Potential Energy Surfaces, Newton Trajectories and Catch Bonds in Theoretical Chemistry

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Abstract

The talk begins with a discussion of the problems involved in defining a reaction pathway, in particular the steepest descent, the intrinsic reaction coordinate (IRC) and gradient extremals (GE). As an alternative, we propose Newton trajectories (NT).¹

An NT is a curve where the gradient of the PES points in the same direction at every point.

Other definitions of NTs and further methods for different calculations are reported.²

NTs connect stationary points of the PES, so they can be used to find saddle points.

Another important property of NTs is that singular NTs bifurcate at valley-ridge inflection points (VRI).

Application: NTs describe the curves of the change of stationary points under a mechanochemical force.³

A special application is the study of so-called catch bonds: counterintiutive bonds that become stronger under a mechanochemical force.⁴ Two example PES are explained.

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¹W.Quapp, M.Hirsch, O.Imig, D.Heidrich, J.Computat.Chem. 19 (1998) 1087;

W.Quapp, M.Hirsch, D.Heidrich, Theor.Chem.Acc. 100 (1998) 285.

²W.Quapp, J.Theoret.Computat.Chem. 2 (2003) 385, and 8 (2009) 101.

³W.Quapp, J.M.Bofill, J.Phys.Chem.B 120 (2016) 2644.

⁴W.Quapp, J.M.Bofill, J.Phys.Chem.B 128 (2024) 4097.

Background: what is a Reaction Path?

The chemical bonds emerge by the overlapping of electrons in a molecule. Their description is the Schrödinger equation, together with the Born-Oppenheimer approximation, which separates kernels from the electrons. An N-dimensional molecule has 3N-6 internal degrees of freedom of the atoms. One can calculate to any constellation $(x_1, x_2, ..., x_{3N-6})$ the potential energy, as well as derivatives, for example, the second ones for comparison with spectroscopy. However, for medium or larger molecules one cannot calculate a net of raster-points in all dimensions, to get a 'full' potential energy surface (PES).

What one can do is the definition of a one-dimensional curve in the (3N-6)-dimensional configuration space of the molecule

$$\mathbf{x}(s) = (x_1(s), x_2(s), ..., x_{3N-6}(s))$$

and calculation of the PES profile over this curve, in a (3N-6)+1 dimensional space. If this curve, or 'path' is more or less inside a valley of the PES then we name it Reaction Coordinate.

IRC I

•
$$\frac{d\mathbf{x}(s)}{ds} = -\frac{\mathbf{g}(\mathbf{x}(s))}{|\mathbf{g}(\mathbf{x}(s))|}$$
, **g** is gradient, Start at SP

Does not always follow the valley of the PES



Hirsch, Quapp, CPL 395 (2004) 150

(2D modified PES using the Neria, Fischer, Karplussurface, see JCP 105 (1996) 1902

SD goes over a ridge !

IRC I

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IRC II

► IRC does not indicate bifurcations of a valley



The blue dotted curve is the IRC. It does not see the valle-ridge inflection point, and not the other TS. The black dashed curve is a singular NT bifurcating at the VRI point.

IRC III

▶
$$\mathbf{x}_{k+1} = \mathbf{x}_k - \lambda \frac{\mathbf{g}(\mathbf{x}_k)}{|\mathbf{g}(\mathbf{x}_k)|}$$
, λ any steplength

Shows numerical zigzagging



Left: exact IRC, right: numerically determined IRC (Fig. by Benjamin Schmidt)

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Definition of a Reaction Pathway

Reaction path (RP)

- ► Is a monotone way between Minimum and Transition State
- It looks nice if going through a valley of the PES
- It would be nice if indicating bifurcations of the valley

A synonyme for RP would be Minimum Energy Path. From the point of view of practical calculations, it would also be helpful if we could calculate the RP beginning at the minimum. Examples

- Steepest descent from SP, IRC
- Gradient Extremal
- Newton Trajectory

Note: none of the examples fulfills all properties, in all cases. Thus, we can treat different RP-Examples on an equal footing.

Distinguished Coordinate

- History: Distinguished Coordinate (used up to present!) Choose a driving coordinate direction along the valley of the minimum, go a step in this direction, and perform an energy optimization of the residual coordinates.
 - This leads to problems if the valley ends
 - The Distinguished Coordinate can jump



(Müller-Brown surface, TCA 53 (1979) 75) Alternative

Use another definition: Newton Trajectory.

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Definition of Newton Trajectory

- W. Quapp M. Hirsch O. Imig D. Heidrich, J Comput Chem 19 1998, 1087-1100, "Searching for Saddle Points of Potential Energy Surfaces by Following a Reduced Gradient"
- W. Quapp M. Hirsch D. Heidrich, Theor Chem Acc 100 (1998) No 5/6, 285-299 "Following the streambed reaction on potential-energy surfaces: a new robust method"



- Chose a Search Direction r
- Build the Projector Matrix $\mathbf{P}_r = \mathbf{I} \cdot \mathbf{r} \mathbf{r}^T$. It is $\mathbf{P}_r \mathbf{r} = \mathbf{0}$.
- Search the Curve $P_r g=0$. It is the Newton Trajectory.

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Predictor-Corrector Method I

Predictor

Go along the tangent of the Newton trajectory

$$\mathbf{0} = \frac{d}{ds} [\mathbf{P}_{\mathbf{r}} \mathbf{g}(\mathbf{x}(s))] = \mathbf{P}_{\mathbf{r}} \frac{d \mathbf{g}(\mathbf{x}(s))}{ds} = \mathbf{P}_{\mathbf{r}} \mathbf{H}(\mathbf{x}(s)) \mathbf{x}'(s)$$

the tangent is \mathbf{x}' ; note: $\mathbf{P}_{\mathbf{r}}$ is a constant $n \times n$ matrix.

Corrector

Use the Newton-Method, jump back to the Curve

Both of the steps need the Hessian of the PES, or updates of it.

The method was included in the top level quantum chemistry packet COLUMBUS.

Predictor-Corrector ivietnod II

TASC-method: TAngent Search Concept

- Use the tangent of the Newton trajectory for the next search direction r. Thus, change r at every step.
- The result is a Gradient Extremal (GE). Definition of a GE:
 - At every point the gradient of the PES is an eigenvector of the Hessian.

$$\mathbf{H} \ \mathbf{g} = \lambda \mathbf{g}$$

and λ is the corresponding eigenvalue. Usually, the GE to the smallest eigenvalue is a valley path. GEs follow the eigendirections at stationary points.

- D.K.Hoffman, R.S.Nord, K.Ruedenberg: TCA 69 (1986) 265-279. "Gradient Extremals"
- W.Quapp: TCA 75 (1989) 447-460.

"Gradient Extremals and Valley Floor Bifurcations on PES"

Gradient Extremai

GΕ

At every point the gradient of the PES is an eigenvector of the Hessian: $\mathbf{H} \mathbf{g} = \lambda \mathbf{g}$, and λ is the Eigenvalue. Of course, λ changes along the path.



The fat curves are the GEs, the thin dashes are NTs.

Note a turning of the upper GE.

(only early examples)

- H.Valdes, J.A.Sordo et al.: CPL 309 (1999) 265, 333 (2001) 130, 392 (2004) 236 and JCC 24 (2003) 2044: Cl + nitrobenzene, Cl + propene
- K.Schiele, R.Hemmecke: ZAMM 81 (2001) 291: driven multiple pendula
- M.Dallos et al.: JCC 23 (2002) 576, JCP 118 (2003)1702, CPC 5 (2004) 1365, PP Columbus: formaldehyle, acetylene
- M.Hirsch, W.Quapp: JCC 23 (2002) 887 "Improved RGF Method to Find Saddle Points" HCP, H₂CO, C₄H₁₀, ring opening of sym-tetrazine
- O.Castano et al.: JCC 23 (2002) 732: cyclooctatetraene
- B.Lasorne et al.: JCP 118 (2003) 5831, and 122 (2005) 184304, Chem.Phys.326 (2006) 500: H₃CO, dimerization of cyclopentadiene

String wiethod

- Chose an initial Chain between two Minimums.
- Change the Chain by a controlled Newton-Method, step by step, back to the searched Newton Trajectory.



and Corrector steps

The colored curves are different NTs (W.Quapp, JTCC 8, (2009) 101-117 "The growing string method for flows of NTs by a second order corrector") The PES concerns Alanine-Dipeptide: CH₃CO-NHCHCH₃CO-NHCH₃ The dimension is (3N-6)=60, N=22 atoms One of the blue NTs shows Predictor-

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String wiethod

Effort for the String Method

- Example Alanine-Dipeptide, 60 internal coordinates, (2 dihedrals fixed, thus 58 coordinates optimized)
- Used: GamesUS on PC, DFT calculations B3LYP/6-31G basis set
- Number of chains calculated: 9
- Number of nodes per chain: 30
- Number of corrector steps per node: 2-3



With such a nice convergence velocity, one can calculate many nodes per chain, and many NTs at all, so to say, a flow of NTs.

Higher-dimensional INTS

- Use a path following method in a reduced PES
- Predictor: IRC- or eigenvector-following technique
- Corrector: Newton-Raphson method

The reduced PES is defined by a set of molecular geometry parameters, (bond distances, bond angles, or dihedrals) that undergo the largest change for the reaction. The remainder of the coordinates are forced to have a zero gradient.

- Thus again use $P_r g=0$ in a reduced space.
- Anglada, Besalu, Bofill, Crehuet: JCC 22 (2001) 387.
- Bofill, Anglada: TCA 105 (2001) 463.
- Hirsch, Quapp: TCA 113 (2005) 58, Examples of so called Newton Leaves
- I.Berente, G.Naray-Szabo: JPC A 110 (2006) 772. "Multicoordinate Driven Method for Approximating Enzymatic Reaction Paths: ..."

Applications of N Is (Examples only)

- W.Quapp, D.Heidrich: JMSt, THEOCHEM 585 (2002) 105
 "Exploring the PES of ethyl cation ..."
- D.H.Ess et al.: JOC 73 (2008) 7472, and 7586, Angew.Chem.In.Ed.47 (2008) 7592: dimerization of 1,3-cyclohexadiene, isomerization of methoxy radical to hydroxymethylene radical, semibullvalene, aldaldehyde radical anion additions to alkyl halides, Cyclopropylidene to allene, deazetization of heterocyclic nitrosimines, 1,2,6-heptatriene to 3-methylene-1,5-hexadiene, endo cyclopentadiene dimerization,...
- G.Rossmueller, ..., Ch.Haettig: JPC C 113 (2009) 1418.
 - "... methanol synthesis .. on the .. ZnO(0001j) Surface"

IN IS INDICATE DIFURCATIONS OF the valley

 NTs have a second definition by an explicite differential equation

$$rac{d \mathbf{x}(t)}{dt} = \pm \mathbf{A}(\mathbf{x}(t)) \; \mathbf{g}(\mathbf{x}(t))$$

named the Branin equation.

It uses the adjoint matrix **A** of the Hessian **H**, which is $[(-1)^{i+j} m_{ij}]^T$, where m_{ij} is the minor of **H**. It is **A H** = $Det(\mathbf{H})$ **I**, thus **A** = $Det(\mathbf{H})$ **H**⁻¹.

The singular points of the equation are zeros of A(x) g(x) = 0, thus
 (i) stationary points, if also g(x) = 0, or
 (ii) valley-ridge inflection points (VRI), if g(x) ≠ 0

If $\mathbf{A}(\mathbf{x}) \ \mathbf{g}(\mathbf{x}) = 0$ and $\mathbf{g}(\mathbf{x}) \neq 0$, then an eigenvector of the Hessian to eigenvalue zero is orthogonal to the gradient.

Branin is the desingularized, continuous Newton equation

- A Newton-Raphson step is $\mathbf{x}_1 = \mathbf{x}_0 \mathbf{H}^{-1}(\mathbf{x}_0) \mathbf{g}(\mathbf{x}_0)$
- One may change this difference into a differential equation, the continuous Newton equation

$$\frac{d\mathbf{x}(t)}{dt} = -\mathbf{H}^{-1}(\mathbf{x}(t)) \ \mathbf{g}(\mathbf{x}(t))$$

- what is noting else then the Branin equation.

$$rac{d\mathbf{x}(t)}{dt} = -\mathbf{A}(\mathbf{x}(t)) \ \mathbf{g}(\mathbf{x}(t))$$

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The name Newton trajectory is coming from this approach.

Bifurcation points of NTs are valley-ridge inflection points (VRI) A(x) g(x) = 0 and $g(x) \neq 0$



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Note: the usual way to detect a past TS bifurcation is by hundreds, or thousends of dynamical trajectories. Why they do not use NTs ???



Figure from: Kong, Hu, Guo, Potluri, Schomaker, and Tantillo, Synthetically Relevant Post-Transition State Bifurcation Leading to Diradical and Zwitterionic Intermediates: Controlling Nonstatistical Kinetic Selectivity through Solvent Effects, JACS 2025, see https://doi.org/10.1021/jacs.4c16760

Dimension of Bifurcation Points

Note: in higher n-dimensional configuration space, the definition of VRIs can result in a higher dimensional VRI-manifold. It may be at least (n-2)-dim.



- Quapp, Hirsch, Heidrich, TCA 100 (1998) 285
 3D example of a test PES (derived from malone aldehyde PES)
- Hirsch, Quapp, Heidrich, PCCP 1 (1999) 5291
 3D example: PES of water
- Quapp, Melnikov, PCCP 3 (2001) 2735
 6D example: PES of formaldehyde

Channels and Index Theorem

Index Theorem Let **a** and **b** be stationary points connected by a regular Newton trajectory. Then it holds

 $\textit{index}(\mathbf{a}) \neq \textit{index}(\mathbf{b}) \text{ ,}$ and the difference is one.

Regular NTs connect a SP (index 1) and a minimum (index 0). The PES shows two adjacent SPs of index one. 0.5 There is no regular NT connecting the SPs. 8 Between the SPs a VRI point has to exist. One singular NT leads to the VRI point and branches there. 0

Hirsch, Quapp: JMSt THEOCHEM 683 (2004) 1



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All NTs which connect a minimum and a SP are a Reaction Channel

Channels and Index Theorem

Index Theorem Let **a** and **b** be stationary points connected by a regular Newton trajectory. Then it holds

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Figure by Michael Hirsch (2004)

2D examples – Representation of NTS

In 2D toy examples, one can easyly represent NTs by graphic orders:

In two dimensions holds that the orthogonal direction to the search direction

 $\mathbf{r}{=}(r_1,r_2)$ is unique the direction $\mathbf{r}^{\perp}=(-r_2,r_1)$.

Then the condition that $\mathbf{r} \parallel \mathbf{grad}$ is the zero of the scalarproduct

$$\mathsf{grad}^{\mathcal{T}} \; \mathsf{r}^{\perp} = \mathbf{0}$$
 .

In Mma one can use

 $\begin{array}{l} \mbox{ContourPlot[- g1[x, y] r2[x, y] + g2[x, y] r1[x, y], {x, 0,5}, {y,0,5}, \\ \mbox{ContourShading} \rightarrow \mbox{False, PlotPoints} \rightarrow 30, \mbox{Contours} \rightarrow \mbox{0}, \\ \mbox{ContourStyle} \rightarrow \mbox{Thickness[0.008], Dashed}] \end{array}$

iviecnanochemistry and ivis – linear approach

Mechanochemistry and NTs

If a linear force is applied to a molecule then the simplest approach for the potential energy is

$$V_f(\mathbf{x}) = V(\mathbf{x}) - F \mathbf{f}^T \mathbf{x}$$

where **f** is the force direction and *F* its amount. $\mathbf{f}^T \mathbf{x}$ is the scalar product of the force and the current coordinate point. Stationary points of V_f move along the conditions $\frac{\partial V_f}{\partial x_i} = 0$

$$\mathbf{g}(\mathbf{x}) \mid\mid \mathbf{f}$$
 .

The curve which describes these force moved stationary points is a Newton trajectory. The search direction \mathbf{r} of the NT is now the force \mathbf{f} .

 W.Quapp, J.M.Bofill, J.Ribas-Arino: Int. J.Quant. Chem. 118 (2018)e25775
 "Towards a Theory of Mechanochemistry – Simple Models from the Early Beginnings" Usually, an application of a force leads to a decreasing barrier of a reaction. This is the aim of a mechanochemically action: gain of energy for a reaction, or especially change the direction of a reaction. Action of a force on a 1D Morse potential:



W.Quapp, J.M.Bofill, TCA 135 (2016) 113

BBP means barrier breakdown point, of bond breaking point, where the former PES barrier disappears. It is the aim of many mechanochemical experiments to reach this point.

Change of Reaction Path



(a) The PES has two very different SPs. Left is the ground state. ... (c) An external excitation in direction of the red arrow changes the reaction channel. The former lower SP_{I} and the Maximum move together; the former upper SP_{II} disappears.

W.Quapp: J.Math.Chem. 56 (2018) 1339-1347

A Minimal 2D Model of the Free Energy Surface for a Unidirectional Natural Molecular Motor

curves) which connect two minima over one SP. BBPs are green.



Pulling into a defind direction makes a curve for the movement of minimum and SP named NT. The red arrows point into the constant gradient direction of the corresponding NT. Det(H)=0 (green) depicts the BBPs on the corresponding NT. Force amount *F* should be lowest along the green line. This lowest BBP is called the optimal BBP. The condition of the optimal BBP is quite simple

 $H(\mathbf{x}) \ \mathbf{g}(\mathbf{x}) = \mathbf{0}$

where $\mathbf{g}(\mathbf{x}) \neq \mathbf{0}$. The gradient is an eigenvector of the Hessian with null eigenvalue. The optimal BBP coincides with a point of the gradient extremal (GE) exactly at the intersection point with the $Det(H(\mathbf{x})) = 0$ -line (green) and the 'optimal' NT. The location of optimal BBPs is extremely important in the context of mechanochemistry. These points reveal which is the most efficient way to trigger a reaction by means of a mechanical force.

W.Quapp, J.M.Bofill: Theoret. Chem. Acc. 135, iss. 4, (2016) 113-132,

A Contribution to a Theory of Mechanochemical Pathways by means of Newton Trajectories

J.M.Bofill, J.Ribas-Arino, S.P.Garcia, W.Quapp: J. Chem. Phys. 147, Iss.15 (2017) 152710,

An algorithm to Locate Optimal Bond Breaking Points on a Potential Energy Surface for Applications in Mechanochemistry and Catalysis

Catch bonds

Mechanical forces play important roles in biology. Biological systems have evolved to address a diverse range of mechanical challenges, including materials with exceptional strength and toughness as well as those that strengthen under load. Mechanochemical reactions enable biological systems to sense mechanical signals and to adapt to changes in their mechanical environment (mechanosensing and mechanotransduction). Key players in these processes are proteins that respond to tensile, compressive or shear forces by undergoing specific conformational changes. They can form catch bonds (bonds that strengthen under load), expose cryptic binding or catalytic sites, or become susceptible to cleavage. These mechanisms are mimicked in synthetic systems and mechanically activated catalysts. Citation: Moving mechanochemistry forward, J.Batteas et al., RSCMechanochem (2025)

Catch bonds

Proteins demonstrate a colourful array of multi-phasic bonds, including biphasic catch-slip and triphasic slip-ideal-slip or slip-catch-slip bonds.

An examples is the T-cell receptor, a specificity between agonists and antagonists is enhanced 4-fold when tension is applied, a next example is cell polarization during migration which is determined by direction-dependent tension between vinculin and actin, a next is bacterium E. coli which avoids being flushed out by the high shear stress of urinal tracts while retaining mobility under low shear stress. Cadherins and downstream mechanotransduction proteins such as catenins require catch behaviour to regulate cell-cell communication and maintain tissue integrity.

Overall, catch bonds play a pivotal role in cell adhesion, motility, mechanosensing, communication, and organization across a wide spectrum of biological contexts.

Citation: Engineering tunable catch bonds with DNA, M.Yang et al., Nature Communications (2024) 15:8828

Catch bonds

Catch bonds

Note that all covalent and H-bonds are slip bonds individuelly. They break faster under stress. So, for catch bond search, only combinations of bonds make sense.

W. Quapp, J.M.Bofill: J. Phys. Chem. B 128, 17, 4097-4110 (2024)

"Theory and examples of catch bonds"

W. Quapp, J. M. Bofill, K. C. Dansuk, S. Keten: submitted

"To a mechanical model of synthetic catch-bonds"

Example: T cell receptor (TCR) interaction $V_f(L, d) = V(\theta(L)) + B(d, \theta(L)) - F(L + d)$ V is a harmonic potential, θ an angle, L and d are distances, B is product of harmonic and Morse pot, the last term makes a NT to direction (1,1), F is the amount of the force.



F.J.van Eerden et al. eLife 12 (2023)

PES I cell receptor

Force 10 pN



We obtain a PES where the direction (1,1) of the external force points into the 'mountains' of the PES. The corresponding NT describes the movement of the minimum and the SP together. However, the hight of the SP increases for moderate forces, in comparison to the MEP in this 'one-state-model'. Right is shown the NT to this direction for case F=10. The SP has moved along the NT. It is higher: catch bond character.

A biological example is endothelia-selectin (E-selectin).

Further Example: Tweezer - mechanical model



(A) Lectin domain of FimH: the mannose ligand (orange) is bound to the ligand binding site in both the open and the closed conformations.

(B) During the transition of FimH from its open to the closed conformation, the clamp loop segment (highlighted

in cyan) closes on the ligand forming new interactions.

PES tweezer: geometry

The maximum length of hmax = 22.5. The model starts from the angle of the tweezers

$$\theta(h) = \arcsin\left[\frac{168.75 + h^2}{30h}\right] \,.$$

Distances (xs,ys) of the tweezer arm from the orange part are

$$xs(h) = 22.5cos heta - 2cos(1.997 - heta)$$

and

$$ys(h) = 22.5sin\theta + 2sin(1.997 - \theta)$$
.

The distance of the orange atom from the tweezers is

$$\sigma(h,y) = \sqrt{(y+h-ys(h))^2 + xs(h)^2}$$

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PES tweezer: force potentials We use three potentials for y, h and σ with

$$pot_1(y) = D_1(1 + Exp[-2\alpha_1(y - \sigma_1)) - 2Exp[-\alpha_1(y - \sigma_1)])$$
$$pot_2(\sigma) = D_2(Exp[-2\alpha_2(\sigma - \sigma_2)] - 2Exp[-\alpha_2(\sigma - \sigma_2)])$$
where $\sigma(h, y)$ is a distance to the side arms, and

$$pot_3(h) = (1 - \frac{h}{10})^{20} + D_3(1 + Exp[-2\alpha_3(h - \sigma_3)] - 2Exp[-\alpha_3(h - \sigma_3)])$$

With corresponding parameters adapted to the FimH we get the PES

$$V(h, y) = pot_1(y) + pot_3(h) + 2pot_2(\sigma(h, y)) .$$

A sum of different potentials of the molecule is better to accept than a product, like in the former case.



Left: PES of the tweezers. Variables are y of the orange particle, and h of the tweezers length. M1 is the minimum of the open, M2 of the closed form. The two-state model is necessary to explain the catch-slip behaviour of FimH/mannose.

The NT to direction (1,1) is dashed.

Right: effective PES under the force 1.25 units. The barrier M2-TSz becomes higher; forming the catch bond character.

There is no general theory for the existence of a catch bond on a PES. The examples are found by trial and error. Currently we collect further examples to become capable to develop such a theory.

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Summary: How to find a RP, if You Wust

Properties of NTs

- Describe the RP by (some) Newton Trajectories: it is tractable – in many practical cases.
- Find TS by Newton Trajectories: it is tractable.
- Find Bifurcations by special Newton Trajectories: it is tractable.

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 Dr.M.Hirsch from Mathematics, Leipzig (now London)
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A row of results (which are presented here) are born in discussions with them.

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(1D Frenkel-Kontorova chain)

Appendix: TCR-pivific Catch bond PES formulae

TCR-pMHC: The PES depends on two main variables: the protein extension *L* and the distance *d*. To simplify the expression, the extension $L(\theta)$ is used as an alternative to the hinge angle θ

 $L(\theta) = 2Wsin(\theta/2)$

and inversely

$$\theta(L) = 2 \operatorname{arcsin}(L/2W)$$
.

The total free energy of the TCR-pMHC system, $V_f(L, d)$, combines intrinsic hinge energy, binding site interaction, and work by the external force

$$V_f(L,d) = V(\theta(L)) + B(d,\theta(L)) - F(L+d)$$
.

The hinge energy, $V(\theta)$, prefers a bent conformation:

$$V(\theta) = 1/2k(\theta - \theta_0)^2$$

where $\theta_0 \approx 0.6\pi$ radians.

The ligand-binding interaction, $B(d, \theta)$, is modeled using a Morse potential:

$$B(d, \theta) = D(\theta) [(1 - Exp(-(d - d_0))^2 - 1]]$$

Here, $D(\theta)$, represents the angle-dependent binding strength, uses a Gaussian centered at θ_1 :

$$D(\theta) = D_0 \operatorname{Exp}\left[-\frac{(\theta - \theta_1)^2}{2\sigma^2}\right]$$

This model captures the allosteric communication between the hinge angle and binding site, crucial for modulating TCR-pMHC interaction strength.

It works also for different selectines, compare

 W. Quapp, J.M.Bofill: J. Phys. Chem. B 128, 17, 4097-4110 (2024) "Theory and examples of catch bonds"

However, the product of two single potential parts is somewhat strange. It is avoided in the tweezer model.

Appendix: Example of a distiunguished coordinate

Example of a distiunguished coordinate PES curves with jumps, in a paper in 2021



If You see such curves, You can assume that a very old and questionable method is used.

Appendix: Eigenvectors and Eigenvalues of A

Relation of the matrix H and its adjoint matrix A: λ_i, μ_i are the eigenvalues of H and A.

- *H* is regular then and only then if *A* is regular.
- H and A have the same eigenvectors. Thus, to any λ_i belongs exactly one μ_i.

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$$\lambda_i \mu_i = Det(H) = \prod_k \lambda_k$$