Dynamical reaction theory from micro to macro through mesoscopic levels

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R. Stephen Berry Tribute Symposium

06/23/2015 - 06/27/2015

How did I get to know Steve ?

- Finite time thermodynamics
- Phase space geometry and reaction dynamics

- An email from Steve
- Telluride Summer Research Center(TSRC)

Three body scattering

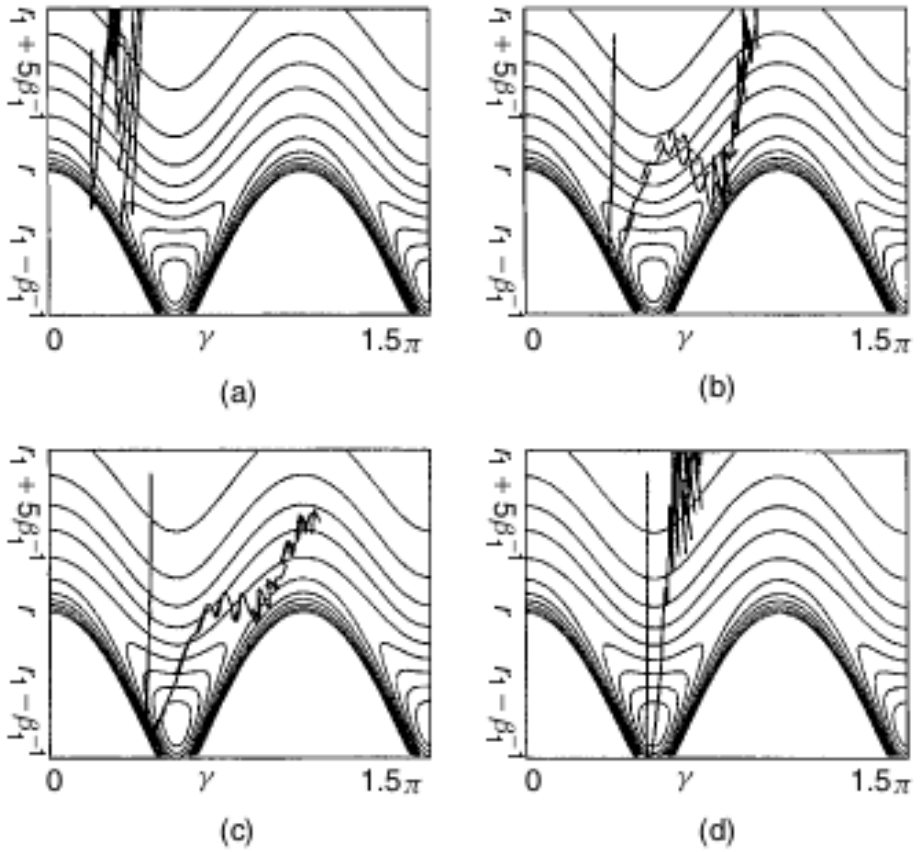

Figure 3.14. The evolution of the unstable manifold shown on the configuration space (r, γ). Thin lines indicate the equi-energy lines of the potential with $R = R_{max}$ (*a*) $\gamma \sim 0$. (*b*) $\gamma \sim 0.3\pi$. (*c*) $\gamma \sim 0.4\pi$. (*d*) $\gamma \sim 0.5\pi$. [Reprinted with permission from M. Toda, *Phys. Rev. Lett.*, Vol. 74 (1995), p. 2670. Copyright © 1995, American Institute of Physics.]

Workshops of TSRC

- The Complexity of Dynamics and Kinetics in Many Dimensions: 08/13/2007 - 08/24/2007
  Tamiki Komatsuzaki, R. Stephen Berry, Mikito Toda

- Geometry of Chemical Reaction Dynamics in Gas and Condensed Phases: 06/10/2013 - 06/14/2013
  Tamiki Komatsuzaki, Mikito Toda, R. Stephen Berry

Contents of my Talk

- Dynamical reaction theory based on phase space geometry

  Going beyond statistical reaction theory

- Collective behavior of Proteins

  Reduction of motions

  to extract sSpace time hierarchy

Dynamical reaction theory based on phase space geometry

Phase space geometry

- Saddle, its stable/unstable manifolds, and how they intersect
- Normally hyperbolic invariant manifolds, its stable/unstable manifolds, and how they intersect

Separation of time scales in unstable behavior represented by Lyapunov exponents

Phase space geometry for 2 dof

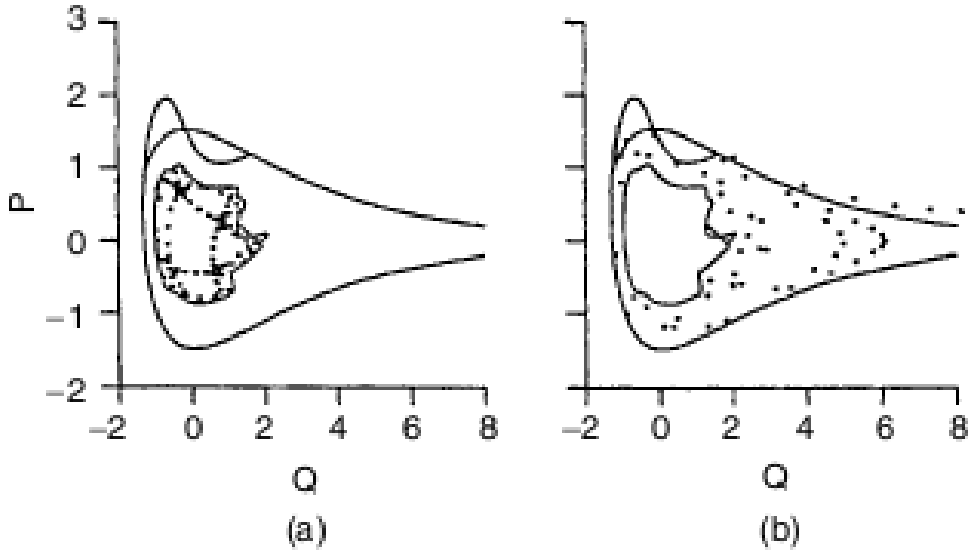

Figure 3.18. Bottleneck in the predissociation of HeI_2 (*a*) orbits trapped within the cantori created by the nonlinear resonance and (*b*) orbits trapped between the cantori and the separatrix. [Reprinted with permission from M. J. Davis and S. K. Gray, *J. Chem. Phys.*, Vol. 84 (1986), p. 5389. Copyright © 1986, American Institute of Physics.]

Phase space geometry for 3 dof

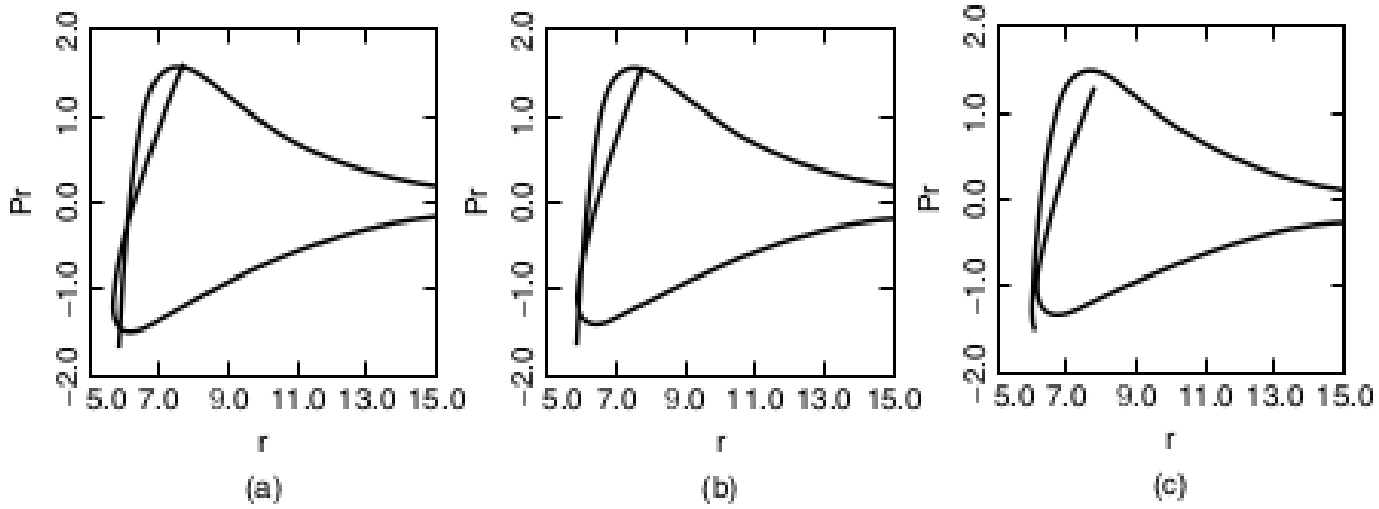

Figure 3.11. An example of homoclinic tangency in a model of HeI_2 that includes the freedom of internal rotation. [Reprinted with permission from R. E. Gillilan and G. S. Ezra, *J. Chem. Phys.*, Vol. 94 (1991), p. 2648. Copyright © 1991, American Institute of Physics.]

Breakdown of separation of time scales

- New phenomena in reaction processes
- Dynamical switching of reaction coordinates

Reaction coordinate vs chaos of vibrational motions

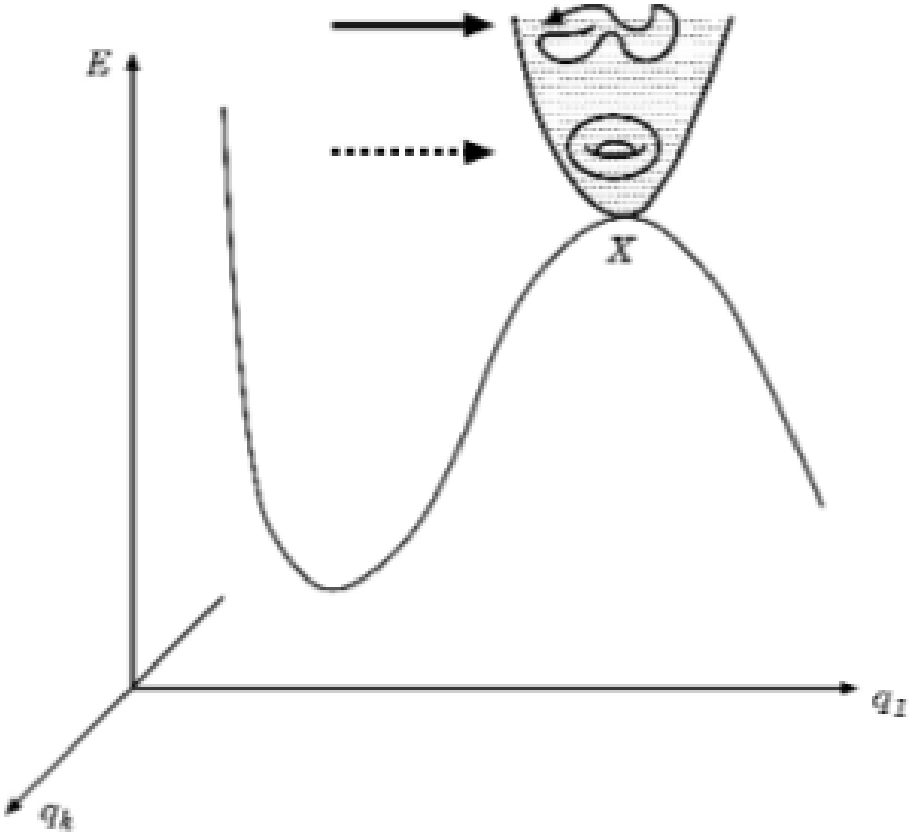

Figure 32. Breakdown of normal hyperbolicity at a saddle.

Beyond Statistical Reaction Theory

- A Dynamical Switching of a Reaction Coordinate to Carry the System Through to a Different Product State at High Energies
  Phys. Rev. Lett. 106, pp.054101, (2011)
  H. Teramoto, M. Toda and T. Komatsuzaki

  Breakdown Mechanism of Normally Hyperbolic Invariant Manifold in terms of unstable periodic orbits and homoclinic/heteroclinic orbits in Hamiltonian Systems
  To appear in Nonlinearity
  H. Teramoto, M. Toda and T. Komatsuzaki

  Experimental Observability of Dynamical Switching
  H. Teramoto, M. Toda, M. Takahashi, H. Kono and T. Komatsuzaki , Submitted

Hydrogen atom in crossed electric and magnetic fields

PRL **106,** 054101 (2011) PHYSICAL REVIEW LETTERS week ending 4 FEBRUARY 2011

Dynamical Switching of a Reaction Coordinate to Carry the System through to a Different Product State at High Energies

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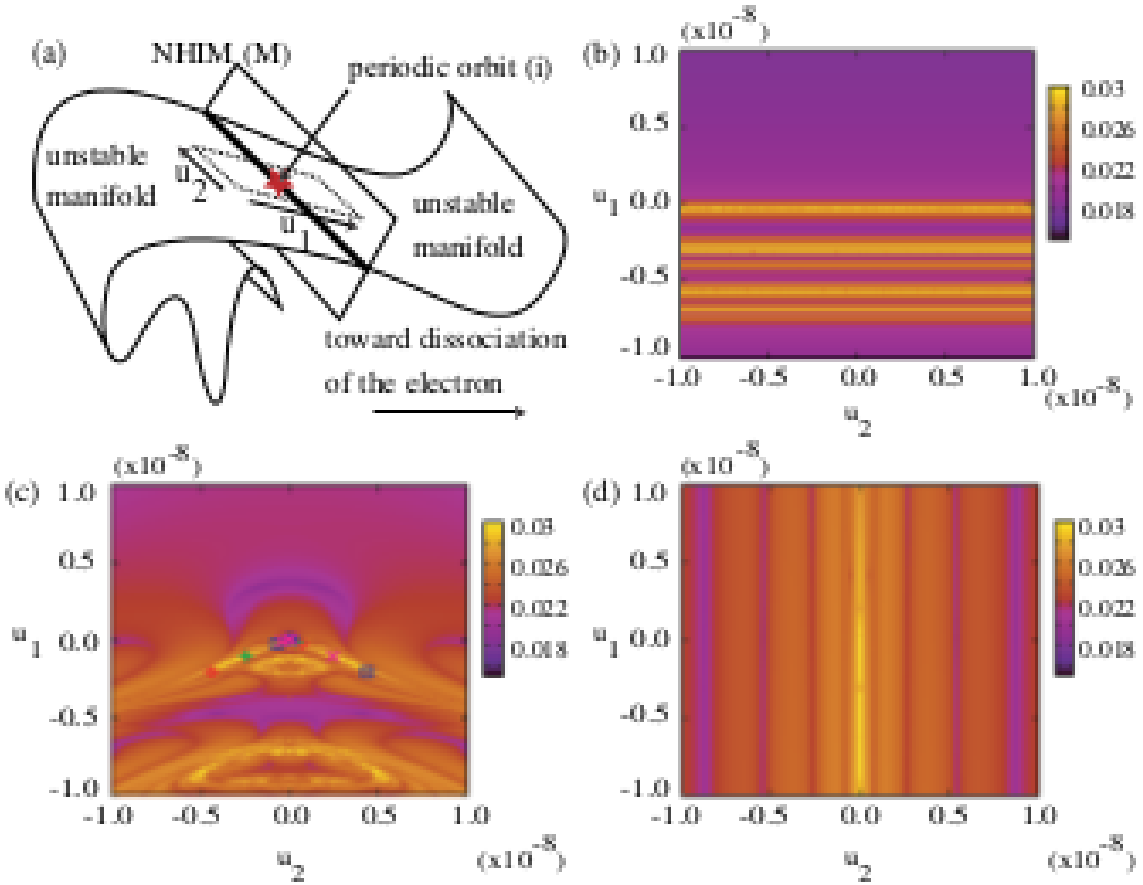
Questions of how the nature of a reaction coordinate that dominates the reaction ceases to exist and whether some new features emerge as an increase of total energy of systems are investigated for many degrees of freedom Hamiltonian systems. As a model system, a hydrogen atom in crossed electric and magnetic fields is scrutinized. It is shown that, when the total energy increases, the reaction coordinate no longer dominates the reaction as did at the lower energies. In turn, a new reaction coordinate emerges, connecting totally different reactant and product states. Furthermore, depending on which parts of the phase space the system traverses through the saddle, the system nonuniformly experiences the switching of the reaction coordinate leading to the different product state. The universal mechanism of the cessation and the switching of the reaction coordinate at high energy regimes above the saddle is investigated.

DOI: 10.1103/PhysRevLett.106.054101 PACS numbers: 05.45.−a, 45.20.Jj, 82.20.−w

Switching of reaction coordinate



Separation of time scales in macroscopic reactions

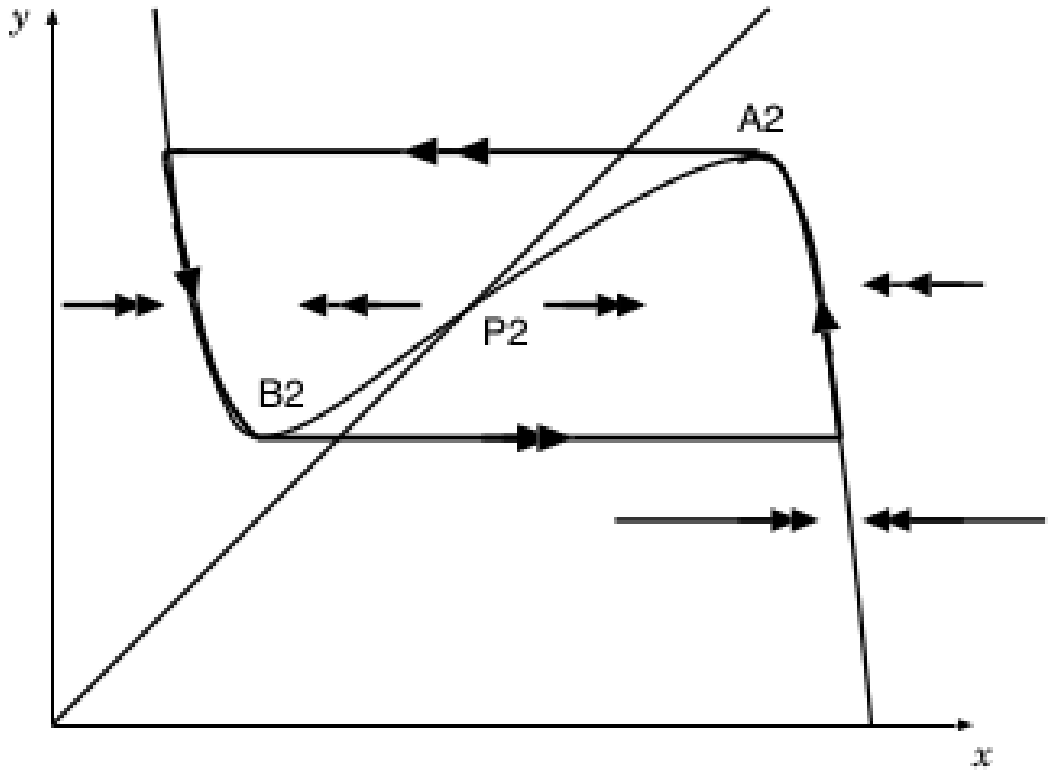


Figure 31. Flow of BZ reaction when limit cycle exists.

Possibility of new mechanism

- Switching of limit cycles
- Chaotic wandering

Phase space structures and dynamical reaction theory

- Possibility of new mechanism in both microscopic and macroscopic description

- Research fields to be explored further both in molecules and rate equations

Collective behavior of Proteins

Motivation of my talk

- Proteins : a tiny existence which performs information processing

  statistical behavior of small systems

  dynamics vs ensemble

- Multiple scales coexist in its behavior without large scale gaps

  emergence of collective motion

Proteins are hierarchical

- Hierarchy of structures of proteins
  multiple hierarchy
- Hierarchy in dynamics ?
- Correspondence between hierarchies of structures and dynamics ?
- Is the hierarchy rigid ?

Problem 1:
How do proteins function ?

- Traditional view of proteins
- Proteins have definite and rigid conformations
- Key vs. key holes
  <= Essential for biological functions

Problem 1:
How do proteins function ?

- Conformation change and fluctuation
- Reaction center is rigid ?
- Relation between conformational change and fluctuation

Problem2:
How do proteins fluctuate ?

- hinges vs. cracking ?
- Random vs. organized ?
- Correlation in space and time ?

Problem3: How are fluctuation related with function of proteins ?

- Functionally important motions ?

Purposes and methods

- Extract collective behavior
  from dynamical viewpoint

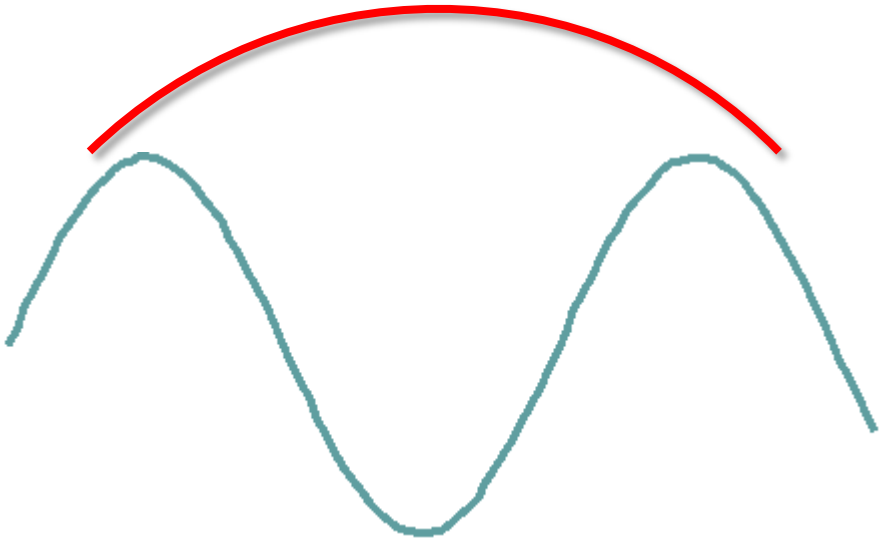
- Resort to
  Wavelet transformation
  and
  Dimensional reduction such as
  SVD, CCA, TICS, Kernel …

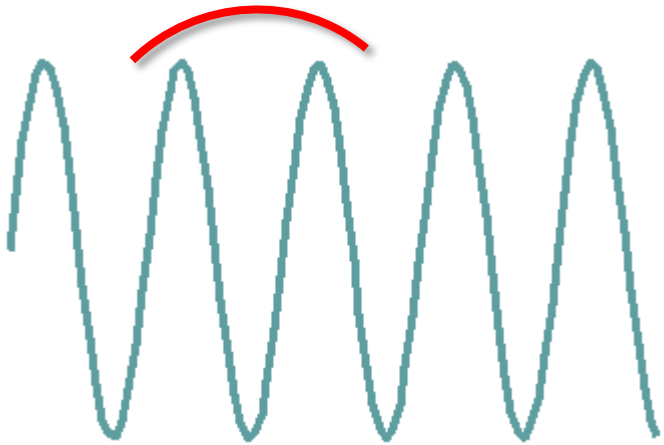
Wavelet Transformation

- Extension of Fourier Transformation to non-stationary time series
- Window to extract local change of oscillation
- Continuous vs. discrete transformation

Morlet Wavelet Transformation

$$(T^{\text{wav}} f)(\omega, t_0) = \sqrt{\frac{\omega}{\sigma}} \int f(t) e^{-\frac{\omega^2}{\pi^2 \sigma^2}(t-t_0)^2} \left(e^{i\omega(t-t_0)} - e^{-\pi^2 \sigma^2} \right) dt \quad (3.54)$$





Singular Value Decomposition

- Extension of eigenvalue decomposition to rectangular matrix（singular values are non-negative real）

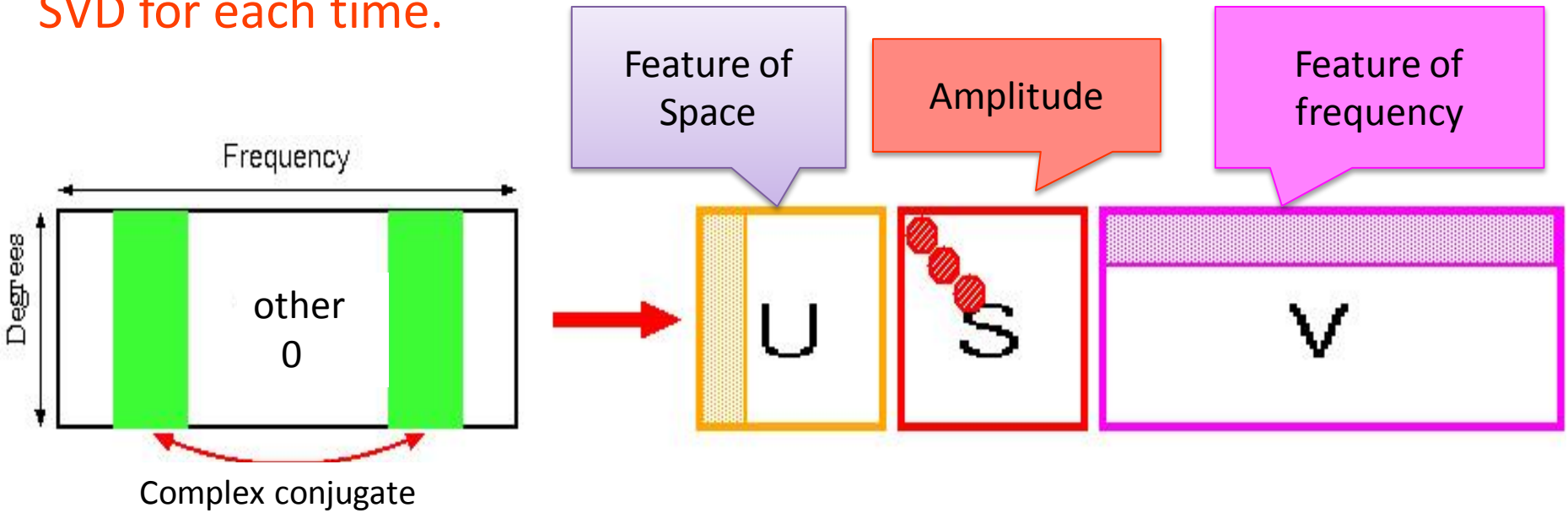
- Wide range of application including reduction of dimensionality, statistical analysis, quantum information

Singular Value Decomposition

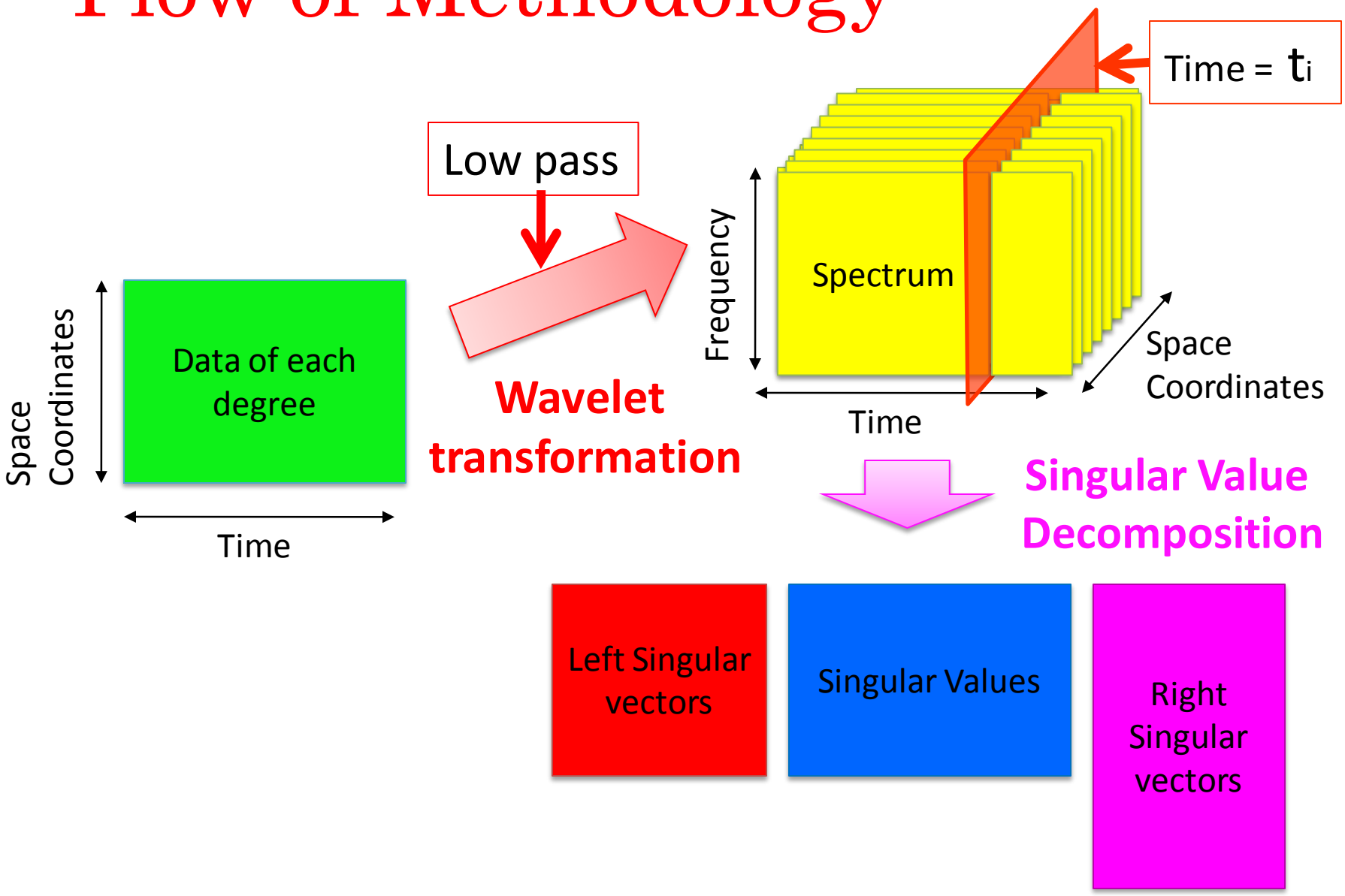
A matrix M can be divided into following form $M = U\Sigma V^{\dagger}$

U : Left Singular vectors
Σ : Singular Values
V : Right Singular vectors

SVD for each time.



Flow of Methodology



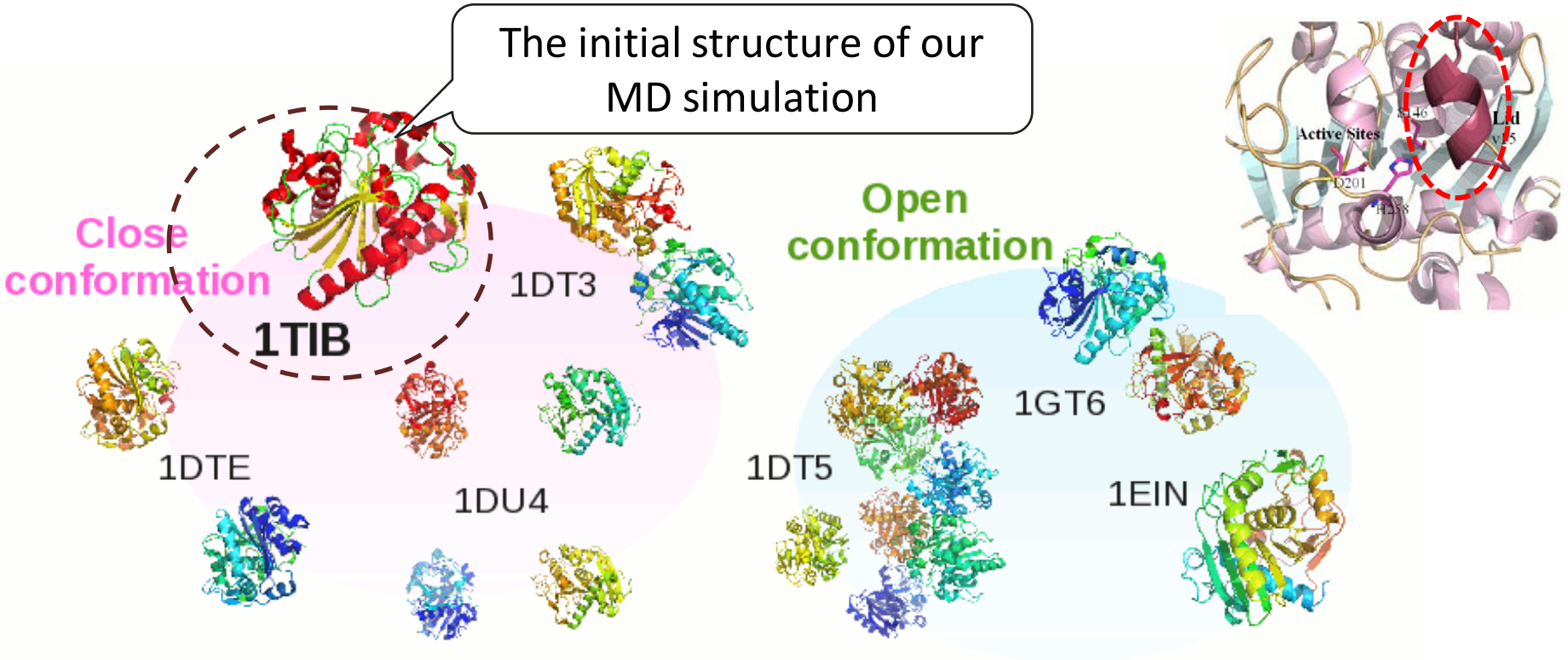
Functional PCA

- Time ordering of data
- Time scales
- Nonstationarity

Target Protein

Thermomyses lanuginosa lipase (TLL)

- 269 residues
- The active sites are covered by the “lid”
- Seven structures **are** reported for TLL in PDB.



Dataset

Time-series Data of Molecular Dynamics Simulation

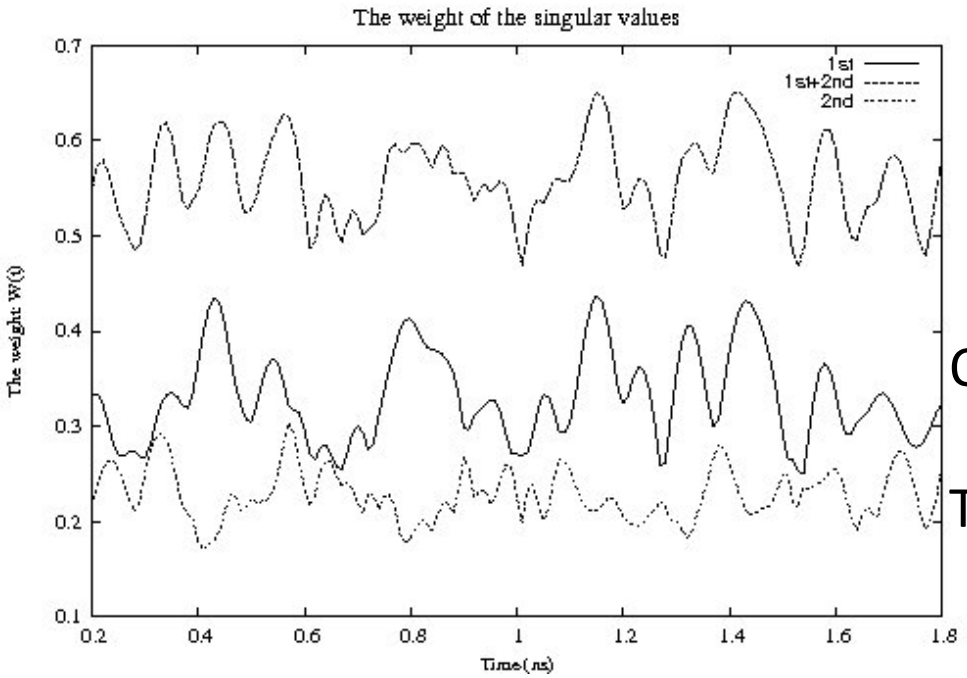
- Software: AMBER9 (SANDER)
- Apply MD to "1TIB" for 2ns
  with the time step of 10ps
  - Temporal sequence data for 200 steps

➔ Apply the feature extraction method to the trajectory data

- Use the data for the time steps between 0.2ns and 1.8ns
- Low-pass filter : M_1=15 and M_2=50
  The frequency range with its period between 133ps and 40ps
- The result of SVD
  - we obtain at most K=min(3N, 2(M_1−M_2+1)) non-zero singular values and their left-singular and right-singular vectors

Reduction of the degrees of freedom

The weight of the first and second singular values



$$W(t) = \frac{\left(\lambda_{1\text{or}2}(t)\right)^2}{\sum_{i=1}^{K}\left(\lambda_i(t)\right)^2}$$

- $\lambda_i(t)$ is the i-th singular value at time t

Only the first singular value
→ about 30%
The first + second singular values
→ 50%

In the following analysis,
we focus on the first singular vector.

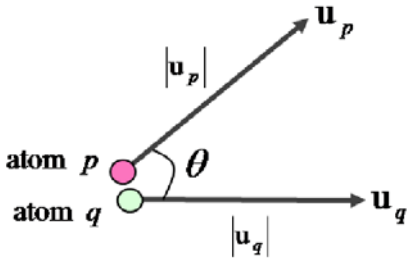
Collective motion of Cα atoms

- The first left singular vector $\mathbf{e}_{i=1}(t)$
  - The first left-singular vector describes the most dominant spatial features of the dynamics

- "Collective motion" of the protein

  The motion when neighboring Cα atoms oscillate along similar directions

- Characterize "collective motion" around the p-th Cα atom
  - The three-dimensional vector: $\mathbf{u}_p(t)$
    - $\mathbf{e}_{i=1}(t) = (\mathbf{u}_1(t), \ldots, \mathbf{u}_p(t), \ldots, \mathbf{u}_N(t))$,
    - We call $\mathbf{u}_p(t)$ "the Oscillation vector"

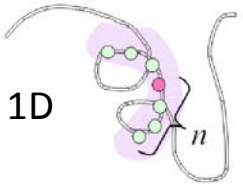


Indexes characterizing collectivity

Neighborhood of the *p*-th Cα atom

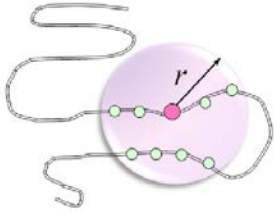
along the sequence of the protein

1D

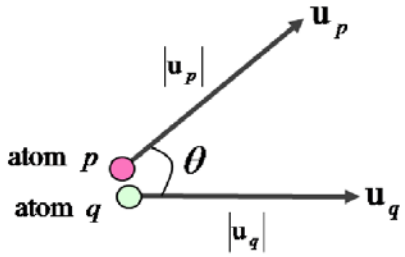


within its three dimensional conformation

3D



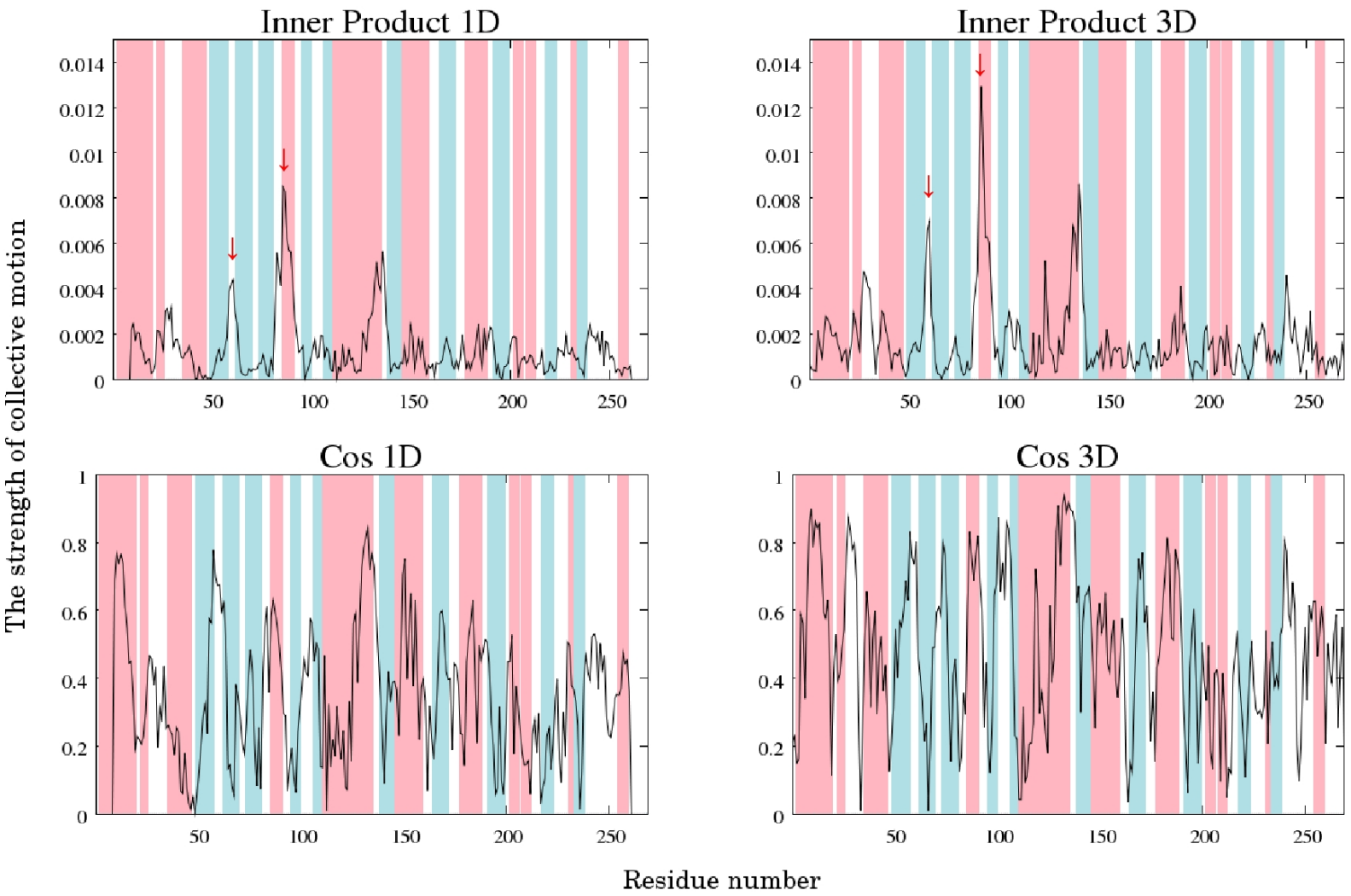
Similarity of the oscillation vectors



	Inner Product	Cosine
	$x_p^{(1)}(t) \equiv \frac{1}{2n-1}\left\lvert \sum_{\lvert p-q\rvert<n} \mathbf{u}_p(t)\cdot\mathbf{u}_q(t)\right\rvert$	$x_p^{(3)}(t) \equiv \frac{1}{2n-1}\left\lvert \sum_{\lvert p-q\rvert<n} \frac{\mathbf{u}_p(t)\cdot\mathbf{u}_q(t)}{\lVert\mathbf{u}_p(t)\rVert\lVert\mathbf{u}_q(t)\rVert}\right\rvert$
	$x_p^{(2)}(t) \equiv \frac{1}{b_{p,r}(t)}\left\lvert \sum_{\lvert \mathbf{r}_p(t)-\mathbf{r}_q(t)\rvert<r} \mathbf{u}_p(t)\cdot\mathbf{u}_q(t)\right\rvert$	$x_p^{(4)}(t) \equiv \frac{1}{b_{p,r}(t)}\left\lvert \sum_{\lvert \mathbf{r}_p(t)-\mathbf{r}_q(t)\rvert<r} \frac{\mathbf{u}_p(t)\cdot\mathbf{u}_q(t)}{\lVert\mathbf{u}_p(t)\rVert\lVert\mathbf{u}_q(t)\rVert}\right\rvert$

※
- n : The number of atoms from the p-th Cα atom
- $b_{p,r}(t)$: The number of atoms within the radius r from the p-th Cα atom
- $\mathrm{r}_p(t)$: The coordinate vector of the p-th Cα atom at time t

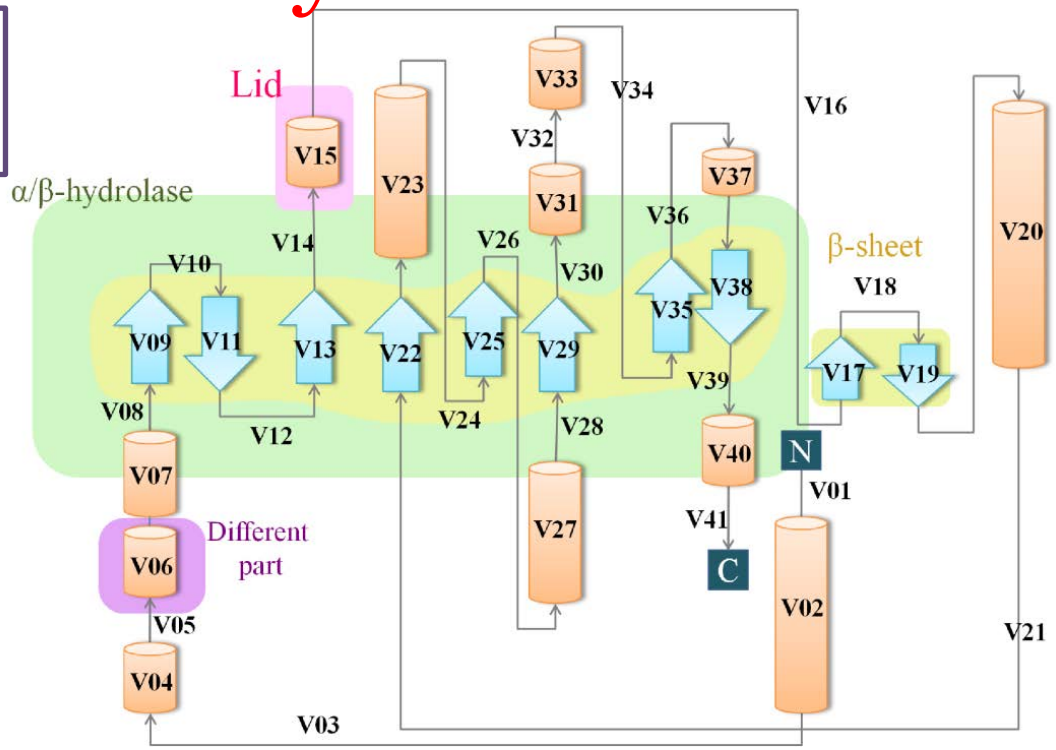
Correspondence with secondary structures



Index for collectivity of secondary structures

Secondary structure of 1TIB

Each structure is identified by the number k=1,..,41 from the N-terminal



New Index of collective motion for the k-th secondary structure

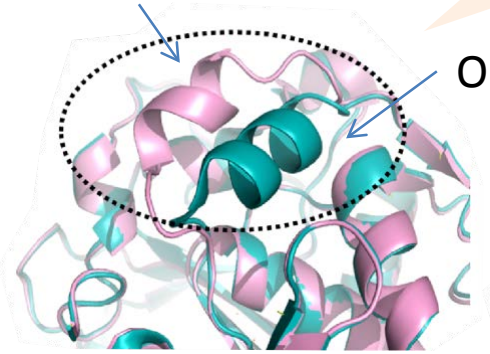
$$R_k^{(i=4)}(t) = \sum_{p=1}^{N} v_{k,p} \cdot x_p^{(i=4)}(t)$$

- Cα atom p belongs to the k-th secondary structure → $v_{k,p} = 1/N_k$,
- * Otherwise → $v_{k,p} = 0$.

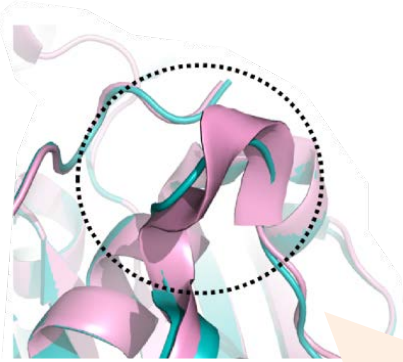
Focus on secondary structures with conformational change

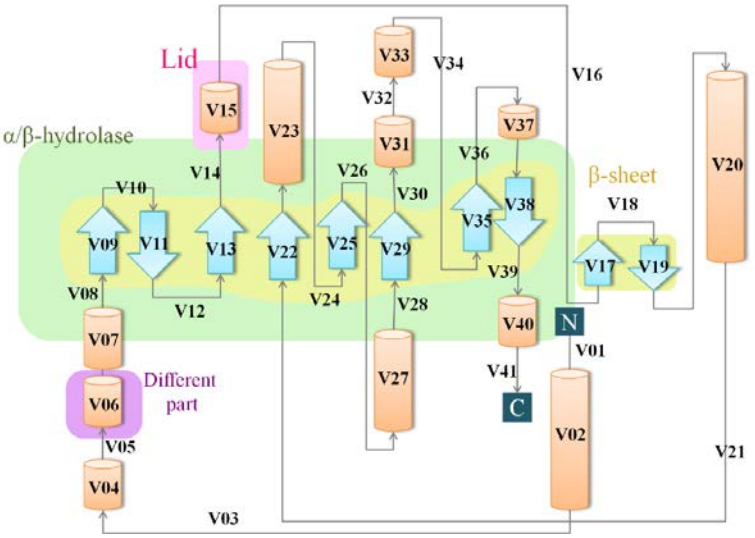
"Lid" (correspond to the structure v15)
varies its form according to conformational changes.

Closed conformations



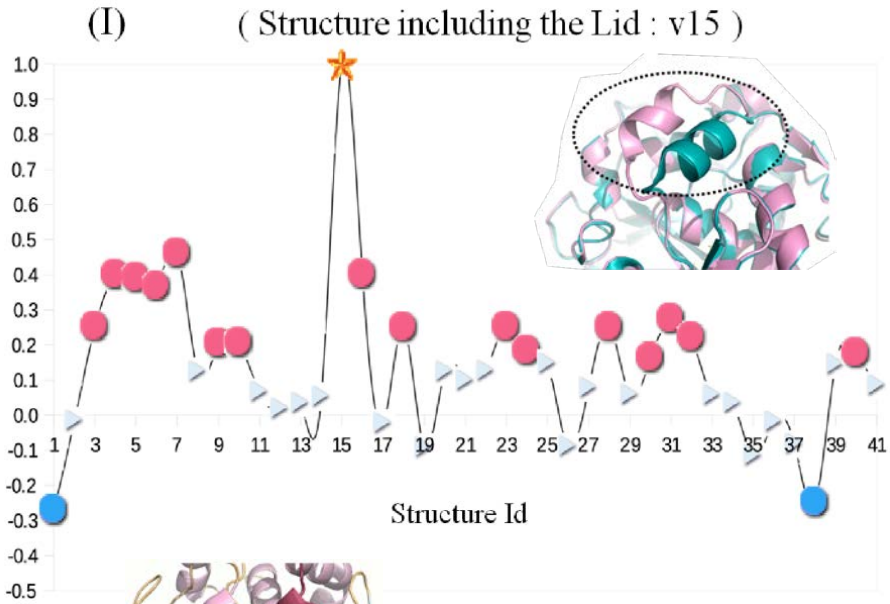
Open conformations

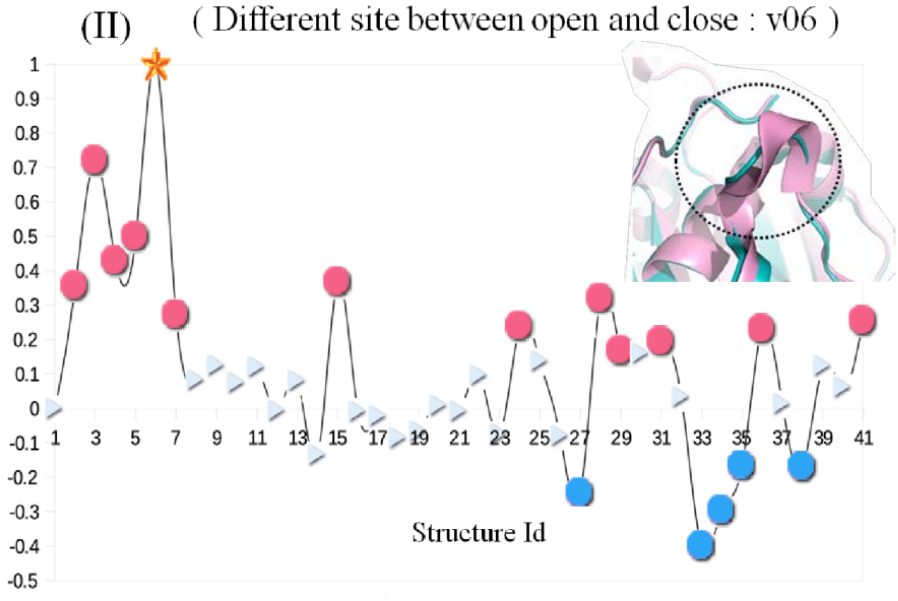


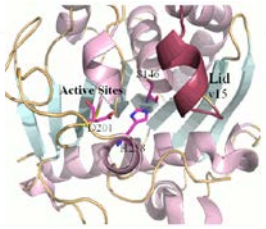


The structure v6 forms a loop in the open conformations, while it forms α-helix in the close conformations

Correlation with other structures







* The structures including active sites are v23, v30, 40.

- v15 and v06 have large correlation with each other.
- Lid v15 has relatively large correlation with functionally important parts.
- v06 does not affect much the motion of functionally important parts.
- Some parts exhibit negative correlation in collectivity

Conclusions

- Method to extract hierarchy of collective motion combining wavelet transformation and SVD
- Correlation of collectivity among secondary structures
- Apply the methods to a protein TLL
  - Index for collective motion within secondary structures indicate not only their collectivity but also show "cracking"
  - Correlation between those with conformational change and functionally important structures
- Future work
  - Correlation network and its modular structure
  - Apply our methods to "intrinsically disordered proteins"
  - Collectivity of higher structures

Dynamics from micro to macro through mesoscopic levels

- Phase space structure enables us to find new reaction mechanism in both microscopic and macroscopic levels

- Various hierarchical structures exist both in space and time
- How do they correlate in mesoscopic levels leading to functionally important movement?

References

- Global Aspects of Chemical reactions in Multidimensional Phase Space
  Adv. Chem. Phys. vol.130(2005)Part A,337-399
  M.Toda
- Dynamics of Chemical Reactions and Chaos
  Adv. Chem. Phys. vol.123(2002)153-198
  M.Toda
- Analysis of motion features for molecular dynamics simulation of proteins
  Chem. Phys. Lett. Vol. 502, 241-247,
  M. Kamada, M. Toda et.al