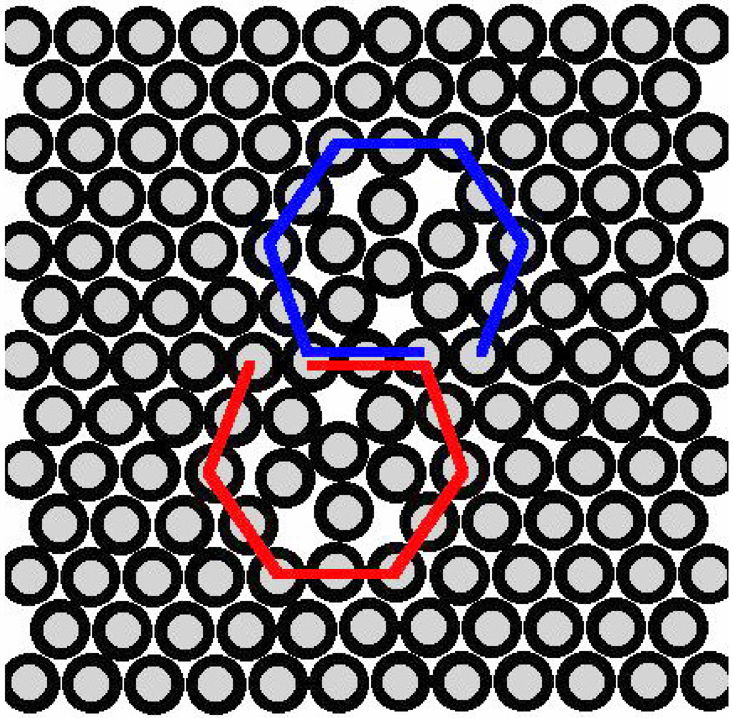
Vacancy-assisted diffusion $T = 0.1\, T_M$
2 spatial dimension soft-core potential

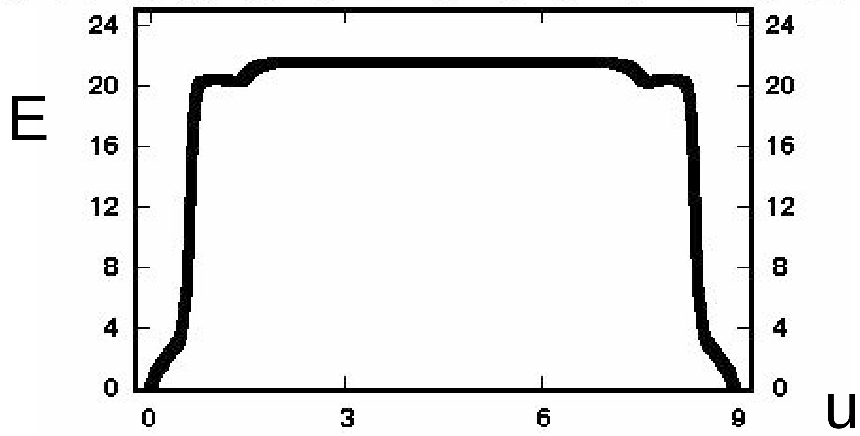
$$V = \epsilon \sum_{i<j} \left(\frac{1}{r_{ij}} \right)^{12}$$

saddle point



same configuration with disclinations highlighted





Energy along the path

Segmented & saddle dominates

LJ_{38} in 3 spatial dimensions Zero Temperature

QuickTime™ and a
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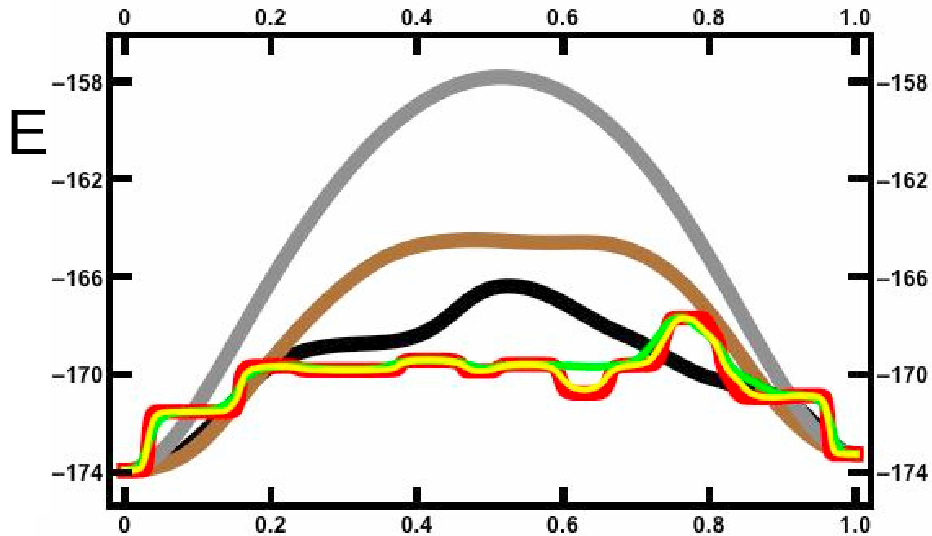
T=0

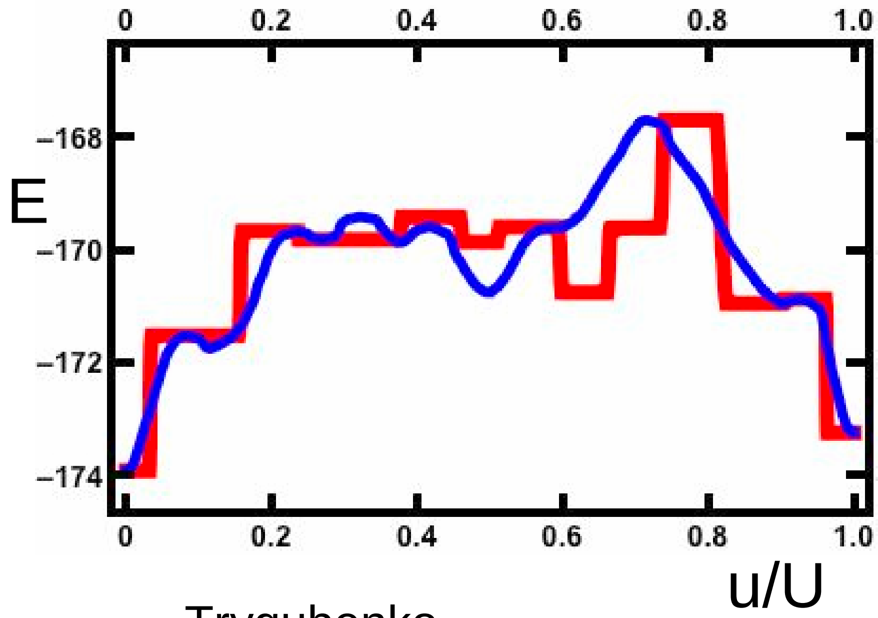
LJ_{38} in 3 spatial dimensions

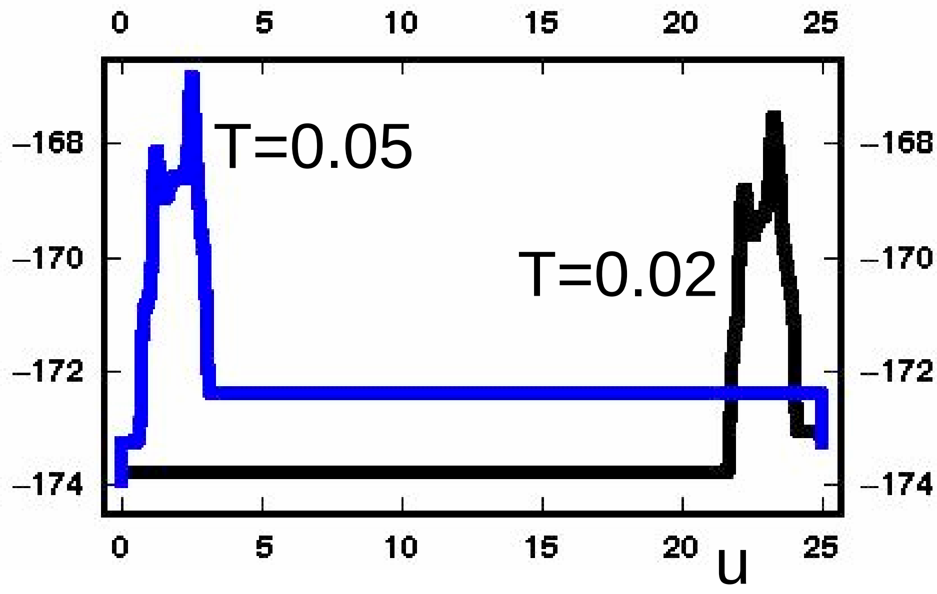


Energy along path

Segmented

T>0 Asymmetric





Trygubenko

http://pdb.trygub.com/pathways/lennard-jones/38/global-second-lowest/3-274sigma/largest-rate-contribution/path-xyz.bz2

Summary and Conclusions

- Using Brownian Dynamics, showed how the Stratonovich formula can be considered to be a ”measure,” providing an expression for the probability of paths.
- Showed how to form an SPDE for path sampling.
- For a variety of examples, looked at the paths that maximized the path probability - but may not be statistically significant.
- Characteristics: the MPPs are
  - Segmented
  - Highly sensitive to small asymmetries
  - Many times, unphysically driven to saddle points, and
  - In one case, driven far away from any minimum of V.
- The MPPs possess many unphysical features. In complex, higher dimensional can they be trusted to give the correct sequence of (transition) states? Remains to be seen.
- This work supports the view of Durr and Bach, Comm. Math. Phys, 1978, and not that of Faccioli, et al. Phys. Rev. Lett, 2006, 2008, J. Chem. Phys., 2009

$$G = \sum_{i\alpha} \frac{1}{2} \left(\frac{\partial V}{\partial r_{i\alpha}} \right)^2 - kT \, \frac{\partial^2 V}{\partial r_{i\alpha}^2}$$

Definition

$$\left\langle \left(\frac{\partial V}{\partial r_{i\alpha}} \right)^2 \right\rangle = kT \left\langle \frac{\partial^2 V}{\partial r_{i\alpha}^2} \right\rangle$$

In equilibrium

$$\int_0^U du \; G = \langle G \rangle$$

If U is big enough

$$\frac{\partial G}{\partial r_{i\alpha}} = 0$$

is an atypical condition