Collective Coordinates and Driving Mechanisms for Conformational Transitions of Complex Molecules

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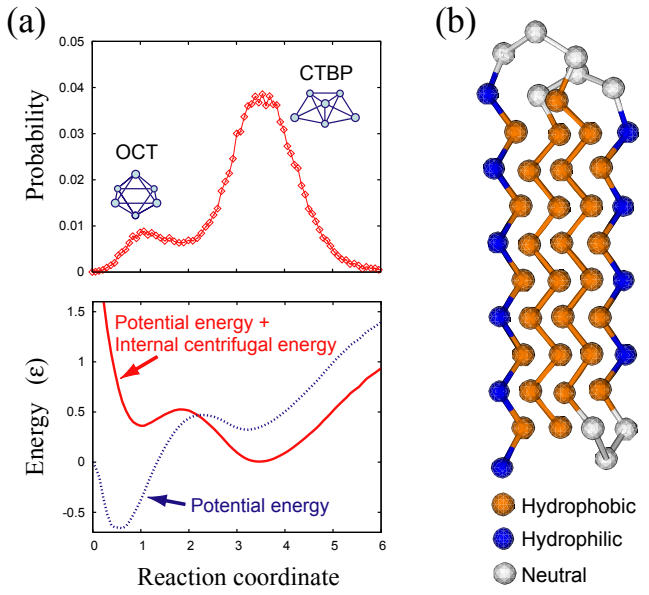
Methods of Geometric Coarse-Graining

- To understand large-amplitude collective motions, from chemical reactions to protein folding, dimension reduction is crucial.
- Develop geometric coarse-graining to overcome curse of dimension
  - appropriately identify
    a small number of important collective variables
  - derive their reduced dynamics
  - use this low-dimensional system
    to clarify mechanisms of large-amplitude motions of molecules.

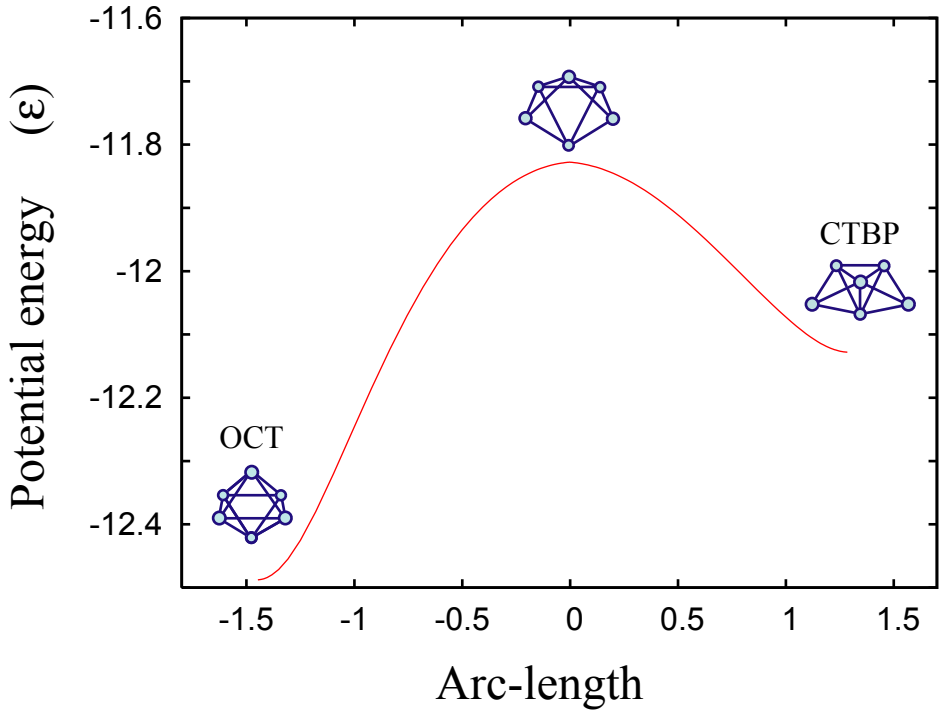


Isomerization Dynamics of 6-Atom Argon Cluster

- Hamiltonian of our model system

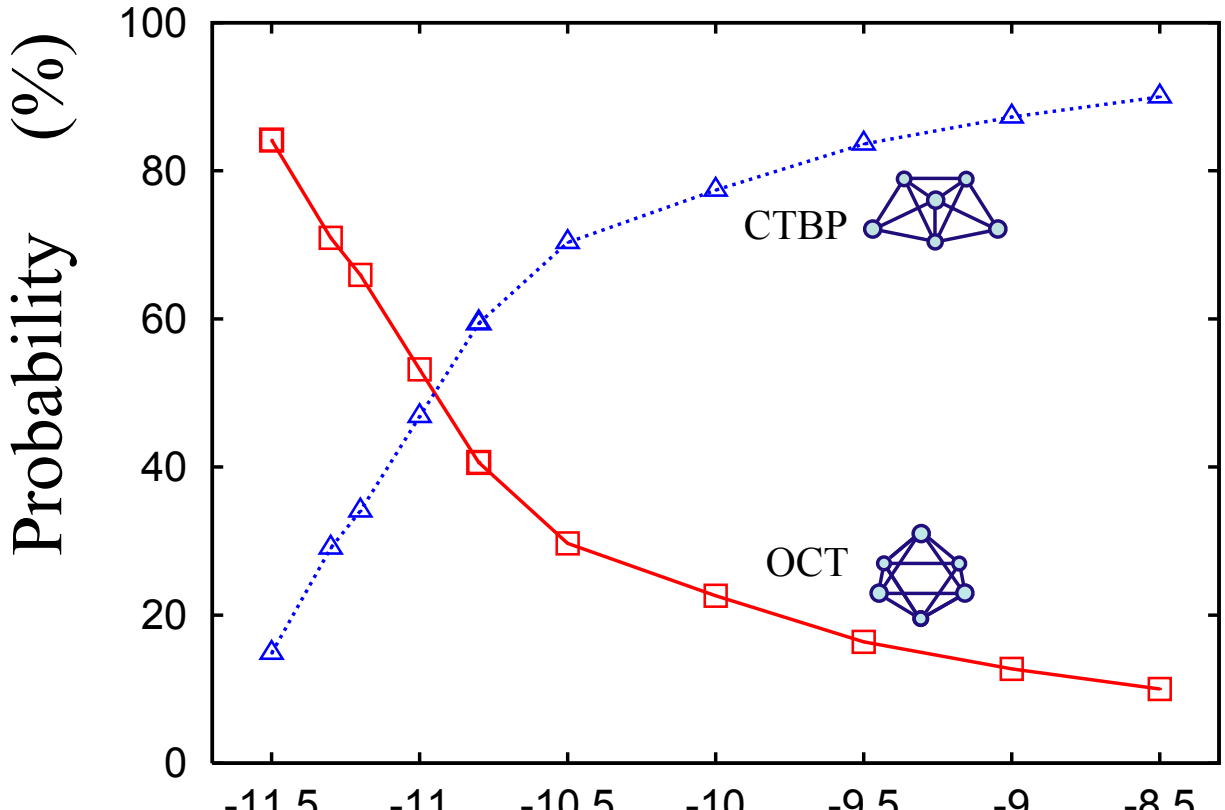
$$\frac{\mathcal{H}}{\varepsilon} = \frac{1}{2}\sum_{i=1}^{6}(\dot{\mathbf{r}}_{si}\cdot\dot{\mathbf{r}}_{si}) + \sum_{i<j}\left[e^{-2(d_{ij}-d_0)} - 2e^{-(d_{ij}-d_0)}\right],$$

- Has 2 geometric distinct isomers:
  OCT (spherical) and CTBP (asymmetric).
- OCT has deeper potential well than CTBP.



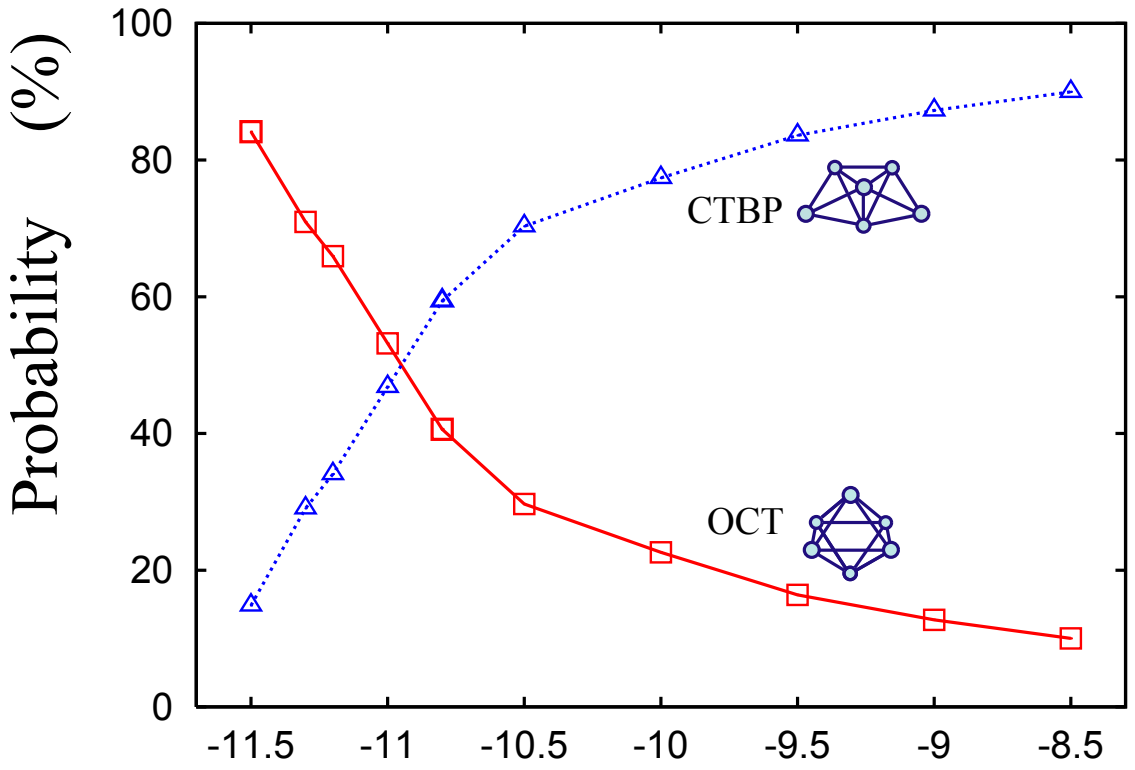
Switching of Structural Preference

- Probability of finding system in each isomer.
- At **low energy**: cluster prefers to be in OCT isomer.
- As energy increases, structural preference switch dramatically.
- At **high energy**: cluster prefers to be in CTBP isomer.
- What is the origin of **switching of structural preference**?



Methods of Geometric Coarse-Graining

- Reduce dimensionality using collective variables: 3 gyration radii.
- Isomerization dynamics are investigated within framework of these reduced dynamics.
- Switching accounted for by a general tendency in polyatomic molecules: Molecules prefer distorted than spherical mass distribuion at high energy range.

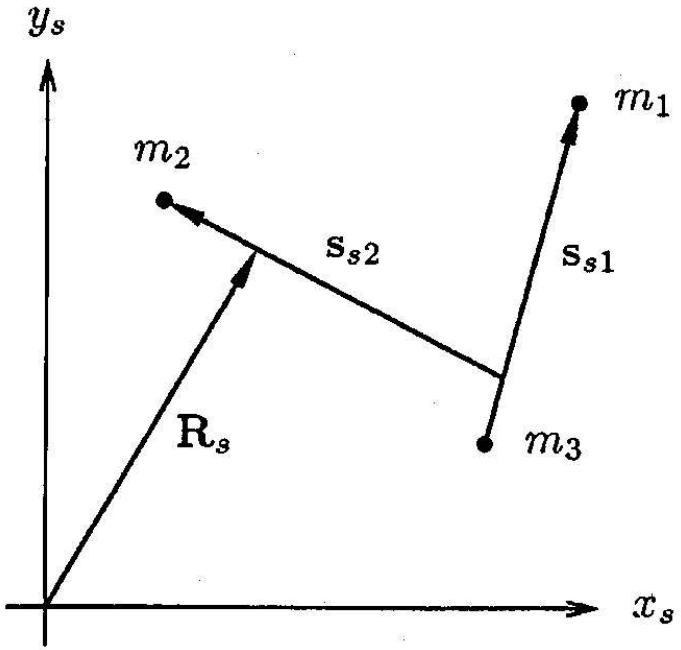


Reducing Translation Dynamics of N-Body Problem

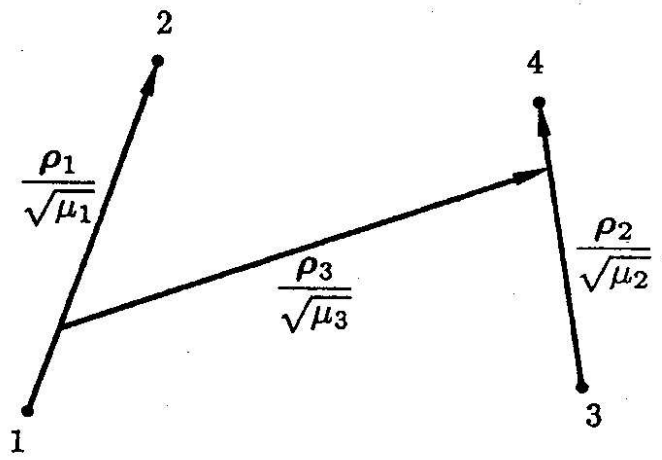
- Eliminate translational d.o.f. via mass-weighted Jacobi vectors

$$\rho_{si} = \sqrt{\mu_i}\left(\frac{\sum_{k=1}^{i} m_k \mathbf{r}_{sk}}{\sum_{k=1}^{i} m_k} - \mathbf{r}_{s(i+1)}\right)$$

where μ_i are the reduced masses, $\mu_i = \dfrac{m_{i+1}\sum_{k=1}^{i} m_k}{\sum_{k=1}^{i+1} m_k}$.



(a)



(b)

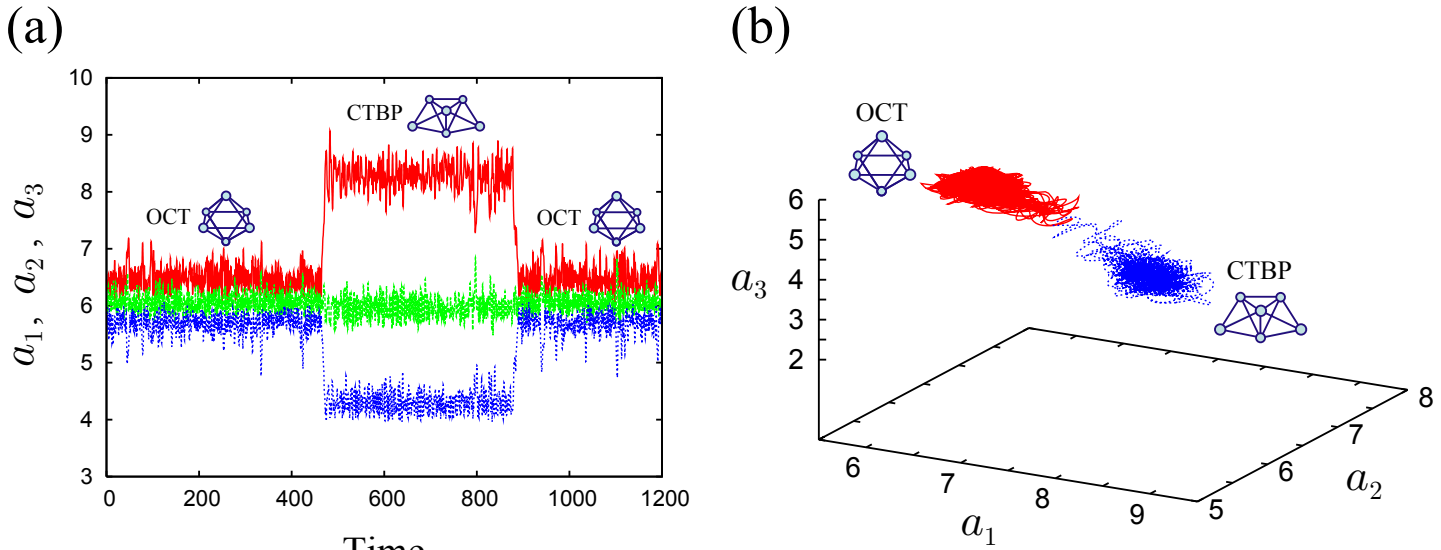
Principal Axis Hyperspherical Coordinates (PAHC)

- Using SVD, Matrix of Jacobi vectors $W_s = (\rho_{si})$ can be written as

$$W_s = RNU^T$$

  - $R = \left(e_1 \; e_2 \; e_3 \right) \in SO(3)$, coincides with principal axis frame, which specifies instantaneous orientation,
  - N is $3 \times (n-1)$ matrix, singular values $a_i$are gyration radii.

$$N = \left(\begin{array}{ccc|ccc} a_1 & 0 & 0 & 0 & \cdots & 0 \\ 0 & a_2 & 0 & 0 & \cdots & 0 \\ 0 & 0 & a_3 & 0 & \cdots & 0 \end{array} \right)$$



Principal Axis Hyperspherical Coordinates (PAHC)

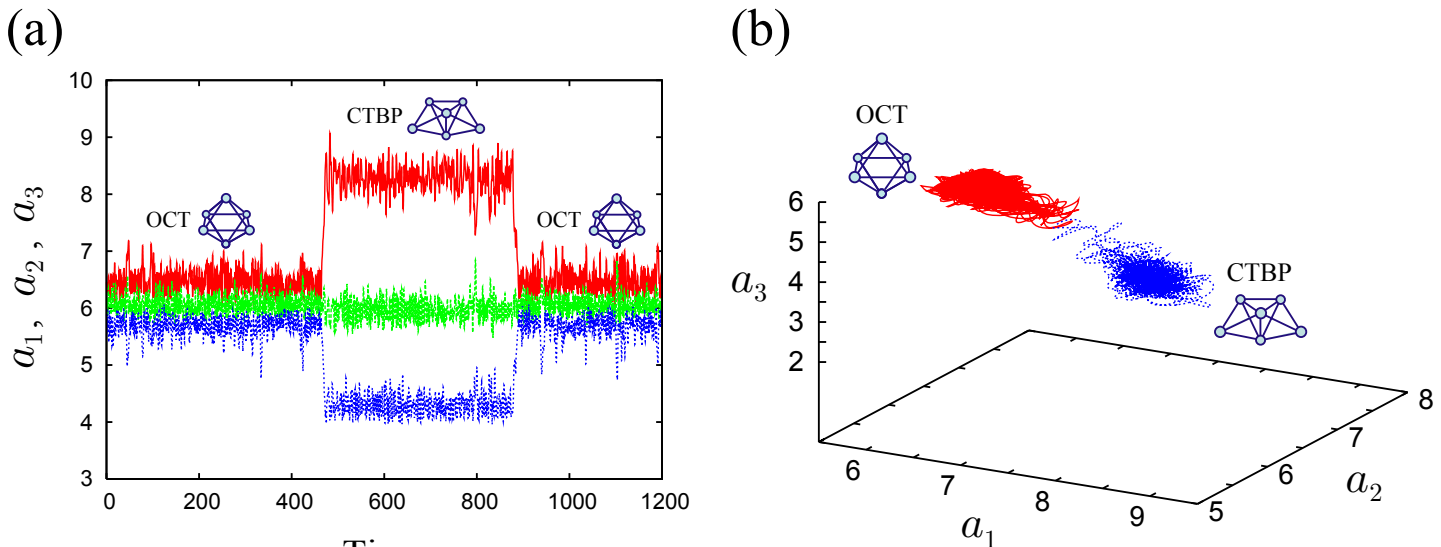
- Using SVD, matrix of Jacobi vectors $W_s = (\rho_{si})$ can be written as

$$W_s = RNU^T$$

  - gyration radii a_i $(a_1 \geq a_2 \geq a_3)$ related to principal moments

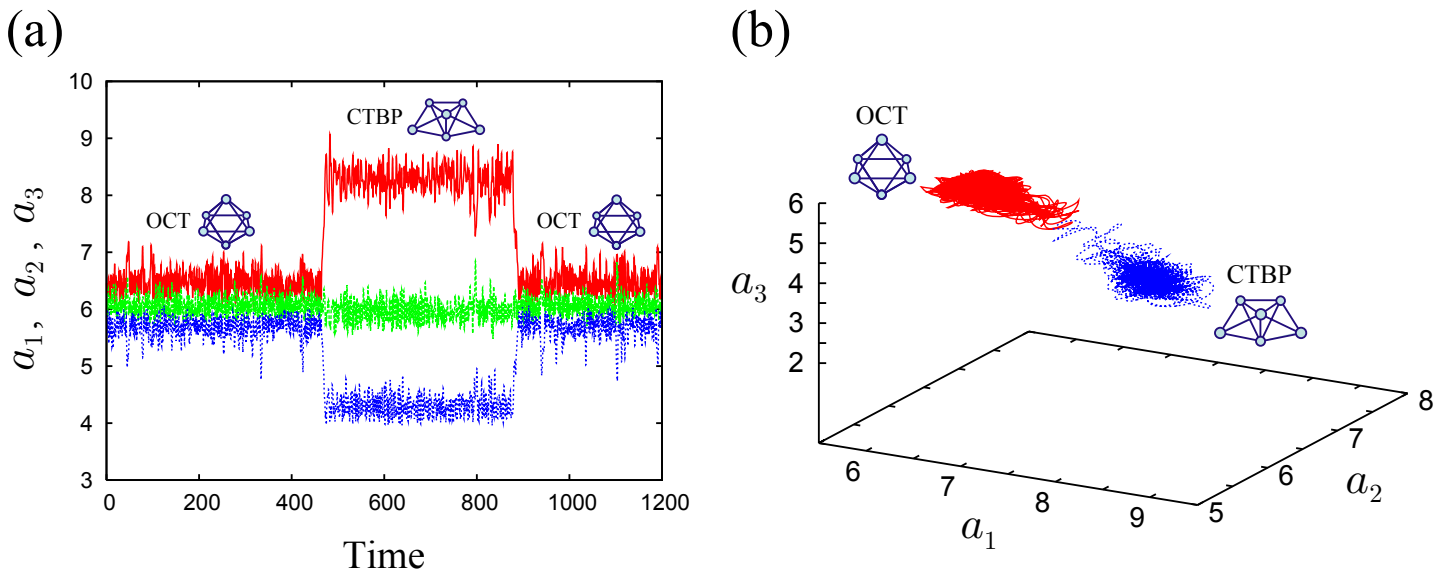
$$M_1 = a_2^2 + a_3^2, \qquad M_2 = a_3^2 + a_1^2, \qquad M_3 = a_1^2 + a_2^2$$

    and measure mass distribution (along principal axis).
  - OCT isomer $(5.97, 5.97, 5.97)$: spherical mass distribution, CTBP isomer $(8.19, 5.89, 4.27)$: asymmetric mass distribution.
  - $U(\phi_1, \ldots, \phi_{3n-9})$ in $SO(n-1)$, specifies shape changes.



Gyration Radii for Coarse-Graining Conf. Dynamics

- PAHC separate rotation/internal motion, and parametrize shape space with 3 gyration radii a_i and $(3n-9)$ hyperangles ϕ_j.
- Isomerization of full system can be captured by transition of trajectory in 3D space of gyration radii.
- Provide 3D space of gyration radii to describe conformational changes in terms of changes in mass distribution.
- If these 9 hidden d.o.f. can be regarded as bath modes, one has a dynamical system of only 3 gyration radii.



Kinetic Energy Has Simple Expression

- Using PAHC, kinetic energy looks simple:

$$2K = \Omega^T M \Omega + (a_1^2 + a_2^2 + a_3^2) + \omega^T \tilde{M} \omega + \sum_{i=1}^{3} \sum_{\beta=4}^{(n-1)} a_i^2 \gamma_{i\beta}^2$$

  where

  - Ω is (external) total angular velocity, M is moment of inertial,
  - a_i are 3 gyration radii (collective variables),
  - $\omega, \gamma_{i\beta}$ are (3n-9) internal angular velocities.

- Under condition of zero total angular momentum,

$$2K = (a_1^2 + a_2^2 + a_3^2) + \omega \tilde{M} \omega + \sum_{i=1}^{3} \sum_{\beta=4}^{(n-1)} a_i^2 \gamma_{i\beta}^2$$

Equation of Motion for Gyration Radii

- Euler-Lagrange equations

$$\ddot{a}_1 = \frac{a_1\left(a_1^2+3a_2^2\right)\left(a_1^2-a_2^2\right)}{\left(a_1^2+a_2^2\right)^2}\omega_{12}^2 + \frac{a_1\left(a_1^2+3a_3^2\right)\left(a_1^2-a_3^2\right)}{\left(a_1^2+a_3^2\right)^2}\omega_{13}^2 + a_1\sum_{k=4}^{n-1}\gamma_{1k}^2 - \frac{\partial V}{\partial a_1},$$

$$\ddot{a}_2 = \frac{a_2\left(a_2^2+3a_1^2\right)\left(a_2^2-a_1^2\right)}{\left(a_2^2+a_1^2\right)^2}\omega_{21}^2 + \frac{a_2\left(a_2^2+3a_3^2\right)\left(a_2^2-a_3^2\right)}{\left(a_2^2+a_3^2\right)^2}\omega_{23}^2 + a_2\sum_{k=4}^{n-1}\gamma_{2k}^2 - \frac{\partial V}{\partial a_2},$$

$$\ddot{a}_3 = \frac{a_3\left(a_3^2+3a_2^2\right)\left(a_3^2-a_2^2\right)}{\left(a_3^2+a_2^2\right)^2}\omega_{32}^2 + \frac{a_3\left(a_3^2+3a_1^2\right)\left(a_3^2-a_1^2\right)}{\left(a_3^2+a_1^2\right)^2}\omega_{31}^2 + a_3\sum_{k=4}^{n-1}\gamma_{3k}^2 - \frac{\partial V}{\partial a_3}.$$

  - LHS are components of acceleration in space of gyration radii,
  - first 3 terms on RHS represent a kinematic force orginated from coupling of gyration radii with internal kinematic rotation,
  - 4th terms represent force orginated from potential energy.

- All kinematic force terms are quadratic in velocities and represent internal centrifugal force (ICF) of kinematic rotation.

ICF Breaks Symmetry of Mass Distribution

- Since $a_1 \geq a_2 \geq a_3$,

$$\ddot{a}_1 = \frac{a_1\left(a_1^2+3a_2^2\right)\left(a_1^2-a_2^2\right)}{\left(a_1^2+a_2^2\right)^2}\omega_{12}^2 + \frac{a_1\left(a_1^2+3a_3^2\right)\left(a_1^2-a_3^2\right)}{\left(a_1^2+a_3^2\right)^2}\omega_{13}^2 + a_1\sum_{k=4}^{n-1}\gamma_{1k}^2 - \frac{\partial V}{\partial a_1},$$

$$\ddot{a}_2 = \frac{a_2\left(a_2^2+3a_1^2\right)\left(a_2^2-a_1^2\right)}{\left(a_2^2+a_1^2\right)^2}\omega_{21}^2 + \frac{a_2\left(a_2^2+3a_3^2\right)\left(a_2^2-a_3^2\right)}{\left(a_2^2+a_3^2\right)^2}\omega_{23}^2 + a_2\sum_{k=4}^{n-1}\gamma_{2k}^2 - \frac{\partial V}{\partial a_2},$$

$$\ddot{a}_3 = \frac{a_3\left(a_3^2+3a_2^2\right)\left(a_3^2-a_2^2\right)}{\left(a_3^2+a_2^2\right)^2}\omega_{32}^2 + \frac{a_3\left(a_3^2+3a_1^2\right)\left(a_3^2-a_1^2\right)}{\left(a_3^2+a_1^2\right)^2}\omega_{31}^2 + a_3\sum_{k=4}^{n-1}\gamma_{3k}^2 - \frac{\partial V}{\partial a_3}.$$

  - 1st and 2nd terms of 1st equation
    are always positive or zero: enlarge a_1,
  - 1st and 2nd terms of 3rd equation
    are always negative or zero: diminish a_3.
  - To elongate in most massive direction and
    to collapse in least massive direction.

- 3rd terms are always positive:
  inflate molecules in all 3 principal-axis directions.

- Inflating effect becomes greater as number of atoms increases.

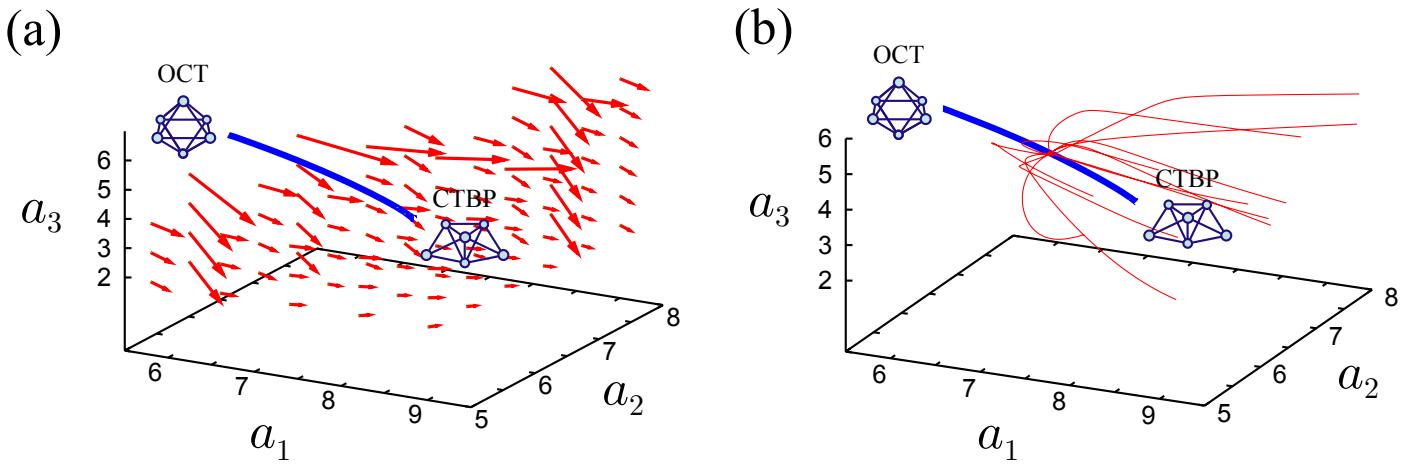
Averaged Field of Internal Centrifugal Force (ICF)

- Gyration radii are subject to 2 kinds of forces
  - PF works to keep mass distribution compact/symmetric,
  - ICF works to inflate and distort mass distribution.
- Averaged field of ICF pushes cluster out of OCT to CTBP region.

$$\ddot{a}_1 = \frac{a_1\left(a_1^2+3a_2^2\right)\left(a_1^2-a_2^2\right)}{\left(a_1^2+a_2^2\right)^2}\omega_{12}^2 + \frac{a_1\left(a_1^2+3a_3^2\right)\left(a_1^2-a_3^2\right)}{\left(a_1^2+a_3^2\right)^2}\omega_{13}^2 + a_1\sum_{k=4}^{n-1}\gamma_{1k}^2 - \frac{\partial V}{\partial a_1},$$

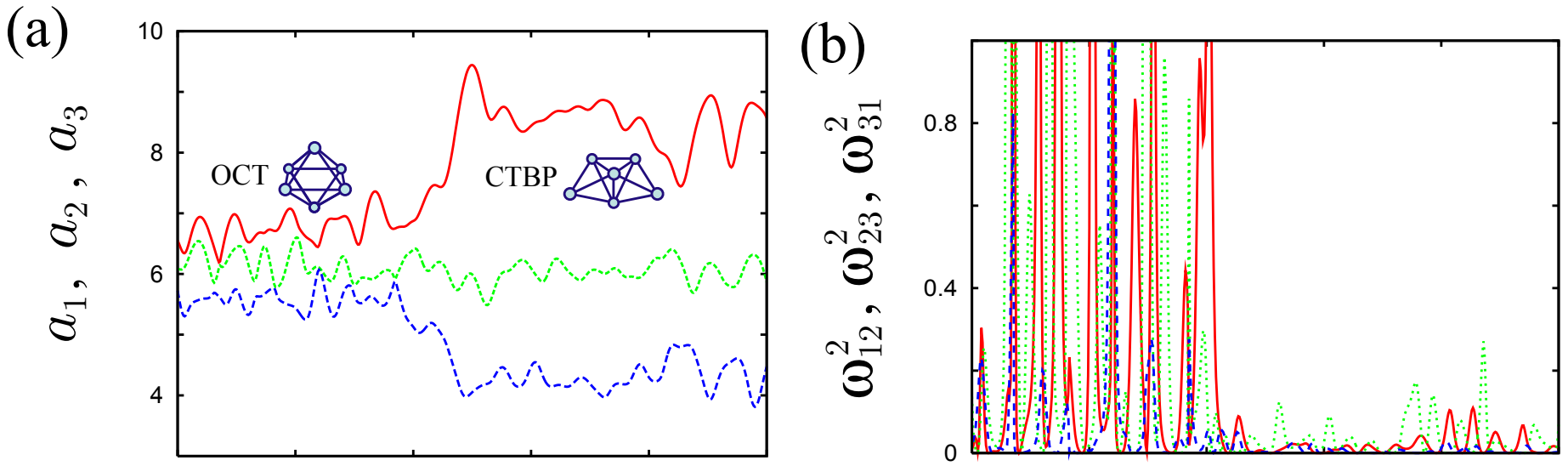
$$\ddot{a}_2 = \frac{a_2\left(a_2^2+3a_1^2\right)\left(a_2^2-a_1^2\right)}{\left(a_2^2+a_1^2\right)^2}\omega_{21}^2 + \frac{a_2\left(a_2^2+3a_3^2\right)\left(a_2^2-a_3^2\right)}{\left(a_2^2+a_3^2\right)^2}\omega_{23}^2 + a_2\sum_{k=4}^{n-1}\gamma_{2k}^2 - \frac{\partial V}{\partial a_2},$$

$$\ddot{a}_3 = \frac{a_3\left(a_3^2+3a_2^2\right)\left(a_3^2-a_2^2\right)}{\left(a_3^2+a_2^2\right)^2}\omega_{32}^2 + \frac{a_3\left(a_3^2+3a_1^2\right)\left(a_3^2-a_1^2\right)}{\left(a_3^2+a_1^2\right)^2}\omega_{31}^2 + a_3\sum_{k=4}^{n-1}\gamma_{3k}^2 - \frac{\partial V}{\partial a_3}.$$



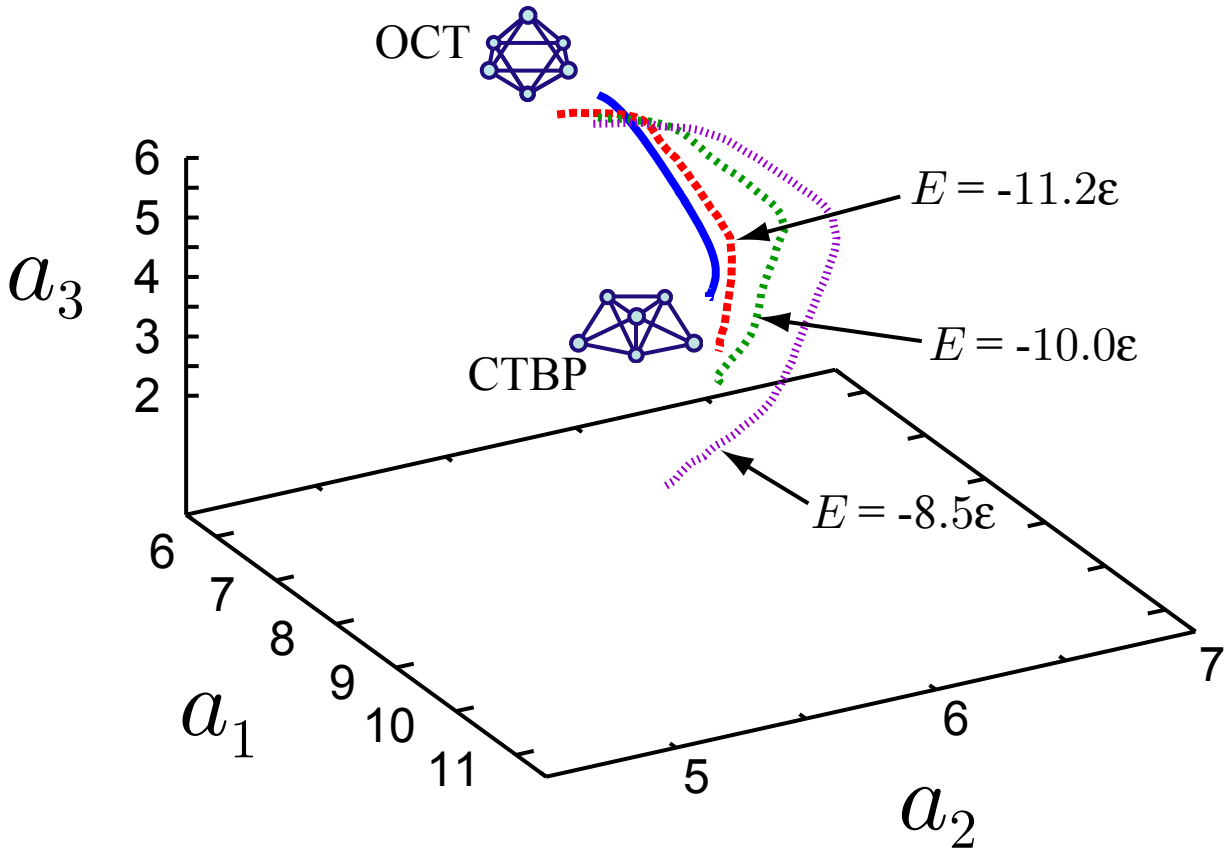
Time-scale Separation of Slow and Fast Variables

- Typical time evolution of
  - 3 gyration radii $a_1, a_2,$ and a_3 (slow variables),
  - squares of quasi-velocities, $\omega_{12}, \omega_{23}, \omega_{31}$ and $\gamma_{i\beta}$ (fast variables)
  - Internal central force $\mathbf{f}_{ICF}$ and potential force $\mathbf{f}_{PF}$ exhibit similar behavior as internal angular velocities.
- Some kind of averaging fast variables can be done.



To Quantify Effects of Internal Centrifugal Force

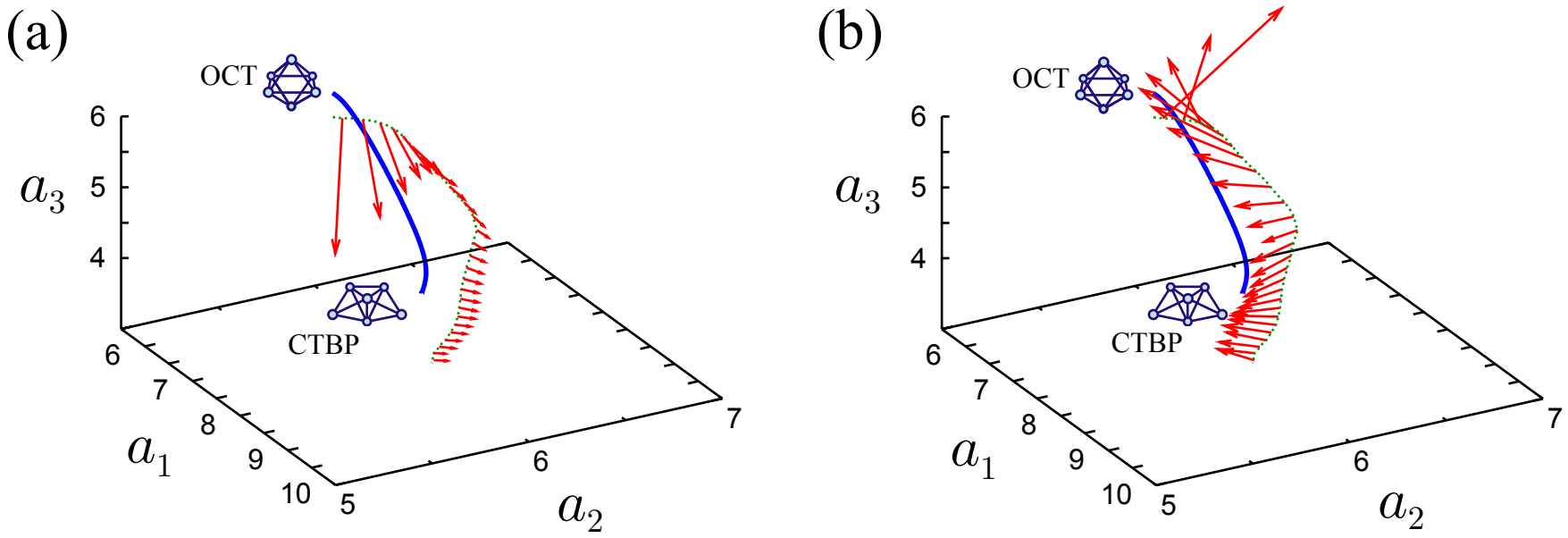
- To quantify effects of ICF
  - determine reaction path in space of gyration radii (a_1 plays an important role),
  - construct effect energy curve along reaction path.
- Note: reaction paths are energy dependent.



Averaged Force Fields along Reaction Path

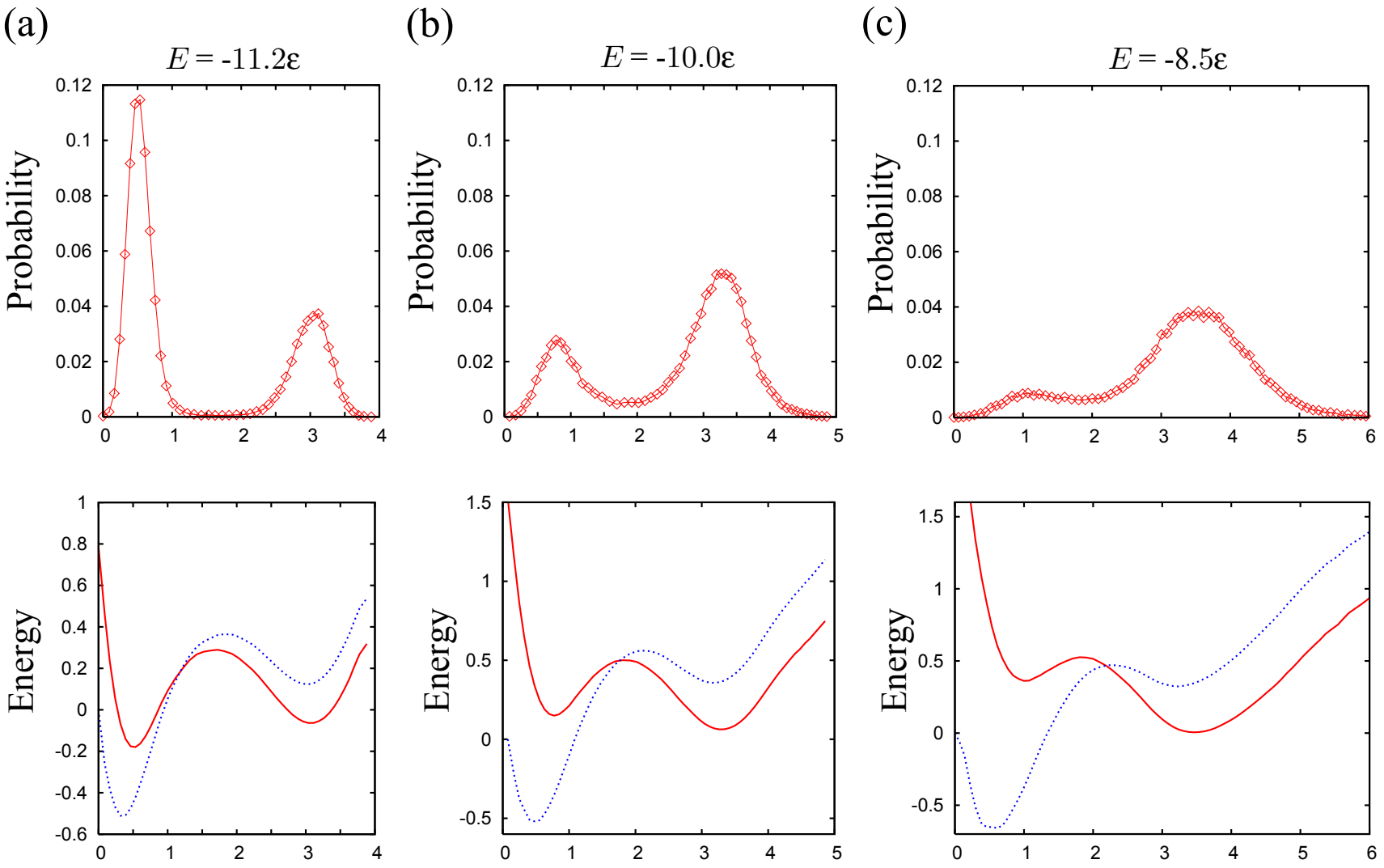
- Average ICF, and average PF along reaction path.
- Reduced potential: $V_{PF} = \int_{path} < \mathbf{f}_{PF} > \cdot \frac{d\mathbf{a}}{ds} ds.$
- Reduced effective potential:

$$V_{PF+ICF} = \int_{path} (< \mathbf{f}_{PF} > + < \mathbf{f}_{ICF} >) \cdot \frac{d\mathbf{a}}{ds} ds$$



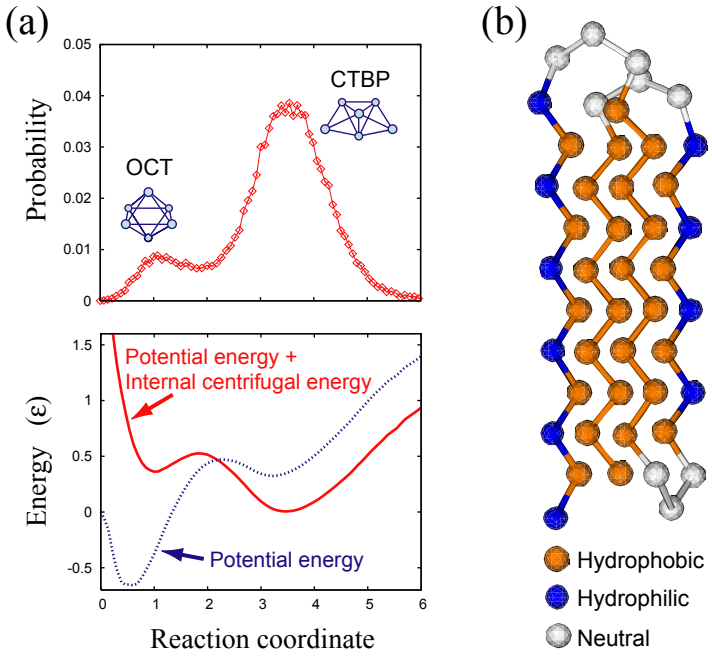
Energy-dependent Switching of Structural Preference

- By integrating sum of 2 force fields along the reaction path, an effective energy curve is deduced.
- Can explain energy-dependent switching of structural preference.



Conclusion: Methods of Geometric Coarse-Graining

- Study isomerization of 6 atoms Argon cluster.
- Geometric coarse-graining to overcome curse of dimension
  - reduce conformation dynamics to 3D dynamics of gyration radii
  - extract interplay between potential force/ kinematic forces (arise from intrinsic geometry, ignored in conventional theories)
  - explain energy-dependent switching of structural preference between symmetric/asymmetric conformations (Argon 6).



Ongoing Work: Methods of Geometric Coarse-Graining

- Develop, extend, and generalize these methods
  - have studied isolated systems, with constant energy, and zero total angular momentum
  - want to study systems with non-zero angular momentum
  - molecules in a thermal environment
- As model molecular systems
  - large clusters (100s of atoms)
  - homopolymers and 3-colored 46 beads biopolymers