

Control of a Model of DNA Division via Parametric Resonance

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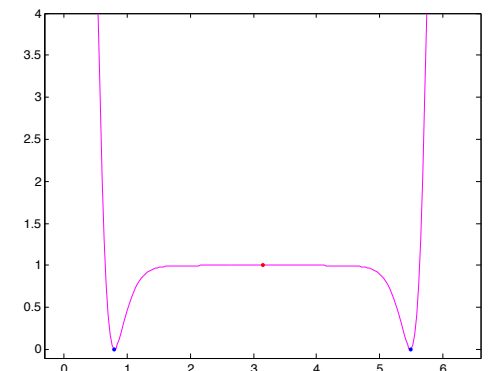
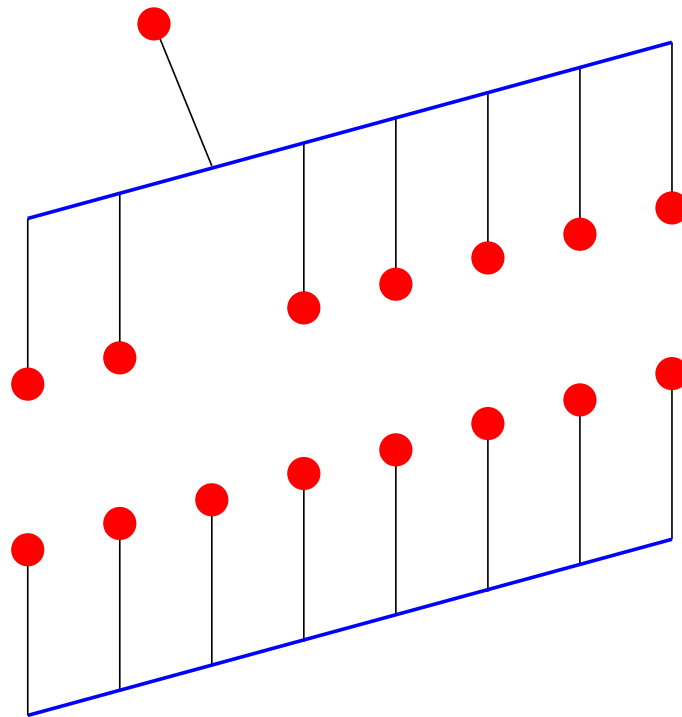
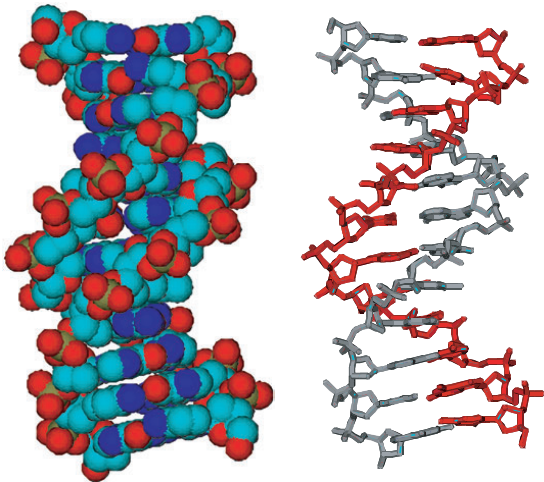
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- ▶ Study internal resonance, energy transfer, activation mechanism, and control of a model of DNA division via parametric resonance.
 - provide a method for controlling real DNA division by EM fields,
 - suggest how enzymes initiate the opening of DNA strands.
- ▶ A Model of DNA Division.

An Intriguing Phenomenon of Structure Activations that the model exhibits in previous numerical studies.
- ▶ Our Results on studying this phenomenon analytically.
 - 0 : 1 resonance, appropriate to use 2-Mode Reduced Models.
 - apply partial averaging to obtain Averaged Reduced Equations.
 - reveal activation mechanism/estimate Min. Activation Energy that match well with numerical simulation of Full Model.
- ▶ By building on our study of its internal dynamics, we are able to control division of this DNA model via Parametric Excitation, that is in resonance with its internal trigger mode.

■ A Model of DNA Division (I)

- ▶ A chain of **pendula** that rotate about axis of a **fixed backbone**, with angle θ_k measured from upward position.
 - The pendula interact with **nearest neighbors** along the backbone through **harmonic torsional coupling**, and
 - with **pendula** on the opposing immobilized strand through a **Morse potential**.



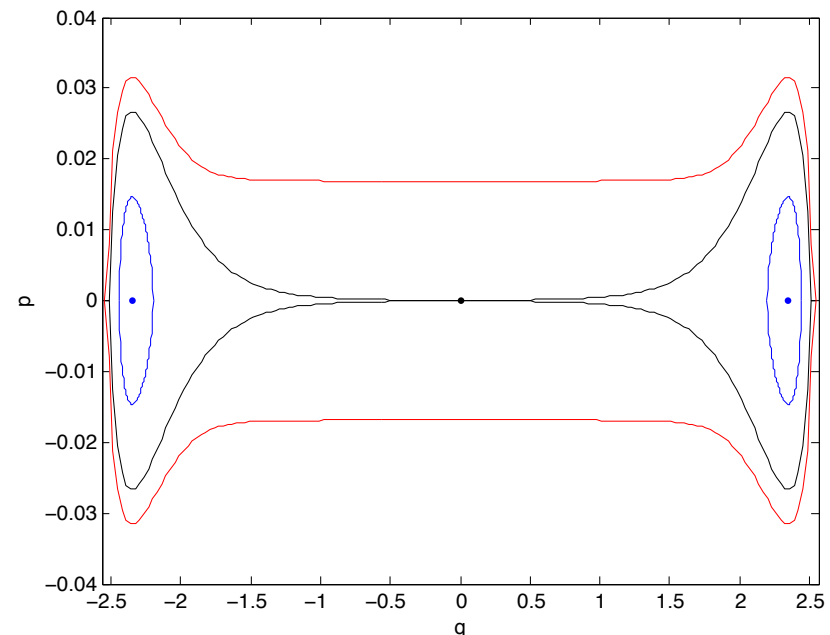
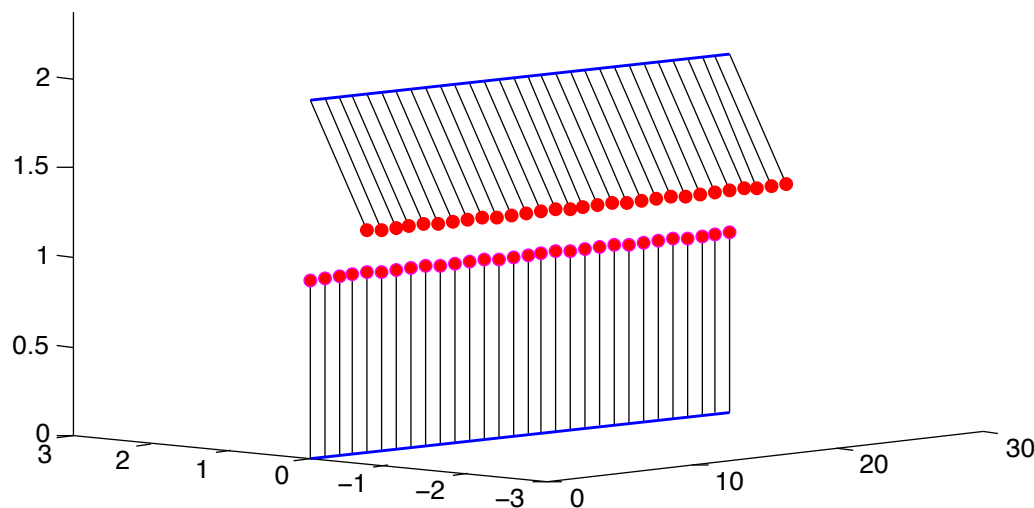
■ A Model of DNA Division (II)

- ▶ Non-dimensional Hamiltonian for these n coupled pendula

$$H(\theta, p_\theta) = \sum_{k=1}^n \left[\frac{1}{2} p_{\theta k}^2 + \frac{1}{2} (\theta_k - \theta_{k-1})^2 + \epsilon \left(e^{-a(1+\cos \theta_k - d_0)} - 1 \right)^2 \right]$$

with periodic boundary condition $\theta_0 = \theta_n$.

- ▶ Parameter values are chosen to best represent typical values for DNA division. Decaying coefficient $a = 7$; Equilibrium distance $d_0 = 0.3$; Amplitude $\epsilon = 1/1400$.

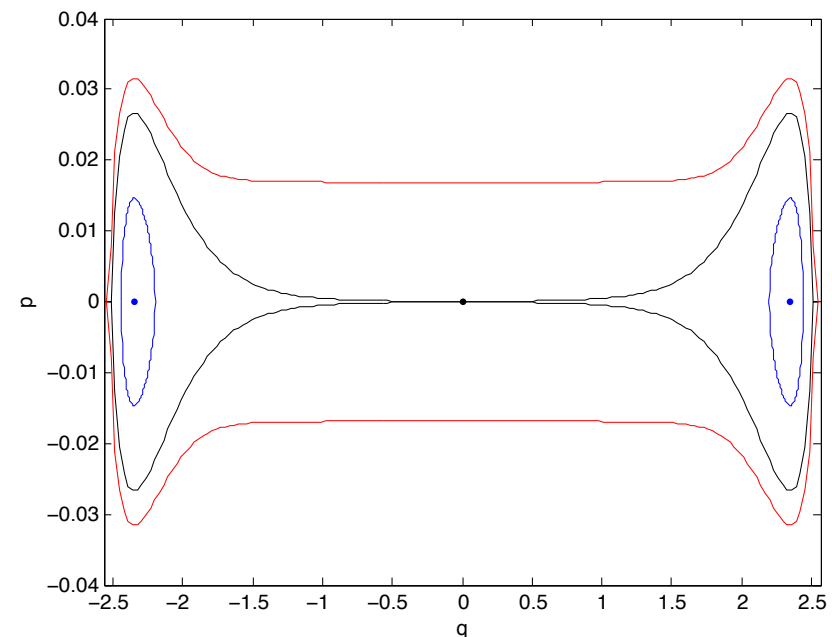
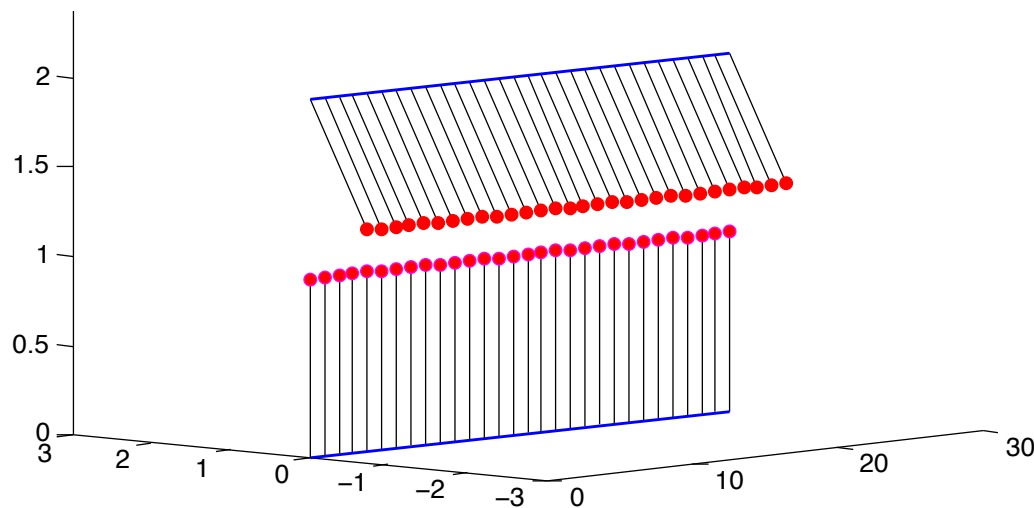


■ A Model of DNA Division (III)

- For analytical study, a Hamiltonian of 30 coupled pendula is used

$$H(\theta, p_\theta) = \sum_{k=1}^{30} \left[\frac{1}{2} p_{\theta k}^2 + \frac{1}{2} (\theta_k - \theta_{k-1})^2 + \epsilon \left(e^{-a(1+\cos \theta_k - d_0)} - 1 \right)^2 \right]$$

- Before studying model, instructive to look at 1 pendulum (n=1).
- Phase space of a pendulum in Morse potential without coupling.
 - 2 stable equilibria at $(\pm\theta_e, 0)$, 1 saddle at $(0, 0)$.
 - **Separatrix**, oscillation near equilibria, flipping across saddle.
- Model of 30 coupled pendula:



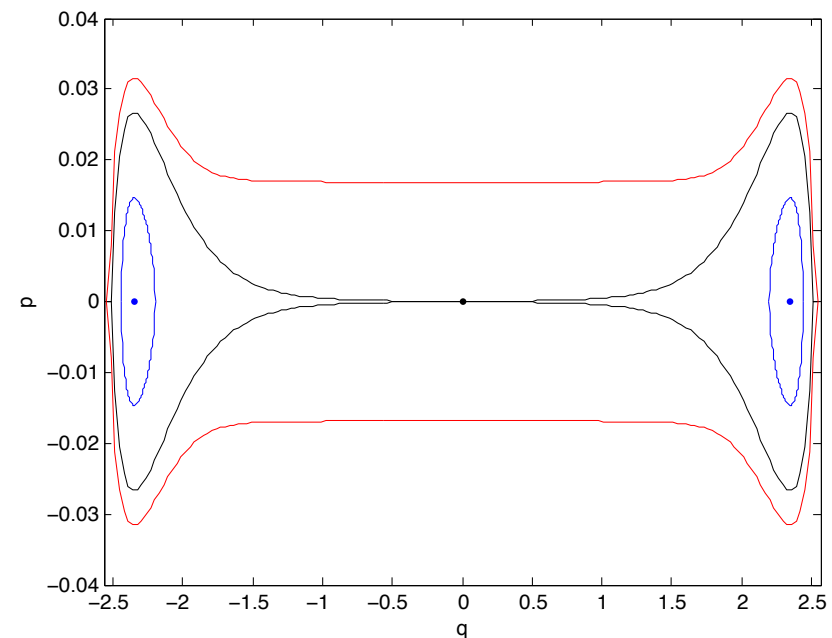
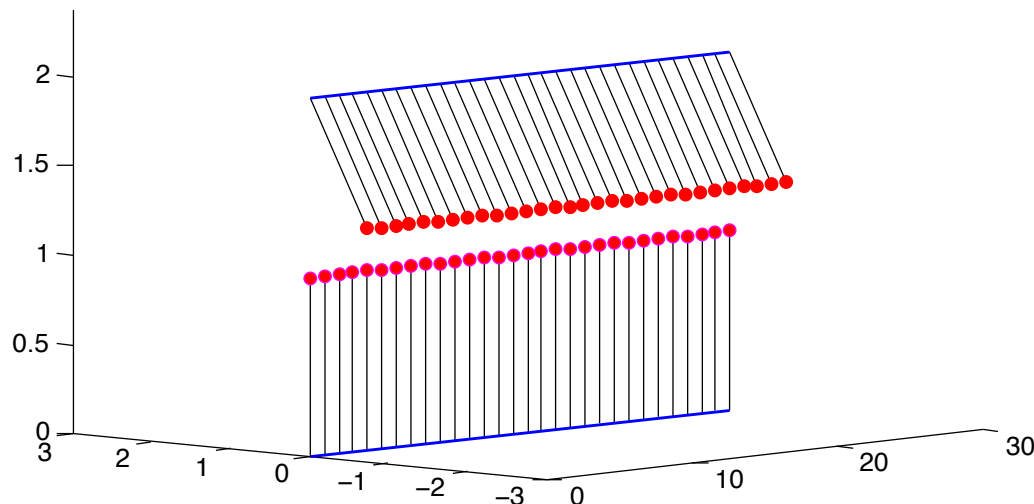
■ A Model of DNA Division (IV)

- **30-coupled** pendula has similar but much complicated behaviors.

$$H(\theta, p_\theta) = \sum_{k=1}^{30} \left[\frac{1}{2} p_{\theta k}^2 + \frac{1}{2} (\theta_k - \theta_{k-1})^2 + \epsilon \left(e^{-a(1+\cos \theta_k - d_0)} - 1 \right)^2 \right]$$

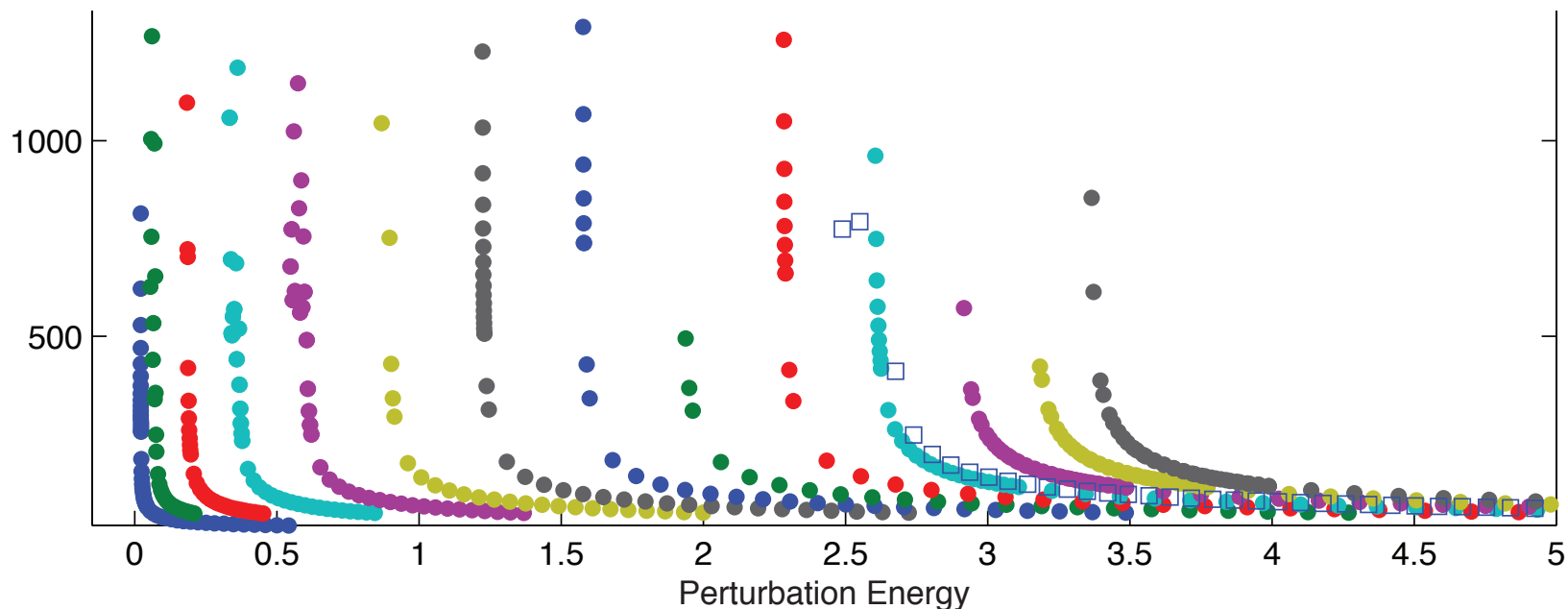
- 2 **stable equilibria** when $\theta_k = \pm\theta_e$, 1 rank one saddle when $\theta_k = 0$.
- For small energy, **liberate near stable equilibria** (global minima).
 - For large enough energy, **move collectively** from one **energy basin** to **the other** and **flip across** a rank 1 saddle.

- Model of 30 coupled pendula:



■ Phenomenon of Structured Activations (I)

- ▶ Previous studies, [mainly numerical](#), showed that this model exhibits an intriguing phenomenon of [structured activations](#):
 - While the system is **robust to noise**, it is [sensitive to certain specific fine scale modes](#) that can trigger the division.
 - See [Mezic \[2006\]](#), [Eisenhower and Mezic \[2007, 2010\]](#), [Eisenhower \[2009\]](#), [Du Toit, Mezic, and Marsden \[2009\]](#).
- ▶ Figure (Eisenhower [2009]): Show initial amount of [energy](#) injected for various [types of activation](#) vs [time to DNA division](#).



■ Phenomenon of Structured Activations (II)

- To appreciate figure and claim shown above, need to introduce **Fourier modal coord. q** related to system coord. ($\theta = Tq$):

$$\theta_k = \sqrt{\frac{2}{n}} \sum_{\alpha=0}^{\frac{n}{2}-1} \left[\frac{q_0}{\sqrt{2}} + \cos \frac{2\pi k \alpha}{n} q_\alpha + \frac{(-1)^j q_{\frac{n}{2}}}{\sqrt{2}} + \sin \frac{2\pi k \alpha}{n} q_{\frac{n}{2}+\alpha} \right].$$

- FMC reveal **natural dynamics** of the system by **diagonalising** linear coupling terms and rewriting the Hamiltonian as follows

$$H(q, p) = \sum_{\alpha=0}^{n-1} \left(\frac{1}{2} p_\alpha^2 + \frac{1}{2} \omega_\alpha^2 q_\alpha^2 \right) + \epsilon \sum_{k=1}^n U \left(\sum_{\beta=0}^{n-1} T_{k\beta} q_\beta \right)$$

where $U(\theta) = (e^{-a(1+\cos \theta - d_0)} - 1)^2$ is Morse potential function.

- **Now**, the model can be seen as a **small perturbation** of n oscillators with frequencies ω_α : $\omega_\alpha^2 = 2 - 2 \cos (2\pi \alpha / n)$, $\alpha = 0, \dots, n - 1$.

■ Phenomenon of Structured Activations (III)

- ▶ This can also be seen clearly if we write EOM in Lagrangian form

$$\begin{aligned}\ddot{q}_0 &= -\epsilon M_0(q_0, q_1, \dots, q_{n-1}) \\ \ddot{q}_\alpha + \omega_\alpha^2 q_\alpha &= -\epsilon M_\alpha(q_0, q_1, \dots, q_{n-1})\end{aligned}$$

with modal frequencies $\omega_\alpha^2 = 2 - 2 \cos(2\pi\alpha/n)$, $\alpha = 1, \dots, n-1$.

- ▶ The coordinate of 0th (Fourier) mode, q_0 , given as follows

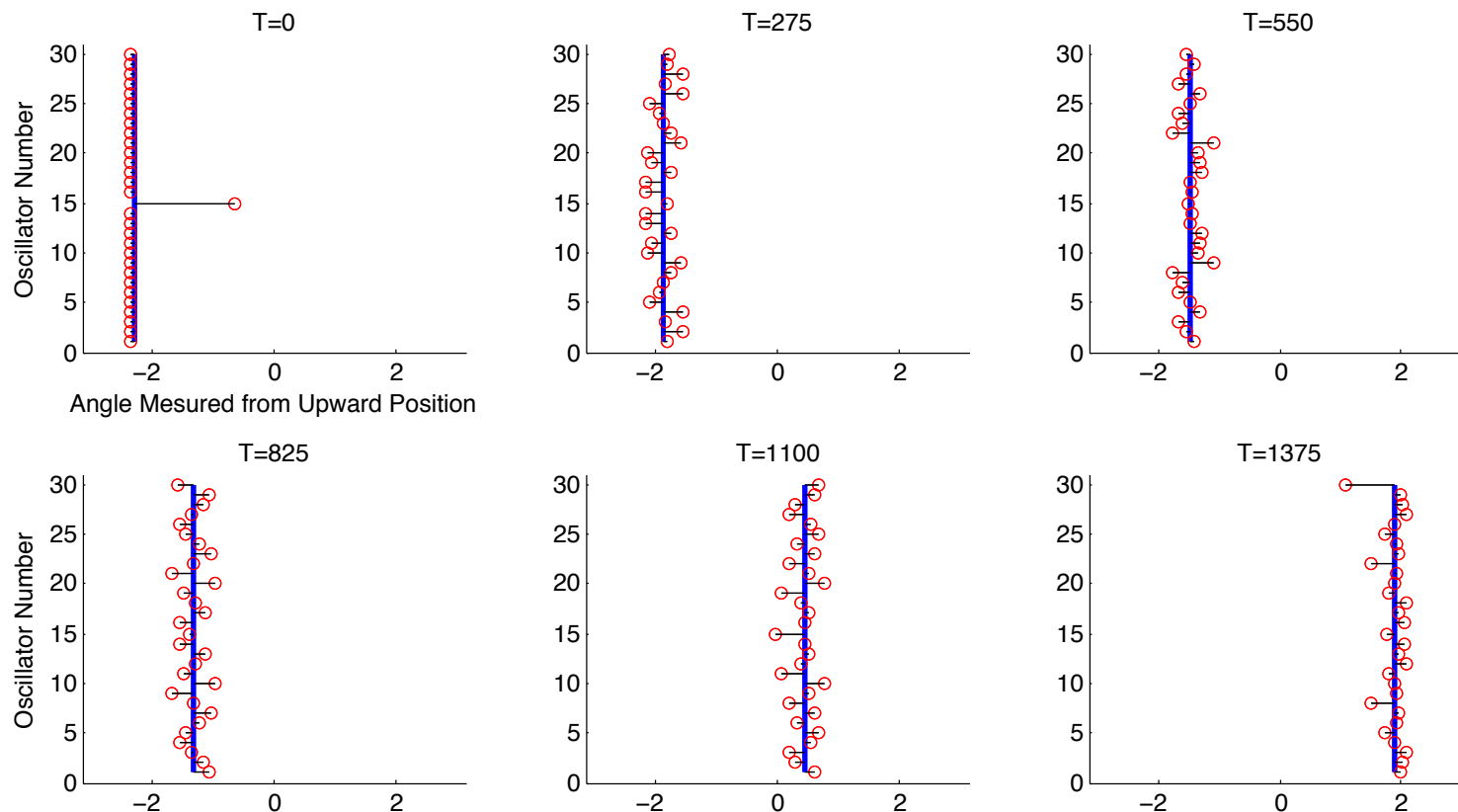
$$q_0 = \frac{1}{\sqrt{n}} \sum_{k=1}^n \theta_k = \sqrt{n} \bar{\theta}$$

is the average angle $\bar{\theta}$ of pendula (except a factor of \sqrt{n}).

- ▶ It plays the special and important role as the collective variable, reaction coordinate, and slow variable, as will be shown later.
- ▶ Other $(n-1)$ modal coordinates q_α are the bath coordinates, and the fast variables.

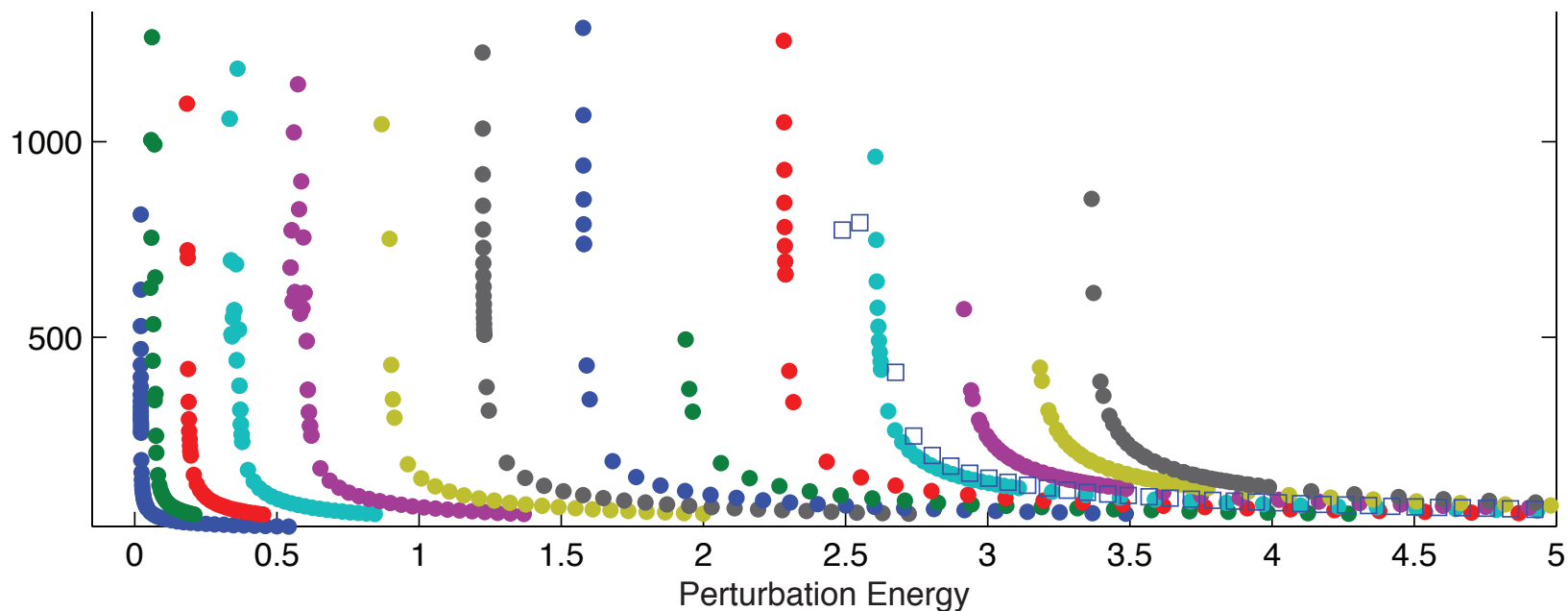
■ Phenomenon of Structured Activations (IV)

- ▶ The role of $q_0 = \sqrt{n\bar{\theta}}$ can be seen from sequence of 6 snapshots of evolution of 30 pendula from equilibria $-\theta_e$ to θ_e across $\theta = 0$.
- ▶ For simplicity, only one pendulum is perturbed as initial activation.
- ▶ Because coupling is much stronger than nonlinearity, transition is collective, closely follow average (thick blue line).
- ▶ Average angle q_0 can be used to mark time to division.



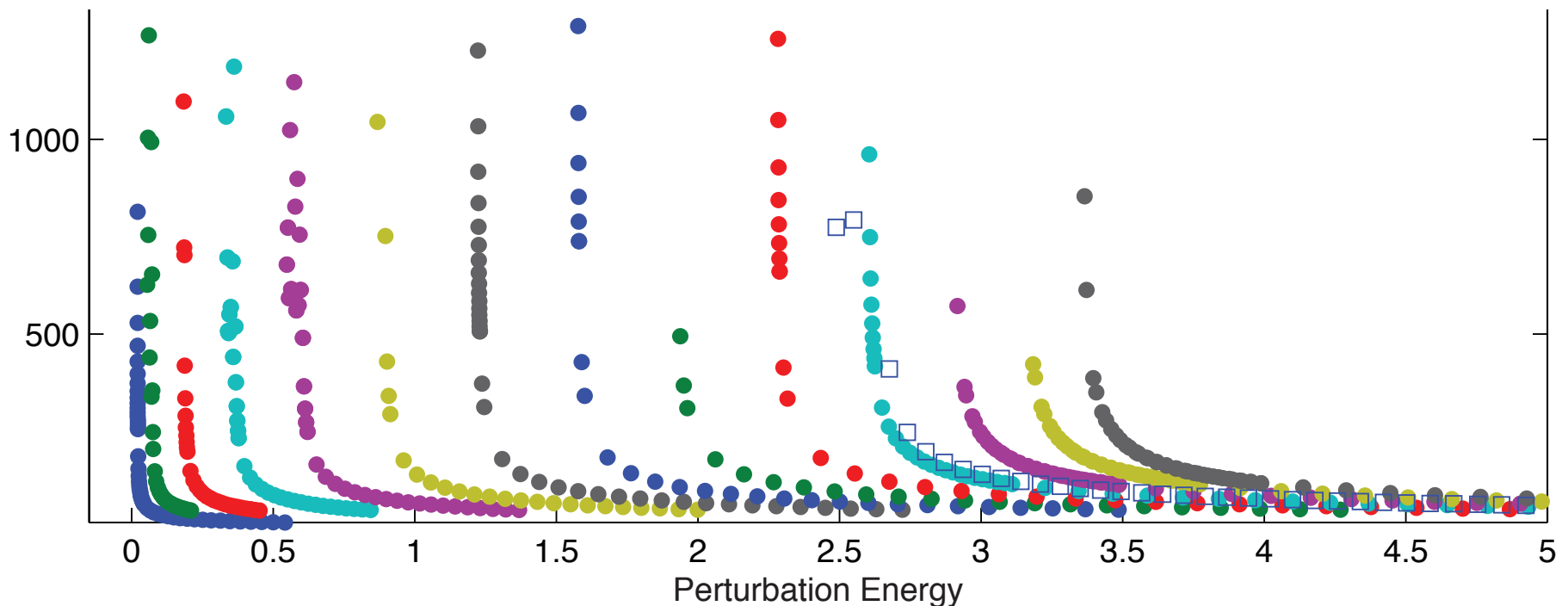
■ Phenomenon of Structured Activations (V)

- ▶ **Now**, initial activation is chosen as a single Fourier mode, $p_\gamma(0)$, and its amplitude modified to vary the amount of activation energy.
- ▶ Time to division determined when average angle q_0 cross $q_0 = 0$.
- ▶ A curve is obtained that shows the amount of activation energy vs the time to DNA division for each Fourier mode (first 14 modes).
- ▶ Each has asymptote at low energy limit (min. activation energy).
- ▶ White "□"s show the data for **random noise**.



■ Phenomenon of Structured Activations (VI)

- ▶ The **minimum activation energy** (MAE) depends on the way this energy is injected into the system.
- ▶ While the system is **robust to noise**, it is **sensitive to certain specific fine scale modes** that can trigger the division.
- ▶ Want to develop **analytical method** to **reveal activation mechanism** and **to compute MAEs**.
- ▶ Want to develop methods for **controlling DNA division via EM fields** and to reveal **how enzymes initiate DNA open state dynamics**.



■ Analytical Study: 0 : 1 Resonance/Partial Averaging

► Recall EOM

$$\begin{aligned}\ddot{q}_0 &= -\epsilon M_0(q_0, q_1, \dots, q_{n-1}) \\ \ddot{q}_\alpha + \omega_\alpha^2 q_\alpha &= -\epsilon M_\alpha(q_0, q_1, \dots, q_{n-1})\end{aligned}$$

which can be seen as a **nonlinear perturbation** of n harmonic oscillators where ω_α varies from 0.2091 to 2.

- The reactive mode (0th mode) forms a nearly 0 : 1 **resonance** with any other mode, each of which has an $O(1)$ frequency

$$m\omega_0 + 0\omega_\alpha = 0, \quad \text{with } m = 1.$$

- This fact leads to **small denominators** and **coupling terms** in the corresponding **averaged equations** or **normal form**.
- Other modal frequencies, are not rationally commensurate and do not have significant time scale separation.

We do not expect strong resonance among them.

- Expect nearly 0 : 1 **resonance** will be main focus of our study.

■ Nearly 0 : 1 Resonance and Partial Averaging

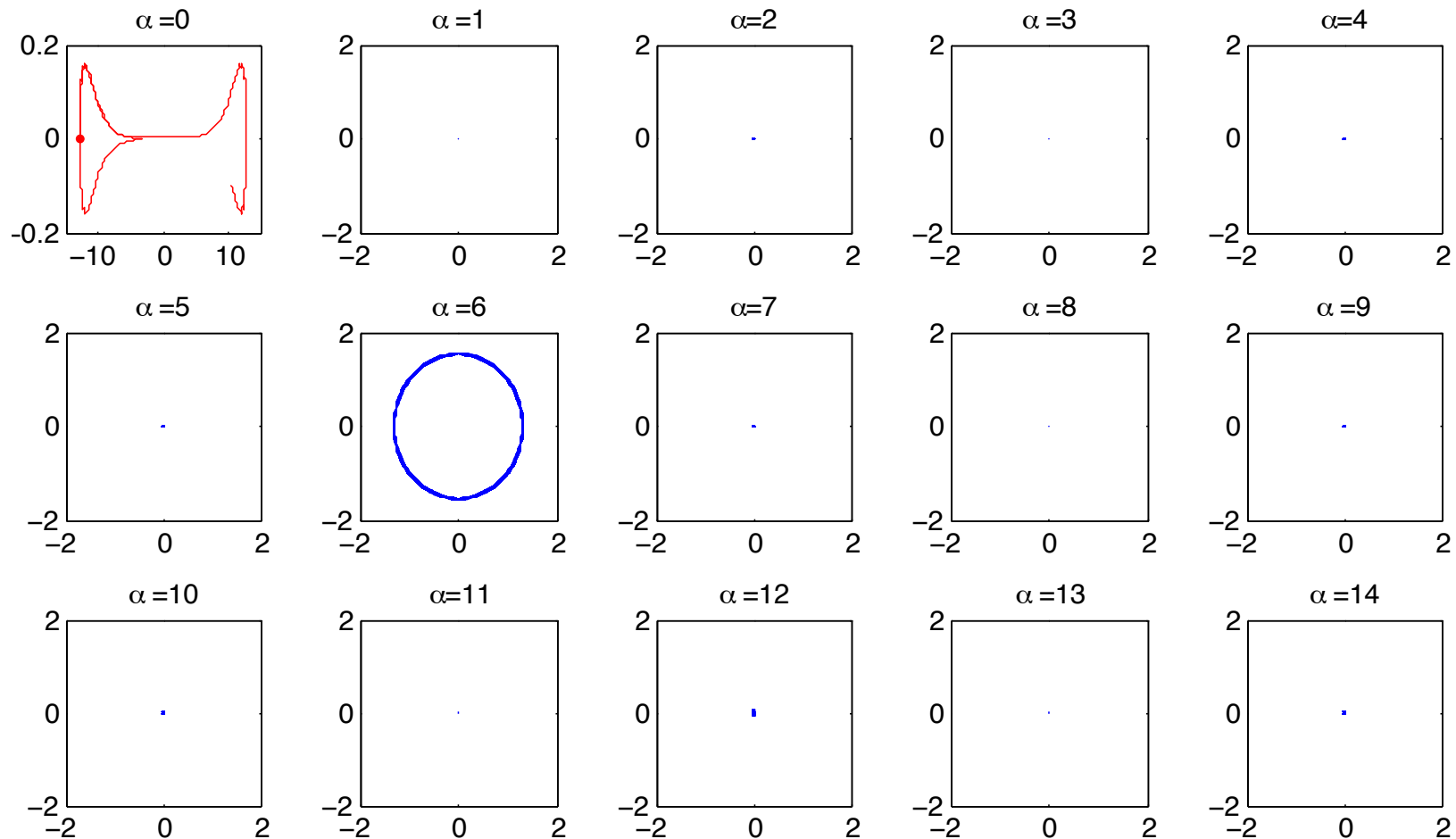
- ▶ Nayfeh & Chin [1995] & Haller [1999] has studied such **degenerate resonance**: they applied a **modified averaging method** to **2 mode truncation** of a mechanical system having this type of resonance.
- ▶ While Eisenhower & Mezic did not mentioned **0 : 1 resonance**, they did apply **Arnold's method of partial averaging** to a **truncated Hamiltonian** in the study of a chain of **Duffing** oscillators.
 - Reason for studying Duffing case: "The exponential form of the **Morse** potential makes analytical progress difficult,..."

Since we have not seen this kind of simplification in DNA literatures, we will keep **Morse** potential (and the added difficulty).

- ▶ To carry out analytical work for such a high DOF system, **reduced model** is needed. The **work** of these researchers, our understanding of nearly **0 : 1 resonance**, our extensive **numerical simulations**, and a rigorous **error estimate** have convinced us that **2 mode truncation** is adequate for our analytical study of structured activations.

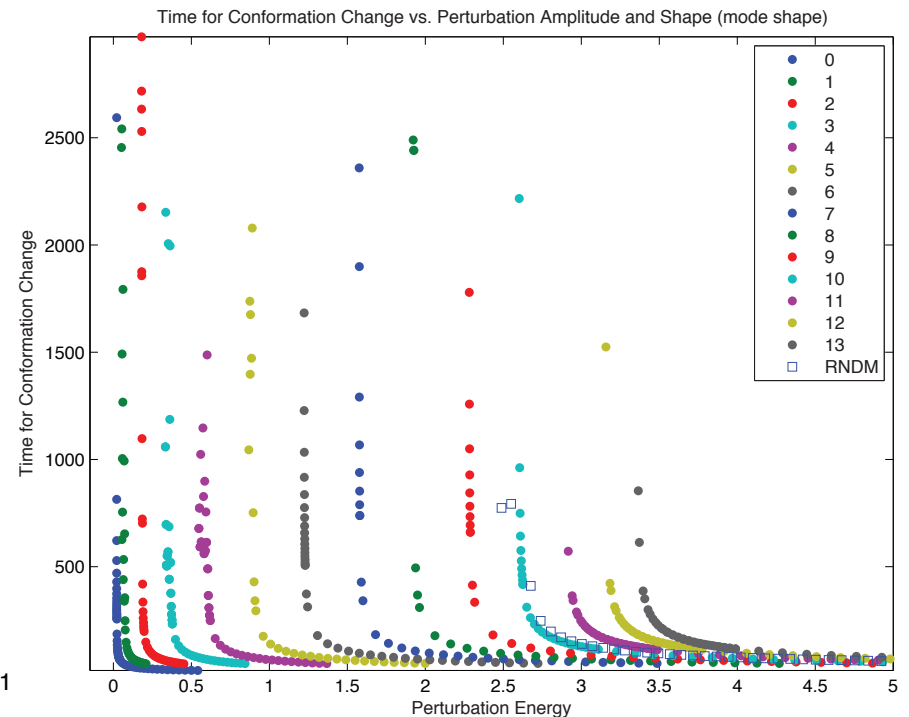
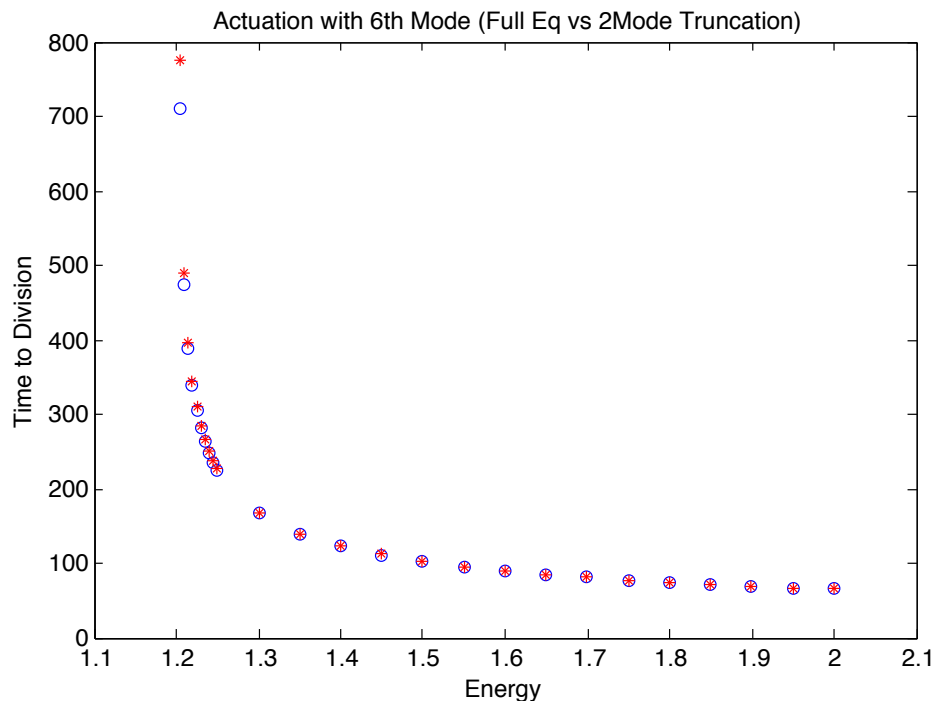
■ Two Mode Truncation Is Adequate (I)

- Projections of a sample trajectory on phase spaces of first 15 modes. Initial activation chosen to be single 6th mode ($q_0^e, \dots, p_6(0), \dots$).
 - energy transfer over-whelmingly from excited to reactive mode,
 - only an extremely small amount of energy transfers from the excited mode to 1 or 2 other modes via near resonances.



■ Two Mode Truncation is Adequate (II)

- ▶ Show **Activation Energy** vs **Time to DNA Division**
 - blue "o"s are data points for **full equations** (30 modes);
 - red "*"s are data points for **2 mode truncation** (0th & 6th mode).
- ▶ Both have almost the same **minimum activation energy** 1.205.
- ▶ Their **time to division** differs very little if **activation energy** is slightly larger than MAE.
- ▶ All data from simulation confirm: **2 mode truncation is adequate**.



■ Averaged Reduced Hamiltonian (I)

► Ready to apply **partial averaging**

- to obtain **averaged reduced equations** for reduced models,
- to study activation mechanism & compute MAE for each mode.

► For 2 mode truncation (0th and γ th mode), Lagrangian EOM is

$$\begin{aligned}\ddot{q}_0 &= -\epsilon M_0(q_0, q_\gamma) \\ \ddot{q}_\gamma + \omega_\gamma^2 q_\gamma &= -\epsilon M_\gamma(q_0, q_\gamma).\end{aligned}$$

Notice: q_0 is the slow variable and q_γ is the fast variable.

► Its correspondent Hamiltonian is

$$H_2^\gamma(q, p) = \sum_{\alpha=\{0,\gamma\}} \left(\frac{1}{2} p_\alpha^2 + \frac{1}{2} \omega_\alpha^2 q_\alpha^2 \right) + \epsilon \sum_{k=1}^n U \left(\sum_{\beta=\{0,\gamma\}} T_{k\beta} q_\beta \right)$$

► Since partial averaging of **Lagrangian equations** is equivalent to partial averaging of its **Hamiltonian**, and our main concern is on energy transfer, we preferred to use Hamiltonian formulation.

■ Averaged Reduced Hamiltonian (II)

- First, **expand** Morse potential U , which involves exponential function, as a polynomial of 26 degrees at $\theta = 0$.

$$H_2^\gamma(q, p) = \sum_{\alpha=\{0,\gamma\}} \left(\frac{1}{2} p_\alpha^2 + \frac{1}{2} \omega_\alpha^2 q_\alpha^2 \right) + \epsilon \sum_{k=1}^n \sum_{j=0}^{26} a_j \left(\sum_{\beta=\{0,\gamma\}} T_{k\beta} q_\beta \right)^j$$

- Then, **use** action angle coordinates

$$q_\gamma = \sqrt{2I_\gamma/\omega_\gamma} \sin \phi_\gamma, \quad p_\gamma = \sqrt{2I_\gamma\omega_\gamma} \cos \phi_\gamma.$$

and **rewrite** reduced Hamiltonian as $H_2^\gamma(q_0, p_0, I_\gamma, \phi_\gamma)$.

- Notice: Besides q_0, p_0 , action I_γ is also a slow variable.
- The **average reduced Hamiltonian** can be obtained by **averaging** the only fast variable ϕ_γ

$$\bar{H}_2^\gamma(\bar{q}_0, \bar{p}_0, \bar{I}_\gamma) = \frac{1}{2\pi} \int_0^{2\pi} H_2^\gamma(q_0, p_0, I_\gamma, \phi_\gamma) d\phi_\gamma$$

■ Averaged Reduced Hamiltonian (III)

► After renaming variables, **average reduced Hamiltonian** is

$$\bar{H}_2 = \frac{1}{2}y^2 + \omega I + \epsilon \left(na_0 + \sum_{k=0}^{13} c_{2k}(I)x^{2k} \right)$$

- $x = \bar{q}_0, y = \bar{p}_0$ are Cartesian coordinates of 0th mode;
- $I = \bar{I}, \omega = \omega_\gamma$ are action and frequency of the other mode;
- $c_{2k}(I)$, polynomials in I ; $\epsilon na_0 = 0.0214$: energy value at saddle.

► **Average reduced Hamiltonian equations** are

$$\begin{aligned} \dot{x} &= y, & \dot{I} &= 0 \\ \dot{y} &= -\epsilon \left(\sum_{k=1}^{13} 2k c_{2k}(I) x^{2k-2} \right) x; & \dot{\phi} &= \omega + \epsilon \left(\sum_{k=0}^{13} \frac{dc_{2k}}{dI} x^{2k} \right) \end{aligned}$$

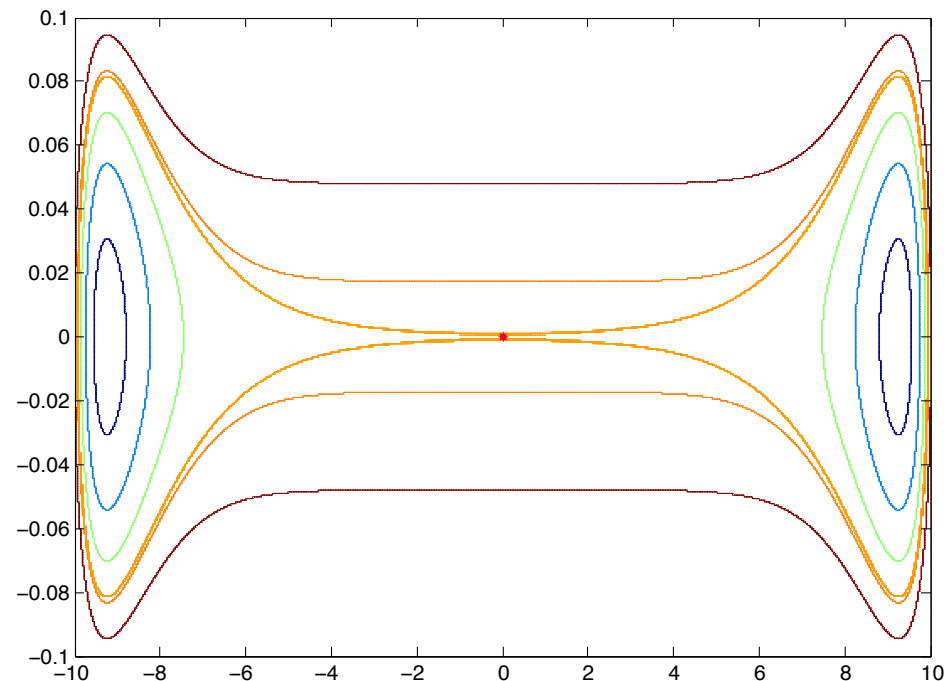
I is a constant of motion. Averaged equations and averaged phase space structures of the reactive mode are parametrized by I .

■ Phase Space of Averaged Reduced Equations (I)

- ▶ Average reduced Hamiltonian is

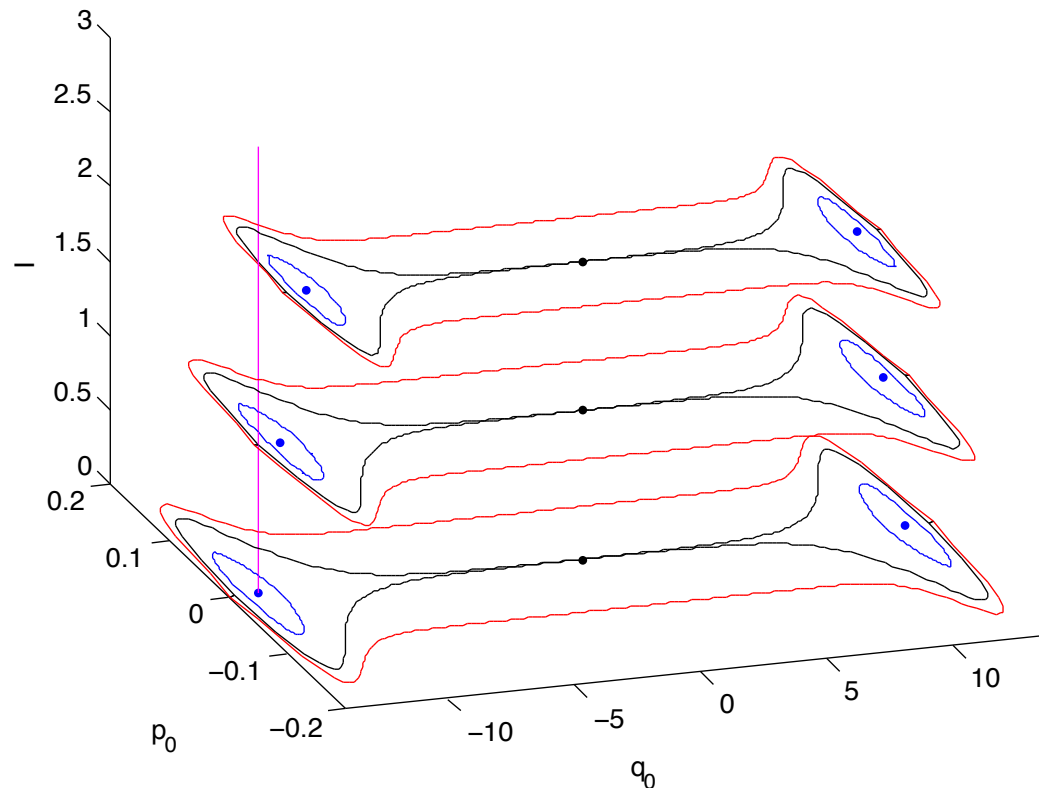
$$\bar{H}_2 = \frac{1}{2}y^2 + \omega I + \epsilon \left(na_0 + \sum_{k=0}^{13} c_{2k}(I)x^{2k} \right)$$

- ▶ Show the **contour plots** for average reduced Hamiltonian which is the **phase space** for average reduced equations. ($I = 5$)
- ▶ **Separatrix**. 2 types of motion: **Liberation** and **Flipping**.



■ Phase Space of Averaged Reduced Equations (II)

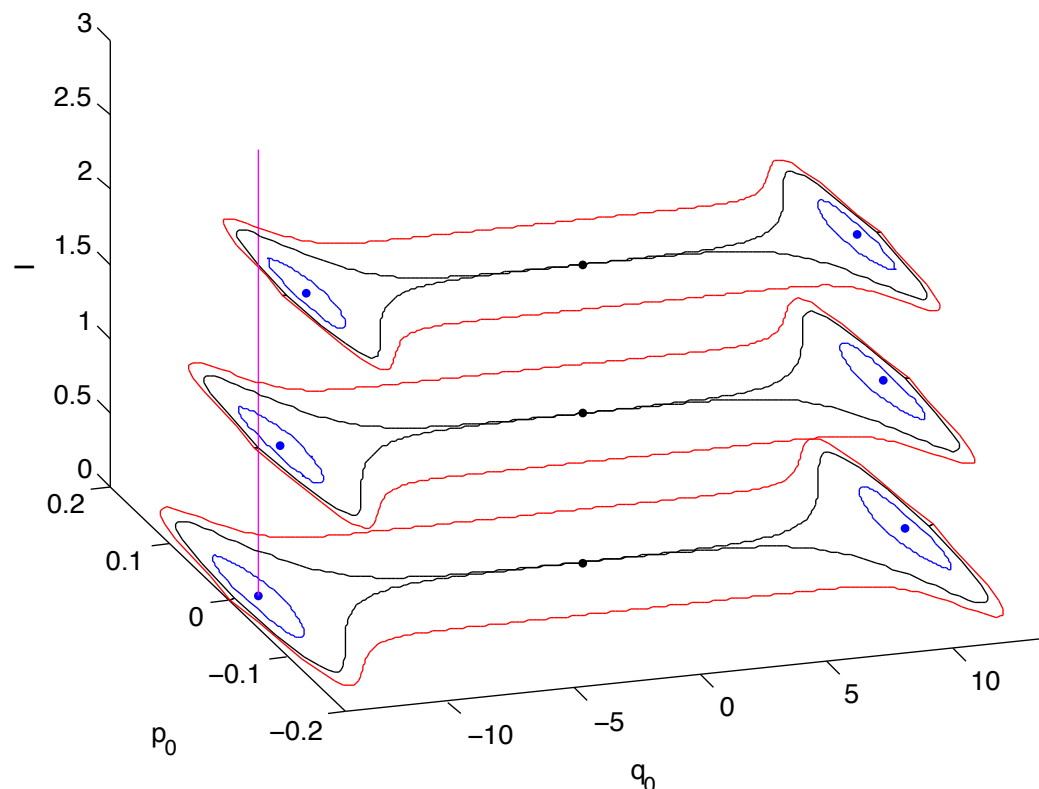
- ▶ If stacked up in increasing I (action of excited mode), we obtain



- ▶ In (x, y, I) space, vertical axis can also be seen as axis of increasing activation energy by scaling with ω , $E_{act} = \omega I$.
- ▶ The **separatrix** "shrinks" towards the saddle as E_{act} increases. Together, ("homoclinic manifold") can be used to study MAEs.

■ Analytical Study of MAE (I)

- ▶ For **averaged reduced system**, this process manifests itself via changes in phase spaces parametrized by I .
- ▶ For **activation energy** slightly larger than **MAE**, ($E_{min} = \omega I_m$), **initial equilibrium** at $(x_e, 0)$, now parametrized by I_m^+ , $(x_e, 0, I_m^+)$, will cross the **separatrix** parametrized by I_m^+ , move into **flipping region** of phase space parametrized by I_m^+ and induce the DNA division.



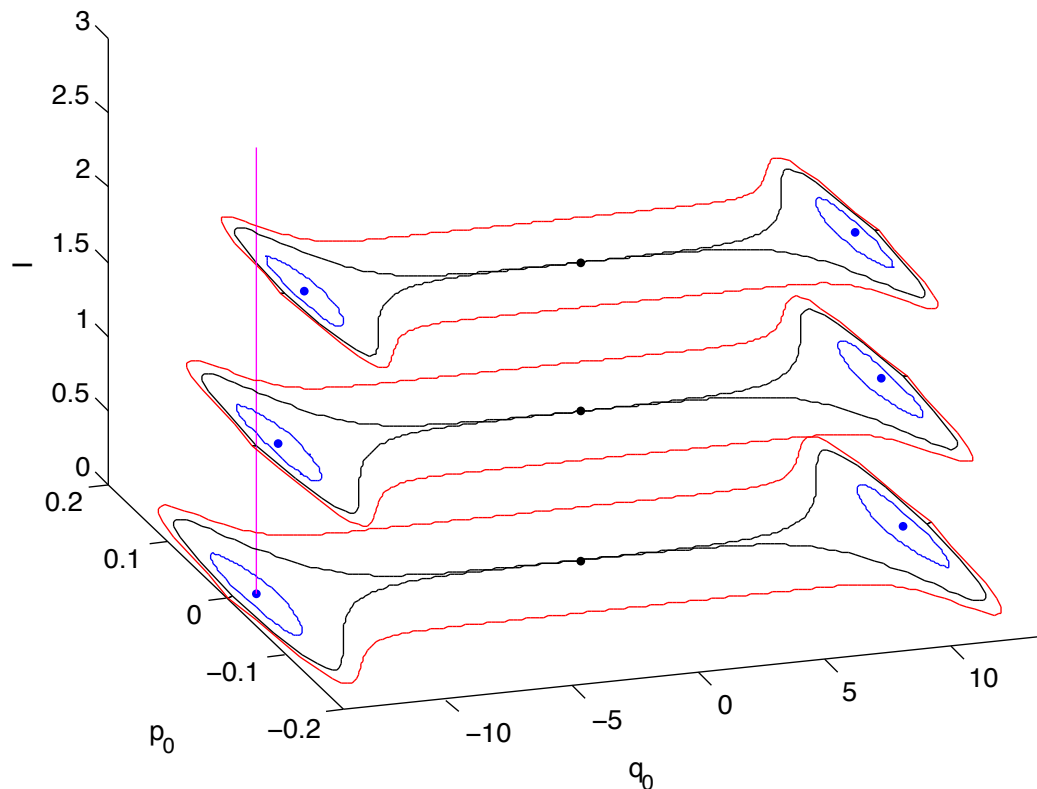
■ Analytical Study of MAE (II)

- ▶ MAE can be found by the **condition** that point $(x_e, 0, I_m)$ is on **separatrix** passing through saddle $(0, 0, I_m)$.
- ▶ Since **separatrix** is a curve (x, y) whose energy is those at saddle:

$$\bar{H}_2(x, y, I_m) = \bar{H}_2(0, 0, I_m),$$

- ▶ MAE can be found by solving for I_m from the **condition**

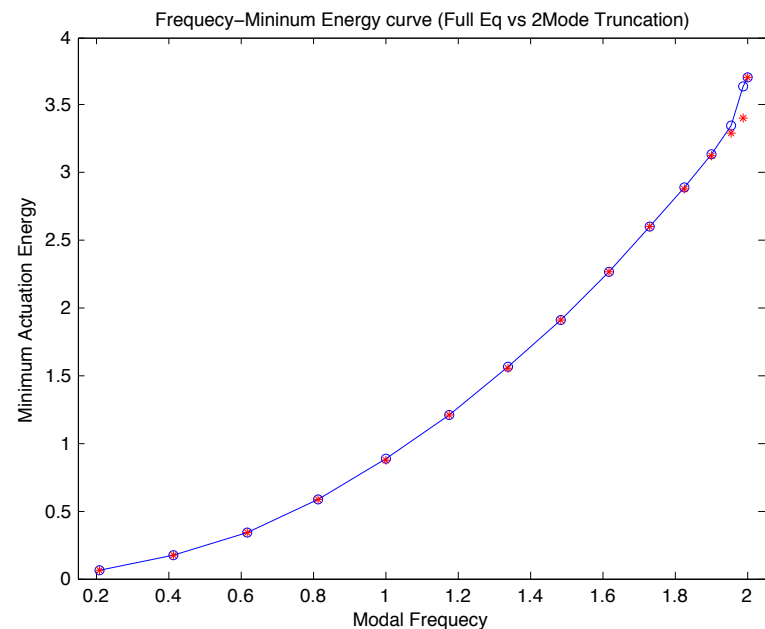
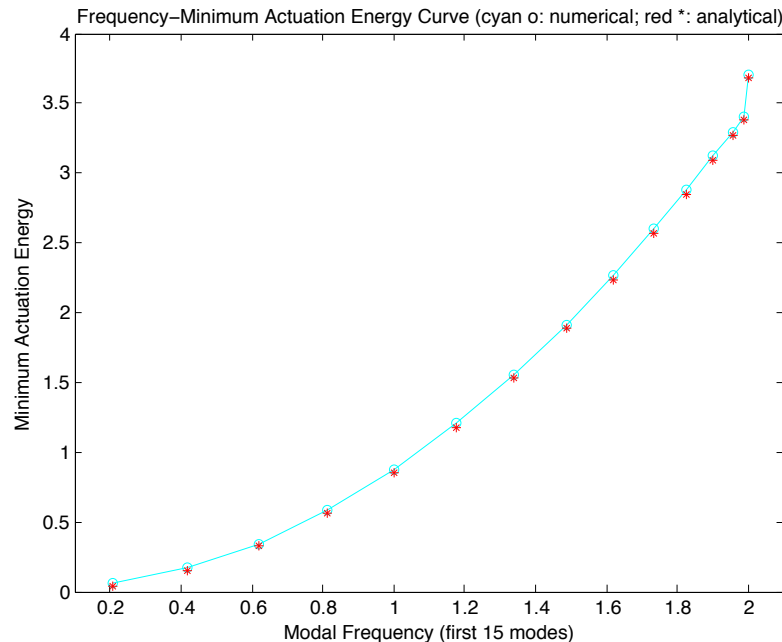
$$\bar{H}_2(x_e, 0, I_m) = \bar{H}_2(0, 0, I_m).$$



■ Analytical Study of MAE (III)

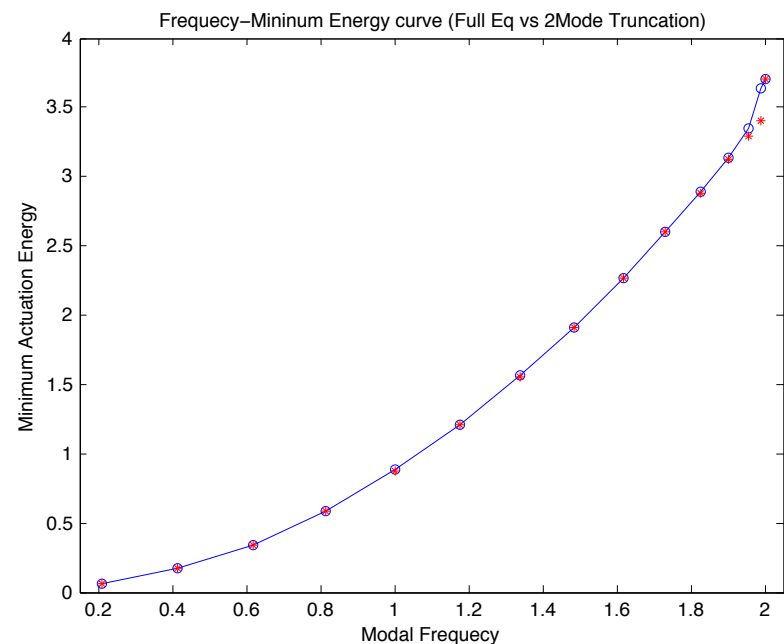
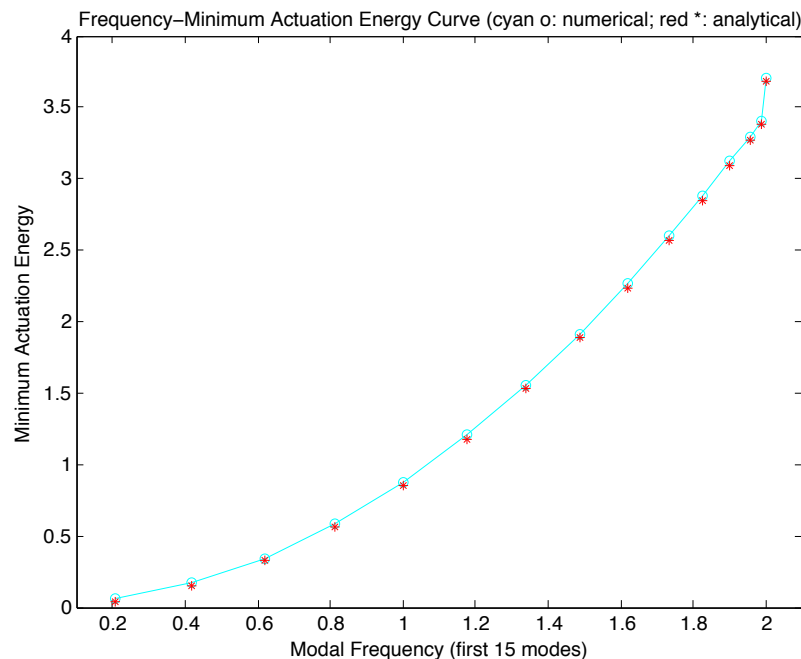
- ▶ Data for cyan "o"s are from simulations (2 Mode Truncation): e.g., 6th data point (6th mode) with $\omega_6 = 1.17$ needs $E_m = 1.205$.
- ▶ Data for magenta "*"s are from analytical computations: 6th data point with $\omega_6 = 1.17$ has $E_m = 1.1801$ (error < 2%).
- ▶ Data from simulations/analytical computations match very well.
- ▶ Also, E_m (except 15th mode) can be approximated as a parabola

$$E_m = 0.8539 \times \omega^2$$



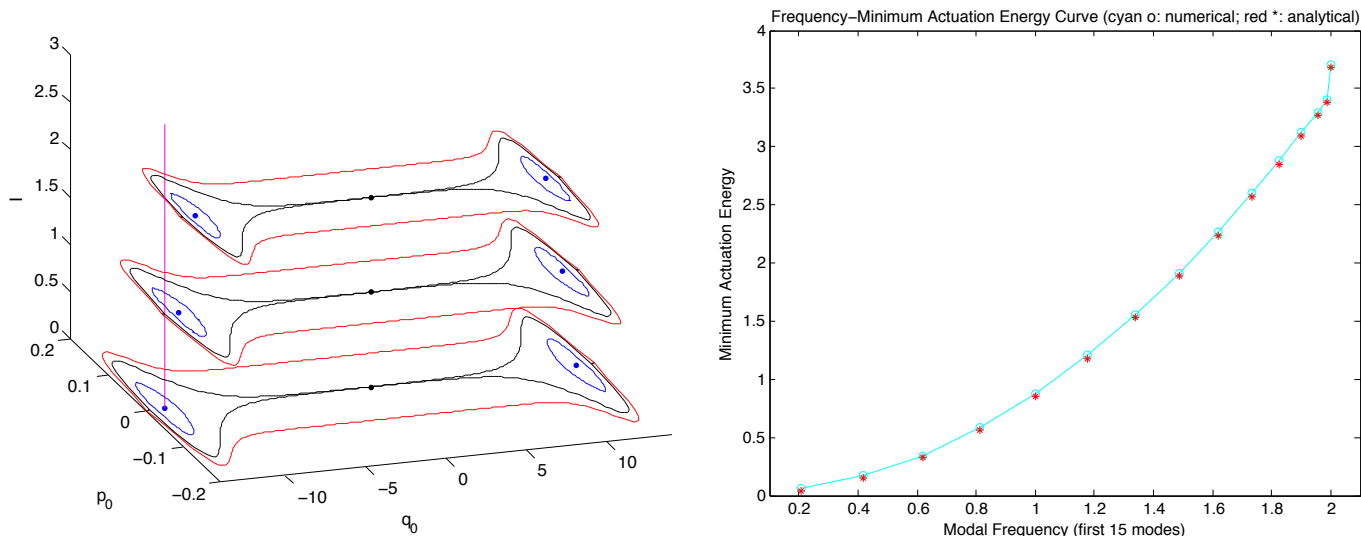
■ Analytical Study of MAE (IV)

- ▶ Blue "o"s are data from simulations of full equations (30 modes): e.g., 6th data point (6th mode) with $\omega_6 = 1.17$ needs $E_m = 1.205$.
- ▶ Red "*" are from simulations of 2Mode truncations. Besides 14th mode, all other data values of blue "o"s and red "*"s have differences less than 1%.
- ▶ **Therefore**, for the study of MAEs, analytical computation provides **accurate prediction** not only for the reduced models, but also for the full system.



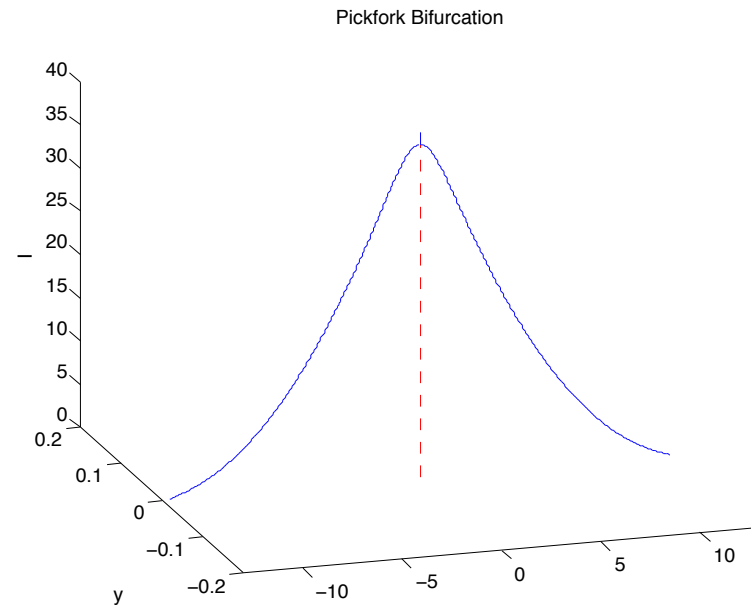
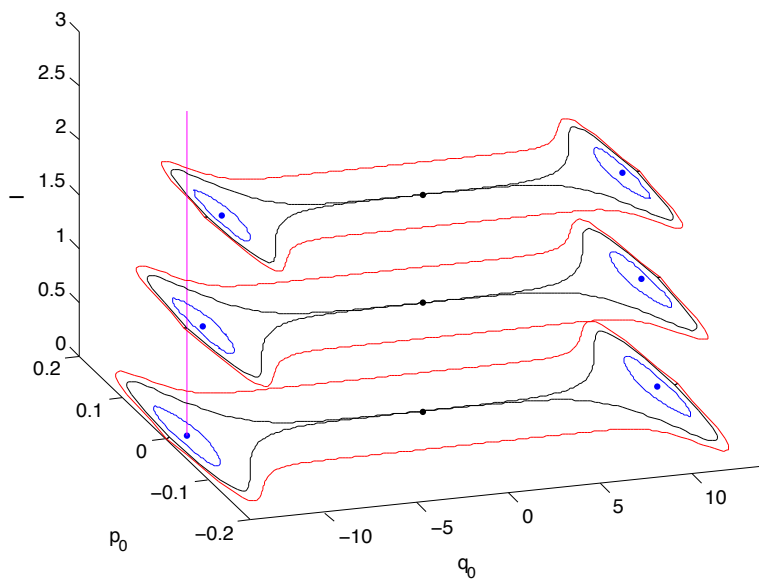
■ Summary: Analytical Results on Internal Dynamics

- ▶ By applying partial averaging, obtained **average reduced equations** for a chain of **Morse** oscillators.
 - Reveal coupling of energy in excited mode/dynamics of reactive mode, as well as **phase space structures of activation mechanism**.
 - Enable to **estimate analytically** MAEs, and discover a relation between frequency of excited mode and MAEs.
 - These **estimates** match very well with numerical simulations obtained from **reduced** and **full model**.
- ▶ Results show **nearly 0 : 1 internal resonance** is responsible for **phenomenon of structured activations** of our DNA model.



■ Control via Parametric Excitation (PE)

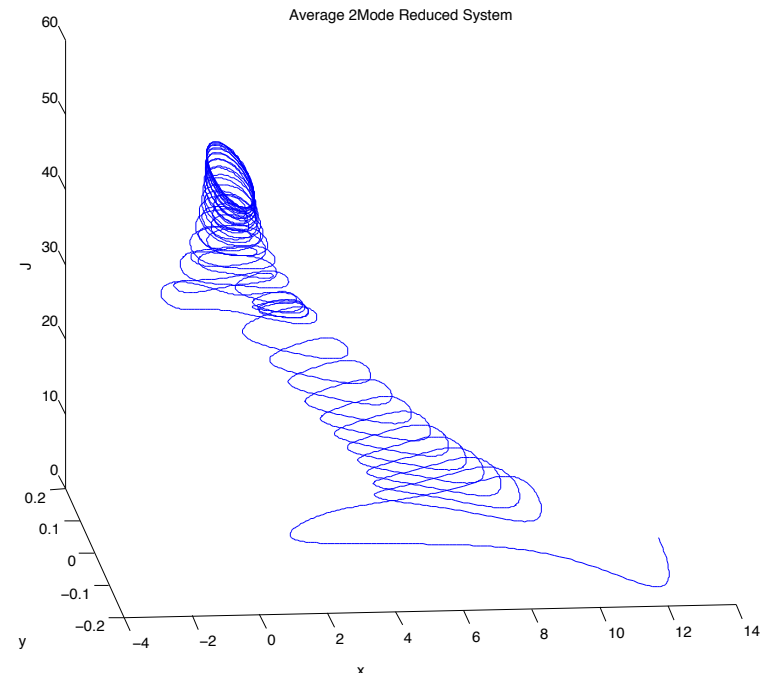
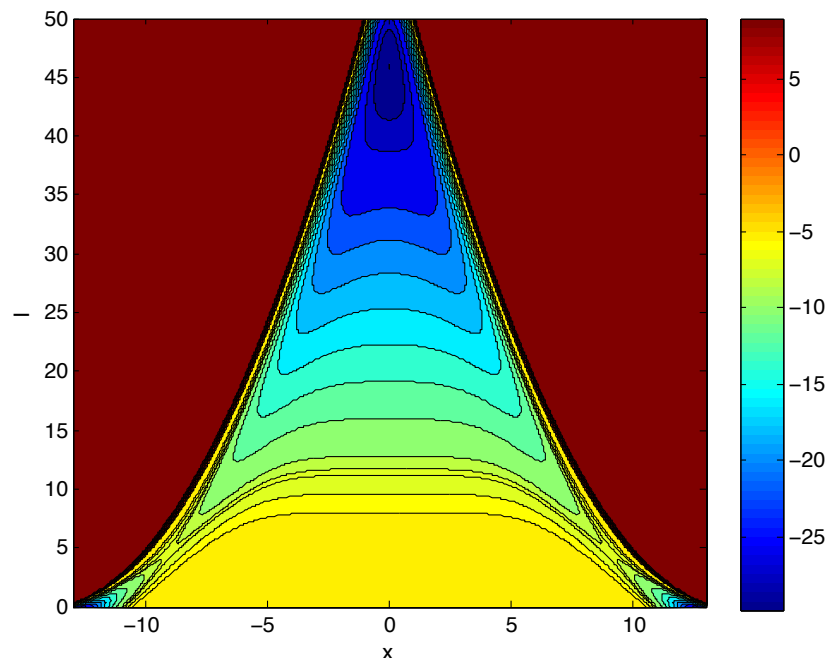
- ▶ Building on understanding of internal dynamics, want to control the division via PE, in resonance with internal trigger modes.
- ▶ This effort is guided by 2 observations and 2 conjectures:
 - Averaged Reduced Eqs has a pitchfork bifurcation at $I_b \approx 38$.
Bif. diagram: curve of stable equilibria; dashed line of saddles.
For $I > I_b$, $(0, 0, I)$ is stable, chain will remain at open state.
 - PR is an efficient way for energy transfer from external source.
- ▶ Conjectures: EM/Enzyme use PR to pump energy into trigger modes and keep DNA at open state (for replication/transcription).



■ 3 Main Results on Control via PE

- ▶ Identify **excitation parameters** and **trajectories** that show how PE drives **Averaged Reduced Model** from its (almost) equilibrium state to its open state near $(0, 0)$.
- ▶ By identifying **effective Hamiltonian** (after PE), able to reveal **global phase space structures** and analyze characteristic **trajectories**.
- ▶ Extend results for **Average Reduced Model** with PE and **friction** to **Reduced** as well as **Full Model** with PE and **friction**.

Findings uncover a method for controlling DNA division via PR.



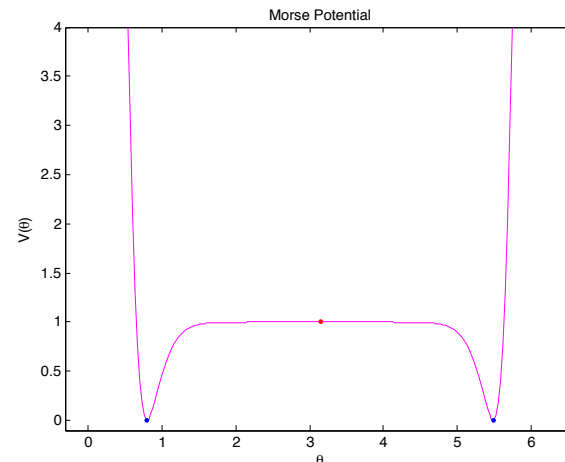
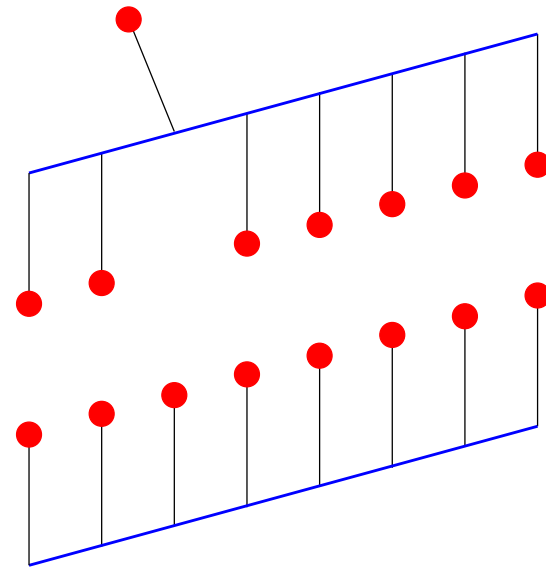
■ EOM of Full Model with PE

► EOM of full model with **PE** and **frictions** can be written as

$$\ddot{\theta}_k - (\theta_{k+1} - 2\theta_k + \theta_{k-1}) - \epsilon U'(\theta_k) = \epsilon \theta_k f \cos \Omega t - \epsilon \mu \dot{\theta}_k$$

where $k = 1, \dots, n; \theta_0 = \theta_n$;

- LHS is original EOM (without PE or frictions);
- f, Ω are **amplitude/frequency** (dipole moment of bases/EM);
 Ω in **nearly 1:2 resonance** with frequency ω_γ of an internal mode.
- μ is **frictional coefficient** (energy loss caused by interaction with surrounding molecules; thermal energy gain is ignored for now).



■ EOM of Reduced/Averaged Reduced Model with PE

- After using FMC, EOM of 2Mode **Reduced Model** is given by

$$\begin{aligned}\dot{q}_0 &= p_0 & \dot{p}_0 &= -\epsilon M_0 - \epsilon \mu p_0 + \epsilon f q_0 \cos \Omega t. \\ \dot{q}_\gamma &= p_\gamma & \dot{p}_\gamma &= -\omega_\gamma^2 q_\gamma - \epsilon M_\gamma - \epsilon \mu p_\gamma + \epsilon f q_\gamma \cos \Omega t.\end{aligned}$$

- Applying partial averaging, we obtain **Averaged Reduced EOM**

$$\begin{aligned}\dot{x} &= y, & \dot{\beta} &= \epsilon(\bar{M}_I - \sigma/2\omega + f \cos 2\beta/4\omega), \\ \dot{y} &= -\epsilon(\bar{M}_x + \mu y), & \dot{I} &= \epsilon I(f \sin 2\beta/2\omega - \mu).\end{aligned}$$

where I, β , action/phase of trigger mode (q_γ, p_γ) ;
 σ is a **detuning parameter**, defined by $\Omega^2/4 = \omega^2 + \epsilon\sigma$.

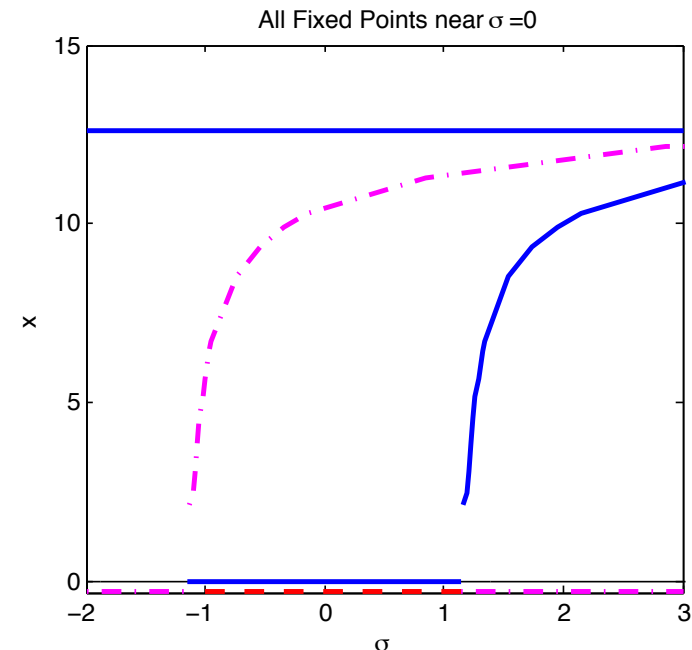
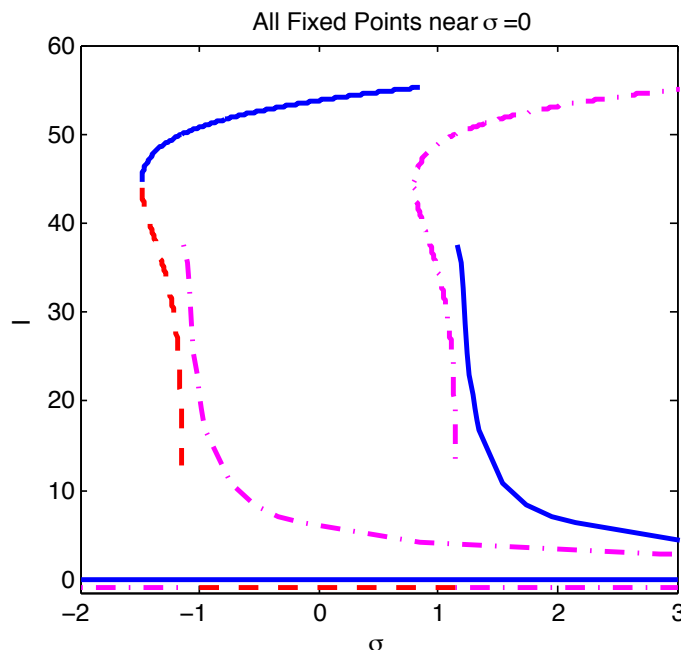
- The Averaged Reduced System (without friction) has an **effective Hamiltonian**

$$H_{PR} = \frac{1}{2}y^2 + \epsilon\bar{M} - \epsilon\frac{\sigma}{2\omega}I + \epsilon f \frac{I \cos 2\beta}{4\omega}$$

that can provide insights on **global phase space structures** of this average reduced model.

■ Bifurcation Analysis of Averaged Reduced Equations

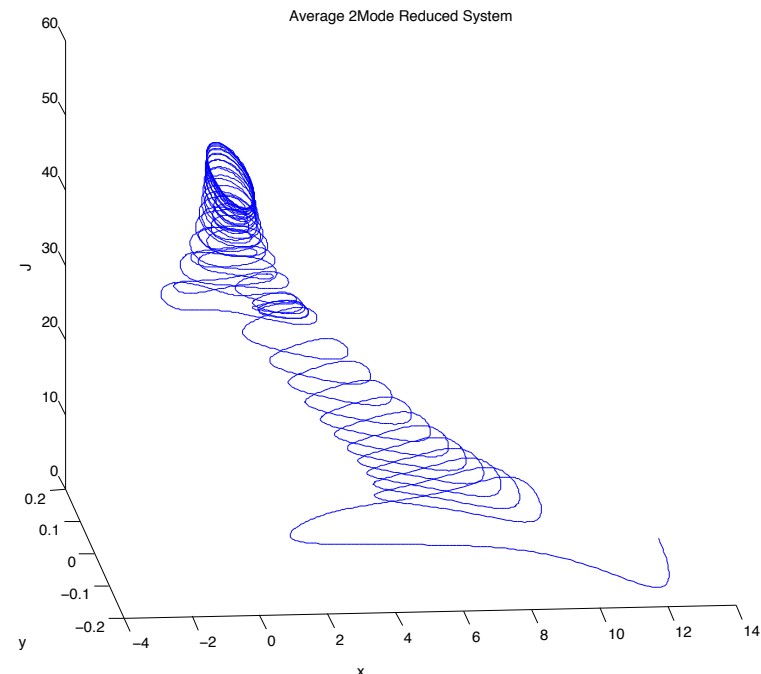
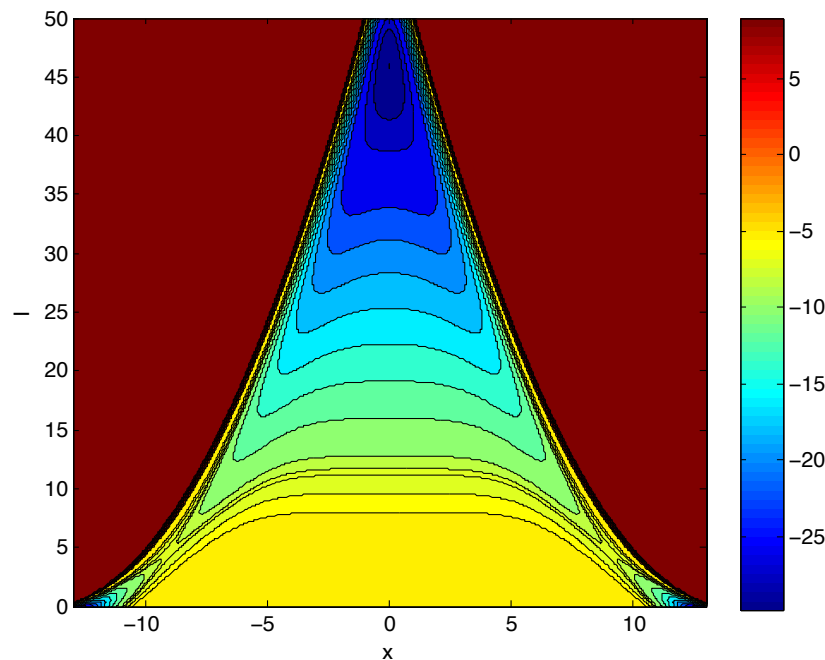
- ▶ Bifurcation analysis can be used to reveal **ranges of σ** and other parameters, f, μ , where **desired dynamics** may be available.
- ▶ Bifurcation Diagrams $(\sigma, I), (\sigma, x)$: how **fixed points** and their **stability** change as σ (Ω) of PE is varied ($y_e = 0, \beta_e$ is a constant).
 - $(x, y, q, p) = (x_e, 0, 0, 0)$: stable foci (bottom of potential well).
 - $(x, y, I, \beta) = (0, 0, I_e, \beta_e)$: stable foci (mark DNA open state).
 - $(x, y, I, \beta) = (x^*, 0, I^*, \beta_e)$: stable foci \times saddle (rank 1 saddle)
- ▶ May provide a pathway from bottom of well to open state.



■ Global Geometry of Effective Hamiltonian

- ▶ While bifurcation analysis provides basic ingredients, it does not give a clear and global picture. **Effective Hamiltonian** is needed.
- ▶ **Energy contours** of **effective potential** show how 3 types of fixed points fit together within **global geometry** of effective Hamiltonian
 - PE turns $(x, J) = (0, J_e)$ which marks DNA division into a **sink**;
 - creates 2 **rank 1 saddles** close to 2 **stable equilibria** $(\pm 12.6, 0)$.

Addition of PE allows trajectory with a little energy to move from an **almost equilibrium state** over the **saddle** and reach the **sink**.

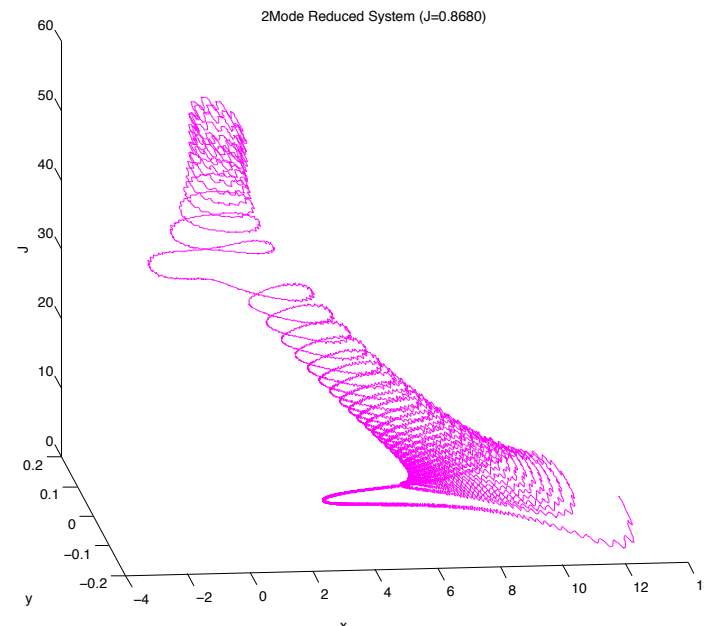
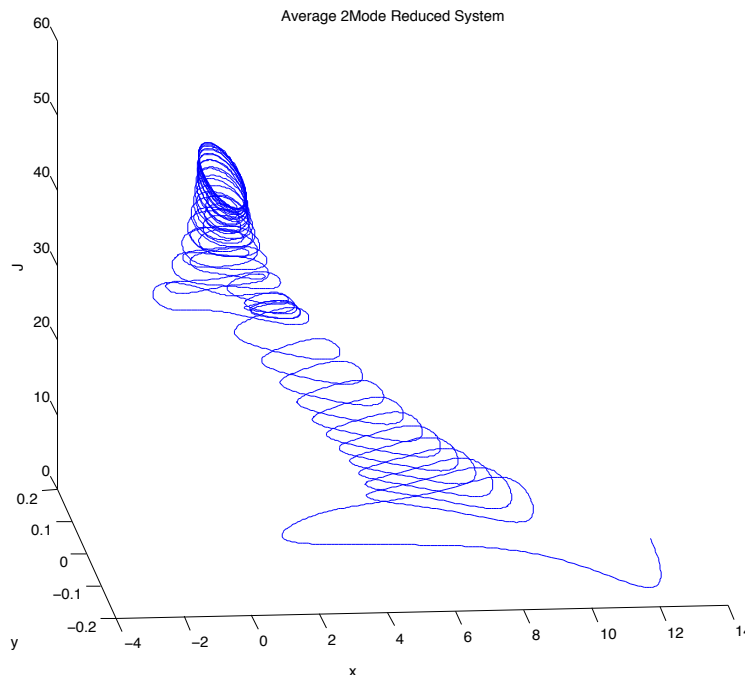


■ Identify a Class of Characteristic Trajectories

- ▶ Insights from bifurcation analysis/global geometry of H_{PR} enable to generate trajectories that show how PR drive averaged reduced system from its almost equilibrium state to its open state.
- ▶ Recall: EOM for Reduced Model are

$$\begin{aligned}\dot{q}_0 &= p_0 & \dot{p}_0 &= -\epsilon M_0 - \epsilon \mu p_0 + \epsilon f q_0 \cos \Omega t. \\ \dot{q}_\gamma &= p_\gamma & \dot{p}_\gamma &= -\omega_\gamma^2 q_\gamma - \epsilon M_\gamma - \epsilon \mu p_\gamma + \epsilon f q_\gamma \cos \Omega t.\end{aligned}$$

- ▶ Right: a corresponding trajectory for reduced model.

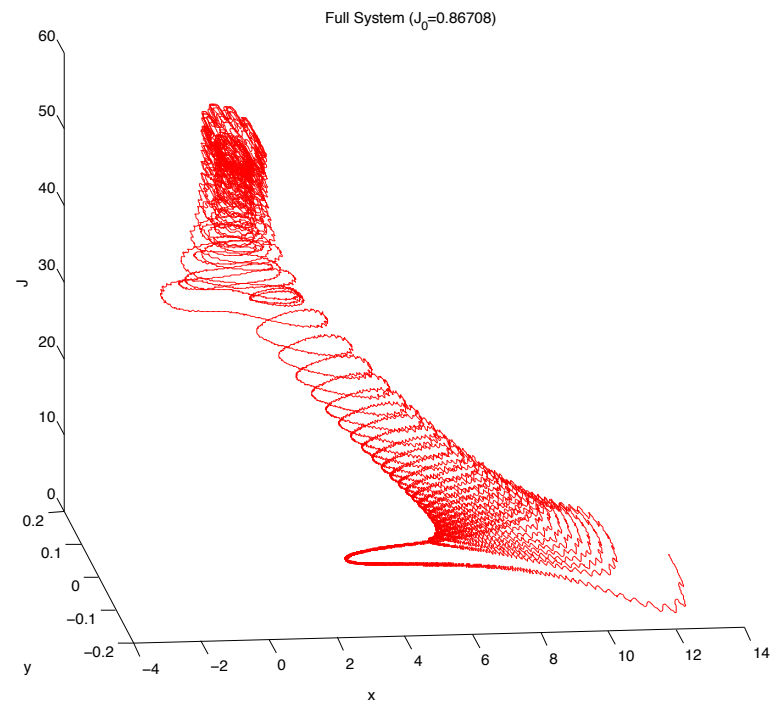
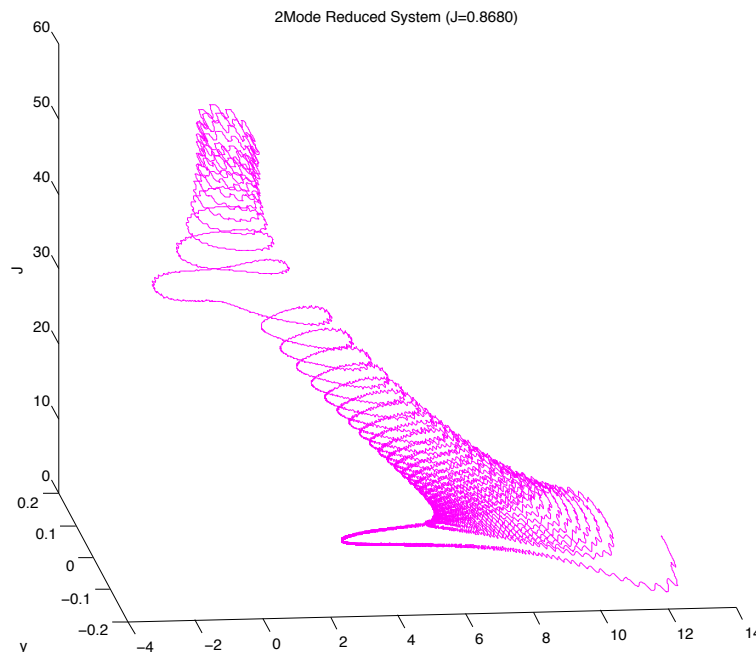


■ Extend Results to Full Model

- ▶ A corresponding trajectory for the **full model**

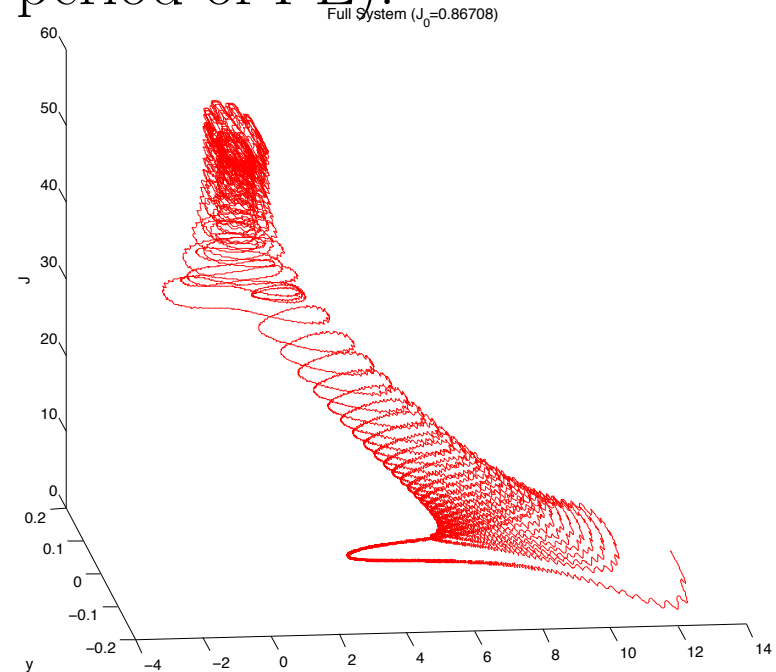
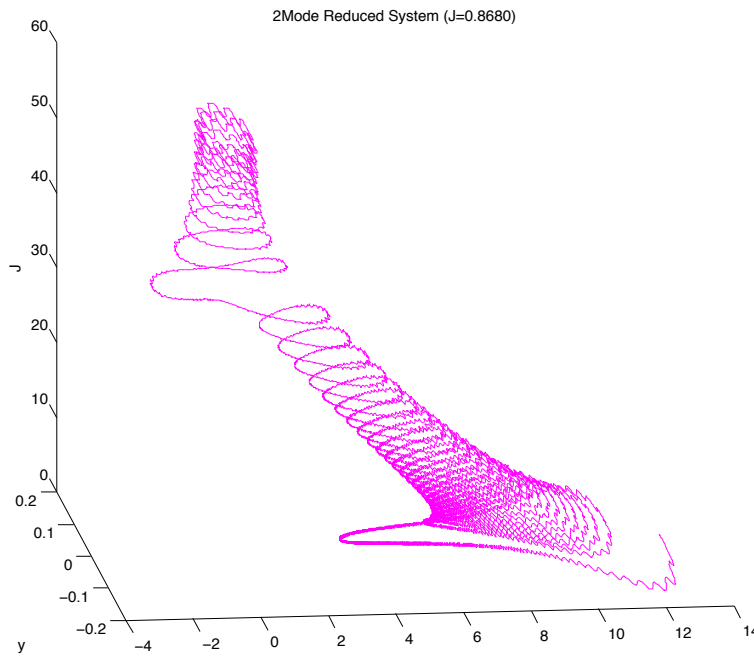
$$\ddot{\theta}_k - (\theta_{k+1} - 2\theta_k + \theta_{k-1}) - \epsilon U'(\theta_k) = \epsilon \theta_k f \cos \Omega t - \epsilon \mu \dot{\theta}_k$$

- ▶ Despite its simplicity (compared to **full system**), **averaged reduced model** is surprisingly accurate by the fact that 3 trajectories are very similar.
- ▶ Without a careful study of **averaged reduced equations**, it may be difficult to guess that such a class of trajectories exist in the **averaged reduced model**, let alone in the **reduced** and the **full model**.



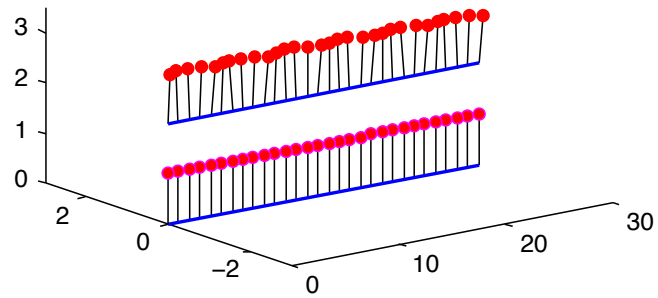
■ Remarks on the Characteristic Trajectories

- ▶ Trajectory starts at **equilibrium position** of **reactive mode** but with small amount of energy in **trigger mode**. Without PE, **liberate** near **equilibrium state** if there is no friction or **die down** if friction exists.
- ▶ With PE, PR inject energy into **trigger mode**, increase I , make trajectory to reach the **region that marks DNA division** ($x = 0$), but with large amount of energy in **trigger mode**.
- ▶ DNA chain that corresponds to this solution is near its **open state**: chain is near **upright position** (with 0 average angle) but with a **periodic swing** (whose period = period of PE).

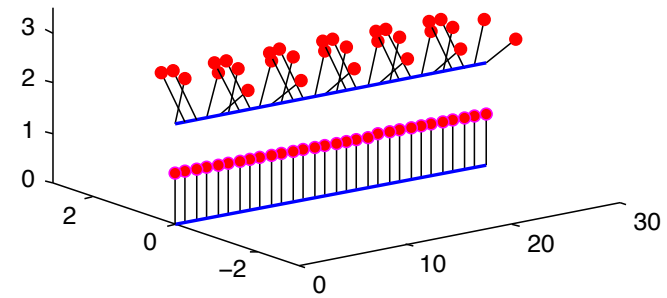


■ Evolution of DNA Chain Near Its Open State

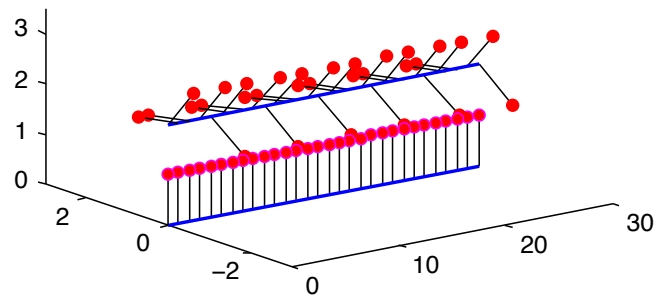
$t=9344.7$



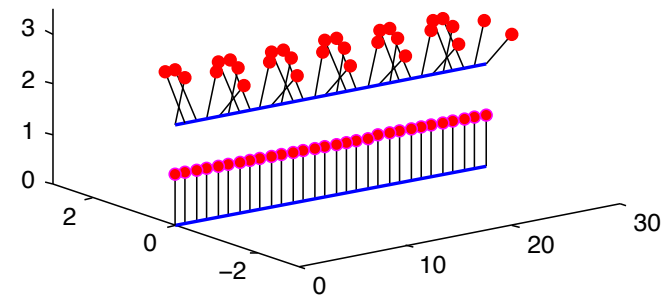
$t=9345$



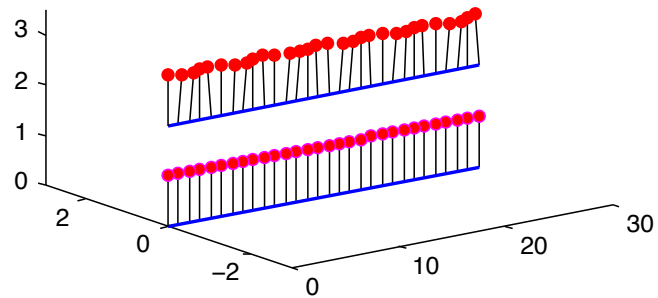
$t=9346$



$t=9347.1$

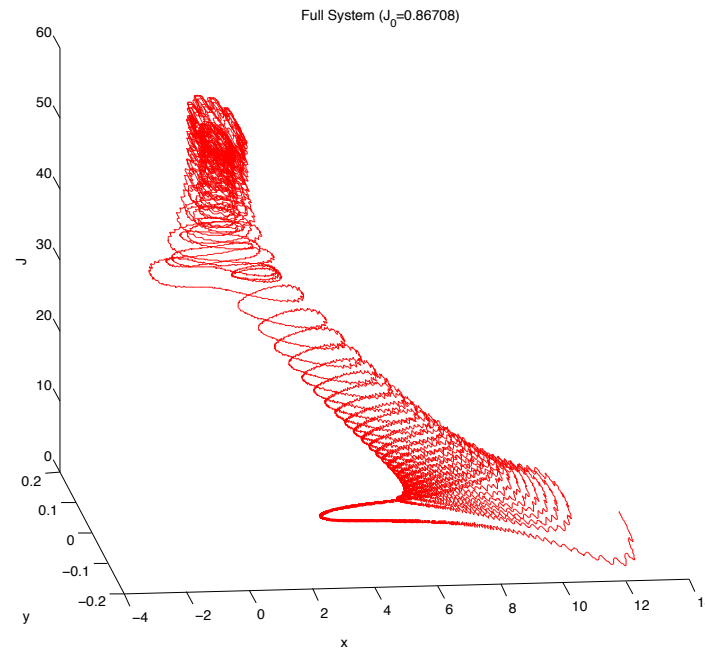
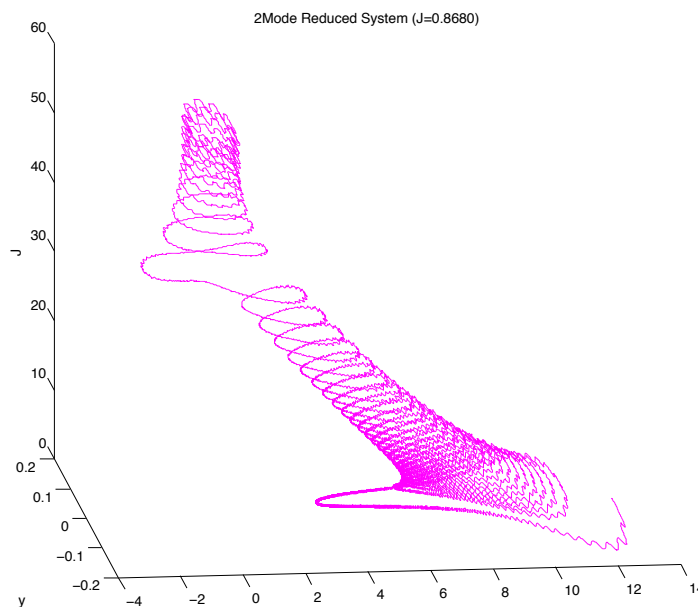


$t=9347.4$



■ Remarks on the Characteristic Trajectories

- ▶ For cases where initial energy is in more than one mode (e.g., 6th and 7th modes), numerical simulation of **full model** shows that this kind of **trajectories** still exist as long as one of the mode is dominant and **PE** is in resonance with the dominant mode.
- ▶ This should not surprise us because while **PR** will inject energy into the dominant mode, **friction** will damp out the other.
- ▶ More studies needed for tradeoffs between amplitude f , detuning parameter σ , frictional coeff. μ on one hand and initial action-phase I_0, β_0 (and mixed modes) on the other.



■ Summary and Future Work

- ▶ Study internal resonance, energy transfer, activation mechanism, and control of a model of DNA division via PR.
- ▶ Future work: add effects of **inhomogeneity** and **helicity**.
 - Moment, torsional/base pair interactions depend on positions.
- ▶ Methodology forged in this study (which merges geometric reduction, partial averaging, chaotic transport, and control via PR) should be applicable to many molecular and biomolecular systems, as well as other mechanical systems involving **multiple-scale**.

