SHAPES AND DYNAMICS OF BIOLOGICAL SYSTEMS

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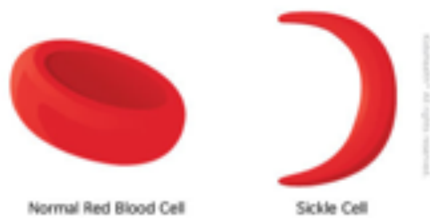
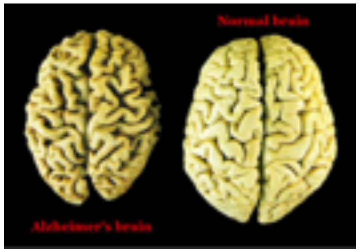
Genome Center

UC Davis

Biology = Quantitative Science ….

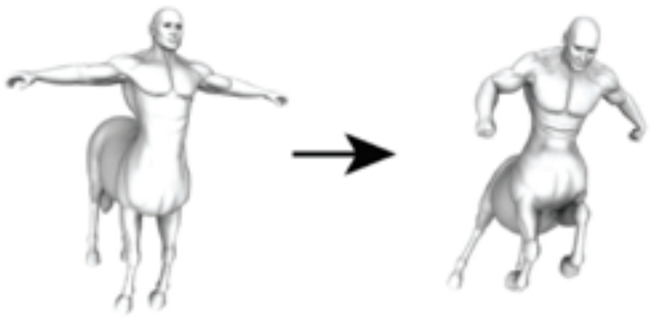
Acetylaminofluorene



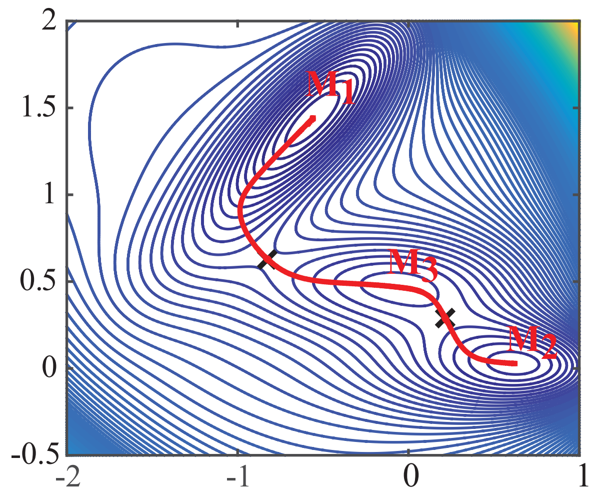


Comparing (biological) shapes

Part I: Optimal diffeomorphism

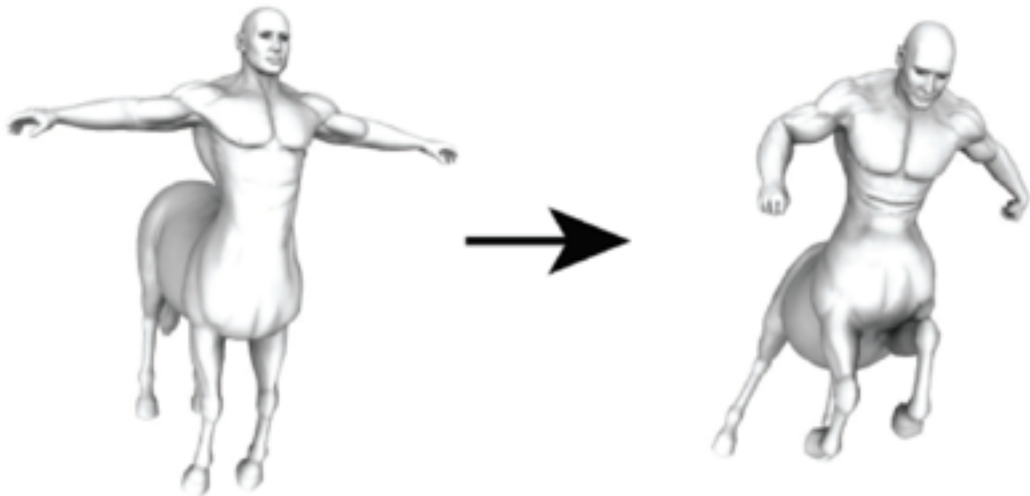


Part II: Geodesics in shape space



Optimal diffeomorphims

We want to compare two surfaces by finding an *optimal diffeomorphism* between them.



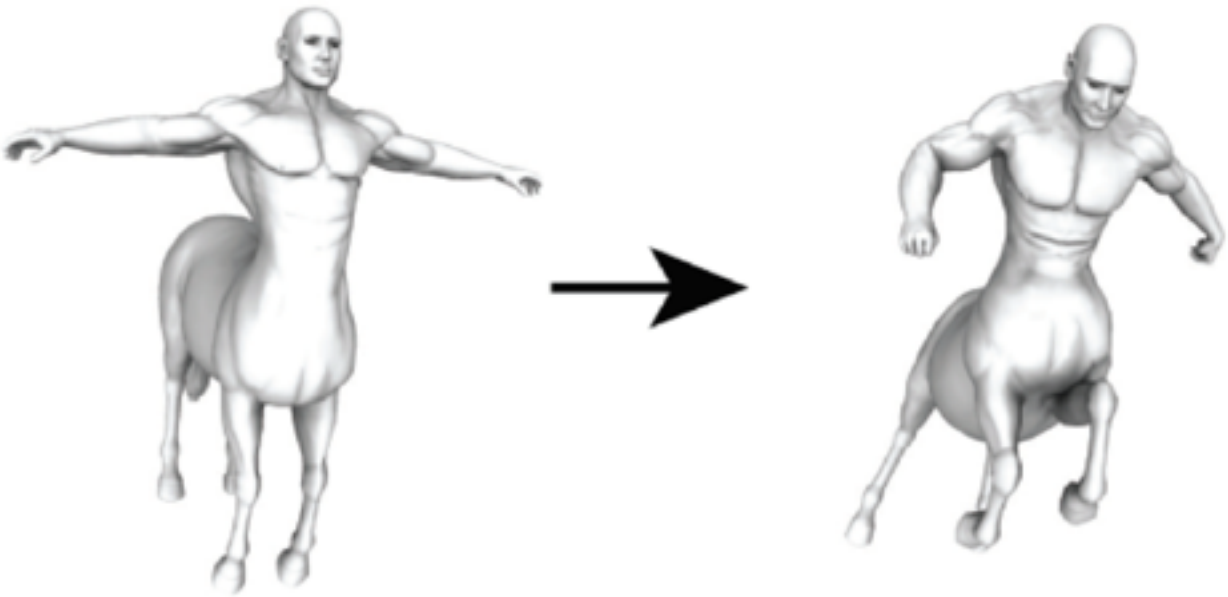
If the surfaces have identical geometry then the optimal diffeomorphism is given by an isometry.

But what if they have different geometries?

What map is *closest* to being an isometry?

Optimal diffeomorphims

Optimal diffeomorphisms do more than give a distance. They also give a *correspondence*.



Diffeomorphic mapping

- General maps between two surfaces deform lengths and angles

- Isometries conserve lengths and angles…. but they are rarely appropriate

- Conformal maps are the next best options, as they distort lengths but preserve angle

The Uniformization Theorem

Theorem [Poincaré, Koebe]

Any two genus-zero surfaces are conformally equivalent

Given any two shapes (with no holes), there is a map from one to the other that preserves angles.

The UC Davis Version…

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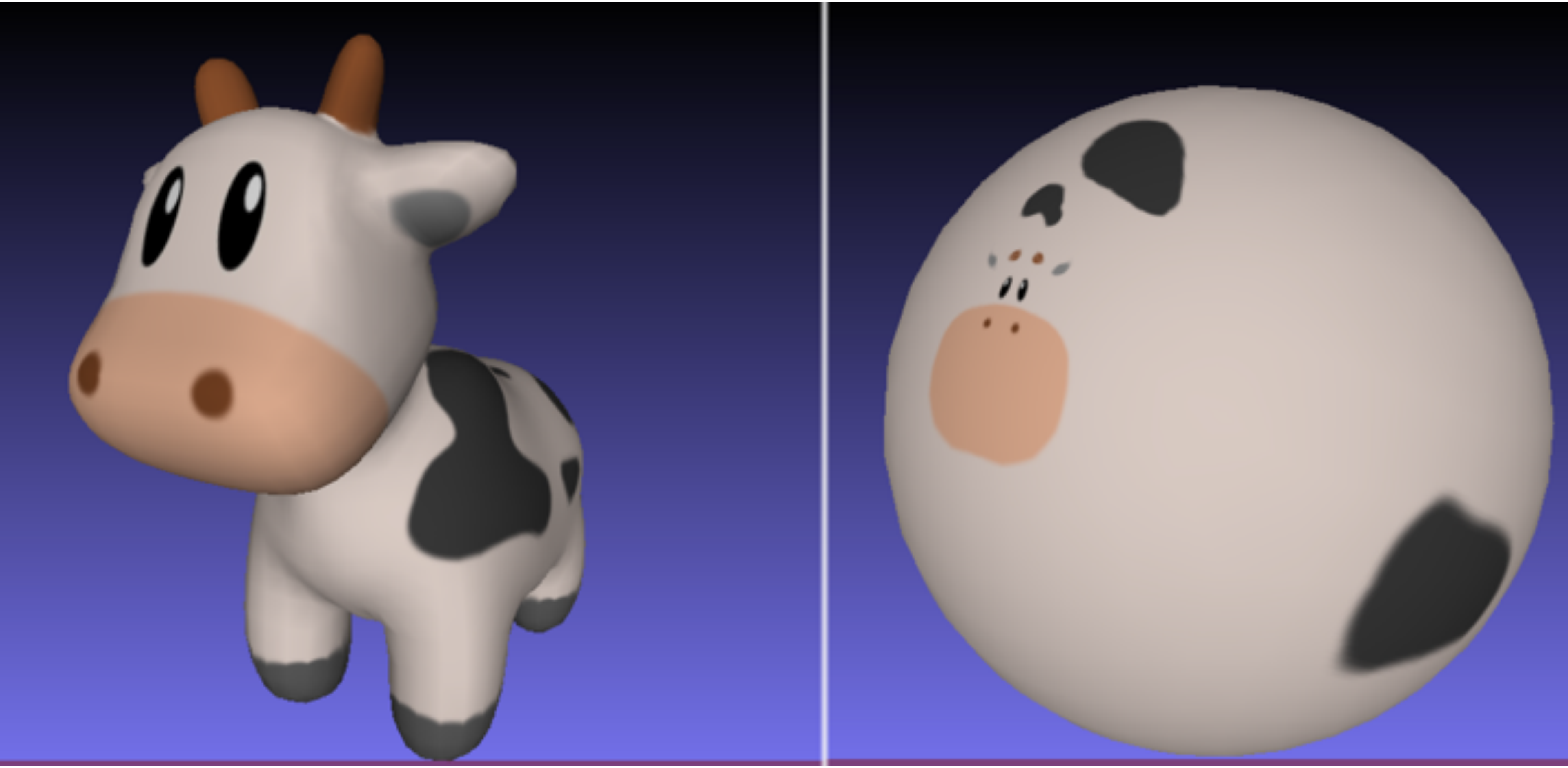
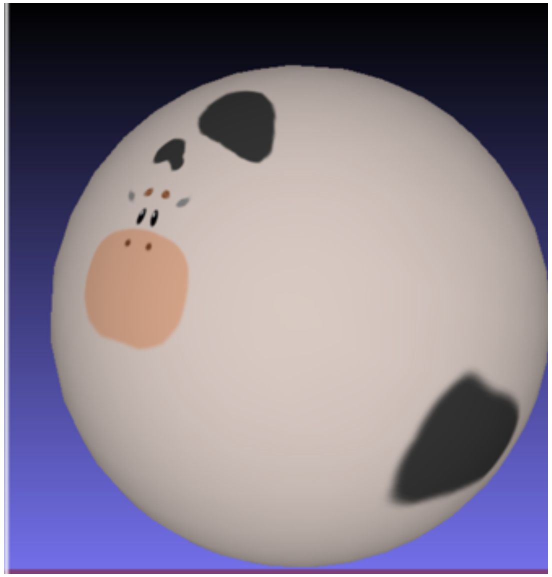


Mapping Genus 0 Surfaces to the Sphere

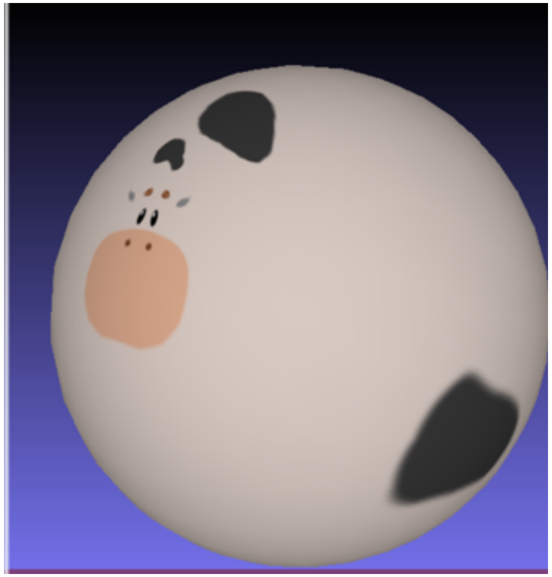
g



$\tilde{g}$

$$\tilde{g} = e^{2u} g$$

Mapping Genus 0 Surfaces to the Sphere



g / g: E -> R+
(i,j) -> l_{ij}

$\tilde{g}$ / g': E -> R+
(i,j) -> l'_{ij}

Continuous:

$$\tilde{g} = e^{2u} g$$

Discrete:

$$l'_{ij} = e^{u(i)+u(j)} l_{ij}$$

Mapping Genus 0 Surfaces to the Sphere

Many algorithms exist:

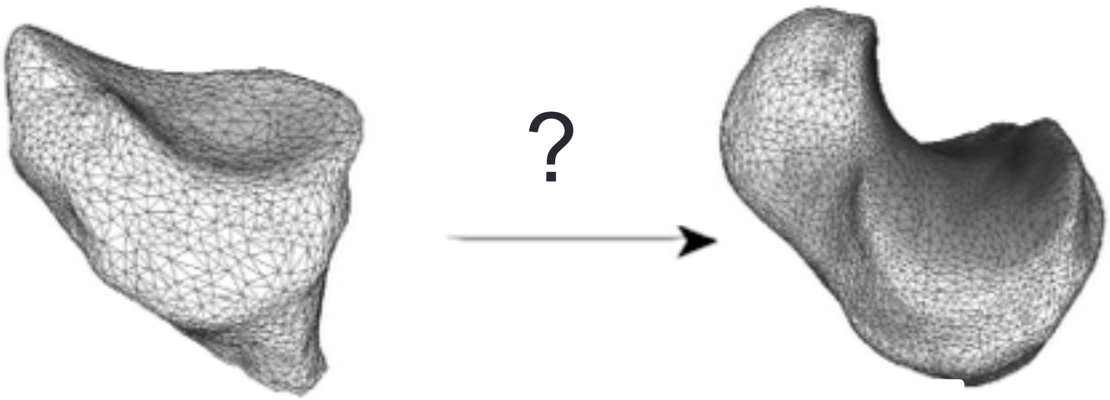
1. Discrete Ricci Flow
2. Discrete Yamabe Flow
3. Conformal Mean Curvature Flow
4. Harmonic Maps
5. Finite Elements
6. Optimize a cost function
7. Discrete Differential Equation
8. Wilmore Flow
9. Circle Packings

Mapping Genus 0 Surfaces to the Sphere

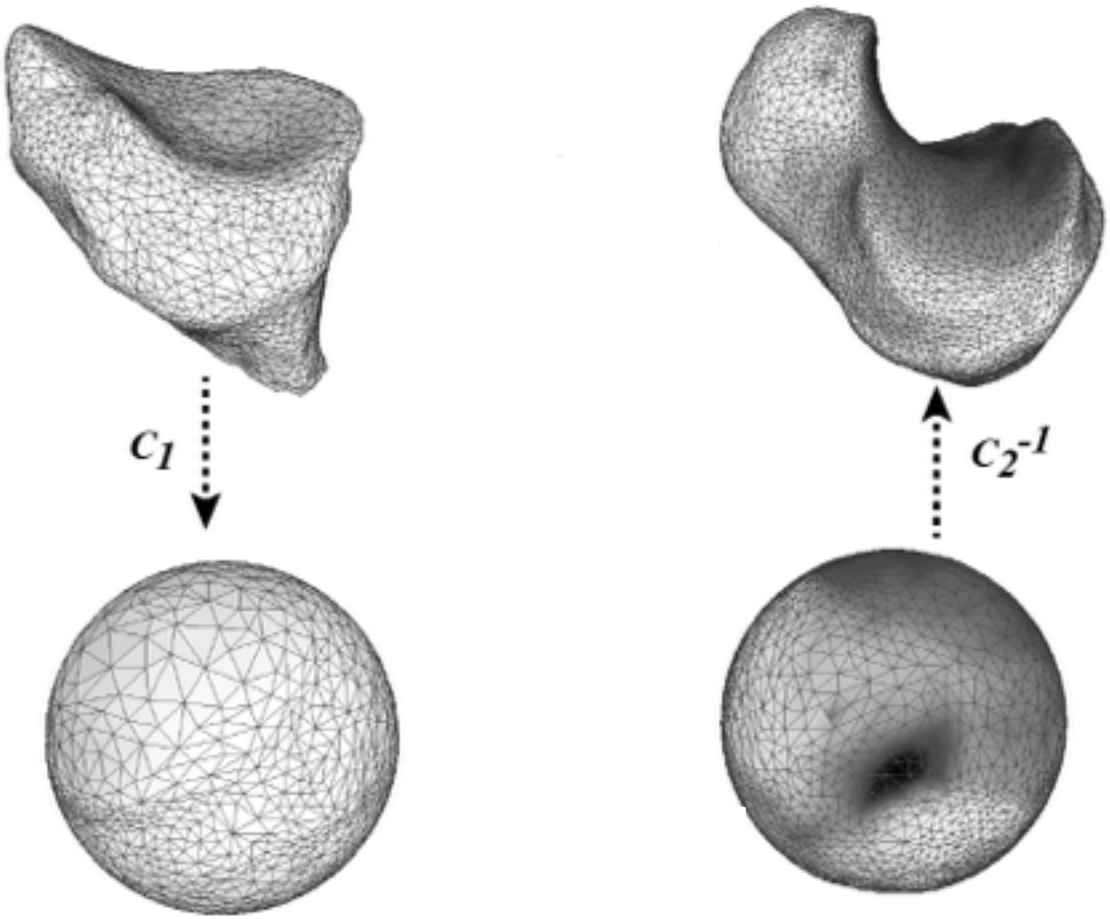
Many algorithms exist:

1. Discrete Ricci Flow
2. Discrete Yamabe Flow
3. Conformal Mean Curvature Flow
4. Harmonic Maps
5. Finite Elements
6. ***Optimize a cost function*** ← ***(Springborn et al, 2008)***
7. Discrete Differential Equation
8. Wilmore Flow
9. Circle Packings

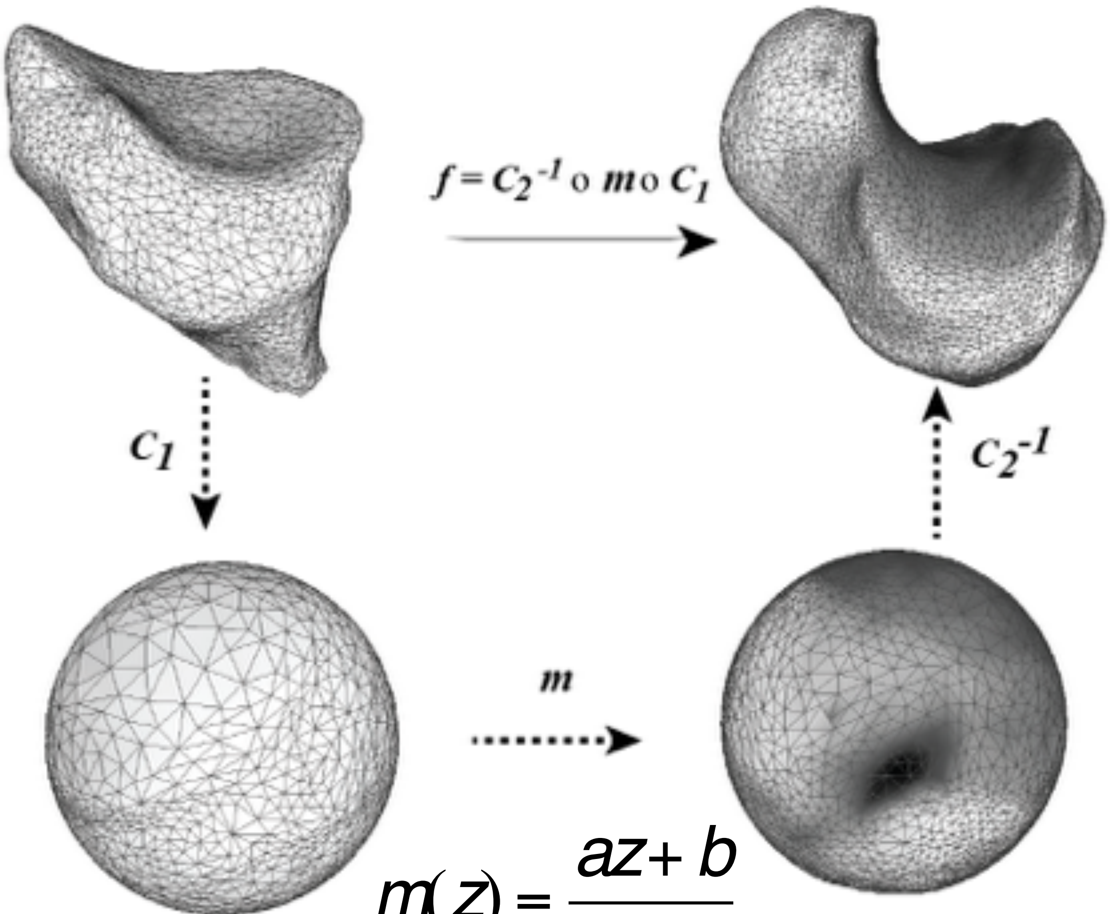
Parametrizing a conformal map between two surfaces



Parametrizing a conformal map between two surfaces

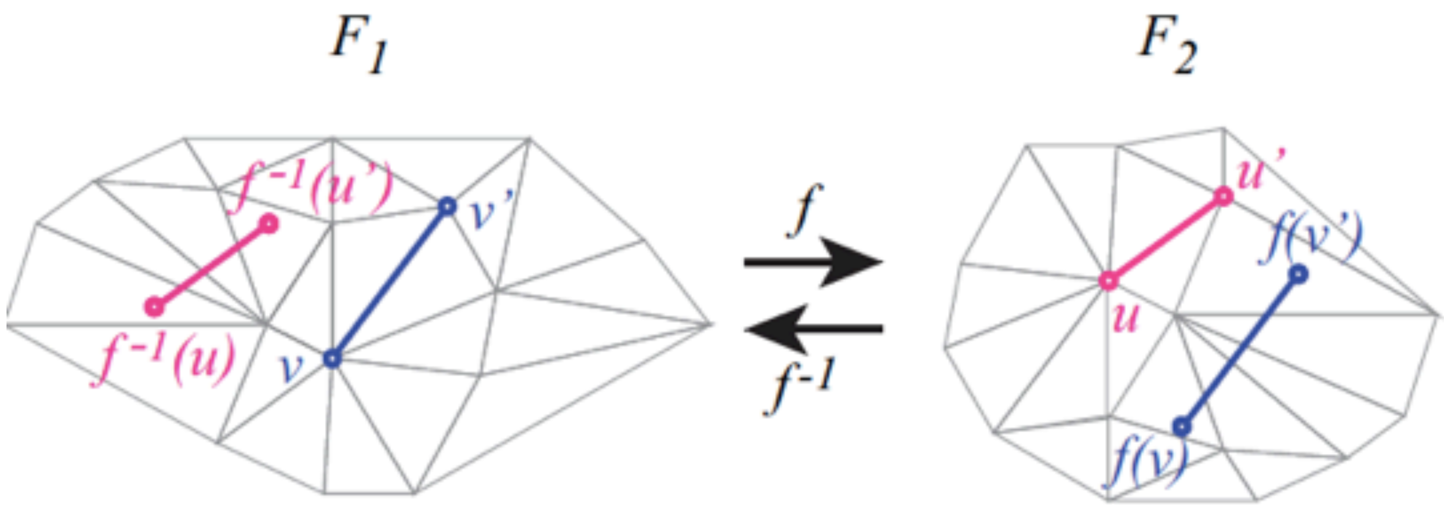


Parametrizing a conformal map between two surfaces



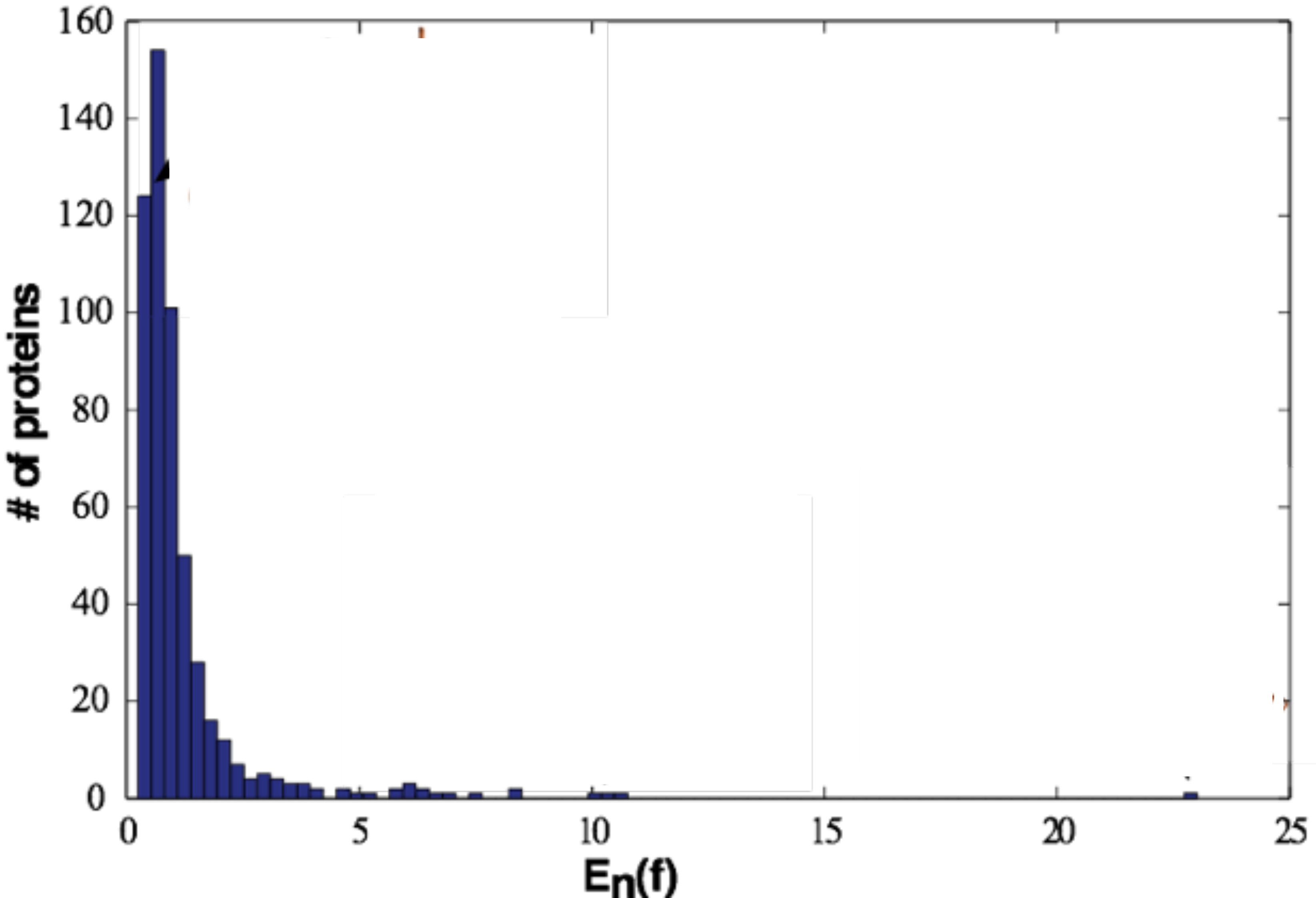
$$m(z) = \frac{az + b}{cz + d}$$

Discrete stretching energy

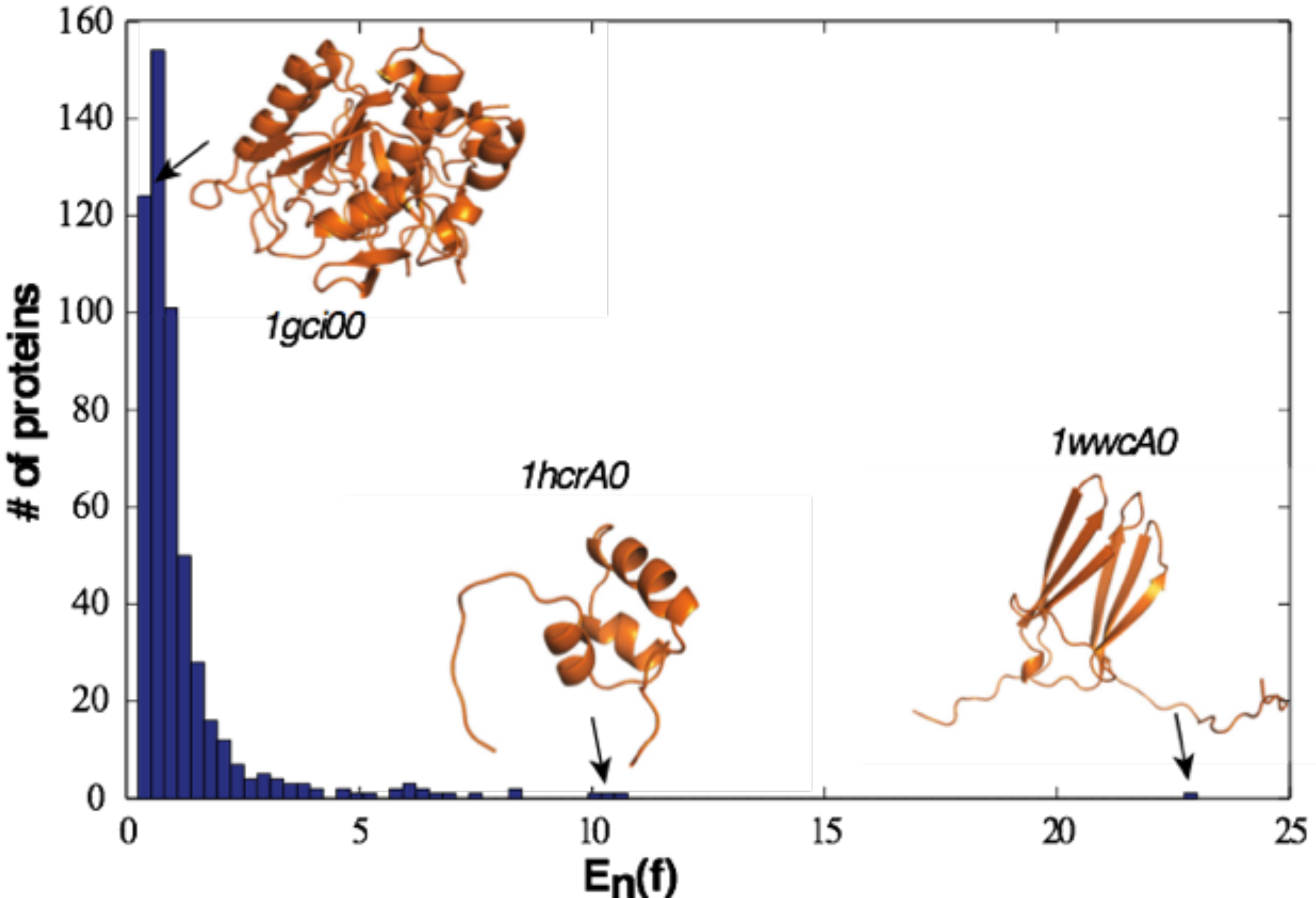


$$E_{sd}(f) = \sqrt{\sum_{(v,v')\in F_1} \frac{A_{vv'}}{3}\left(\frac{l\left(f(v),f(v')\right)}{l(v,v')}-1\right)^2} + \sqrt{\sum_{(u,u')\in F_1} \frac{A_{uu'}}{3}\left(\frac{l\left(f^{-1}(u),f^{-1}(u')\right)}{l(u,u')}-1\right)^2}$$

How round are proteins?



How round are proteins?

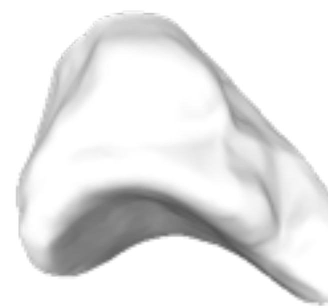


Analysis of anatomical data

Dataset of proximal first metatarsals from 38 prosimian primates, and 23 New and Old World monkeys

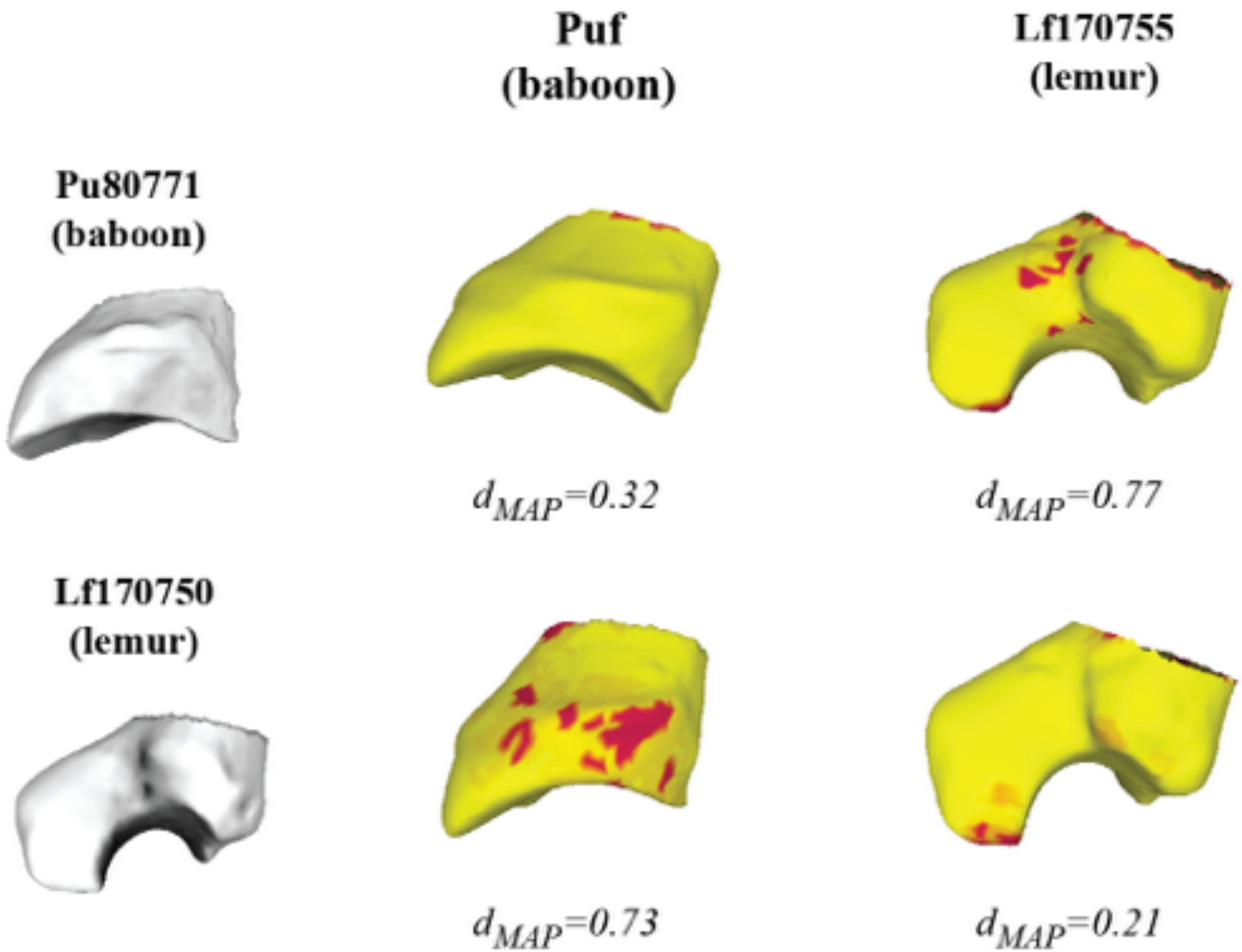
Prosimian:
lemur

Simian:
Cape baboon
(old world)

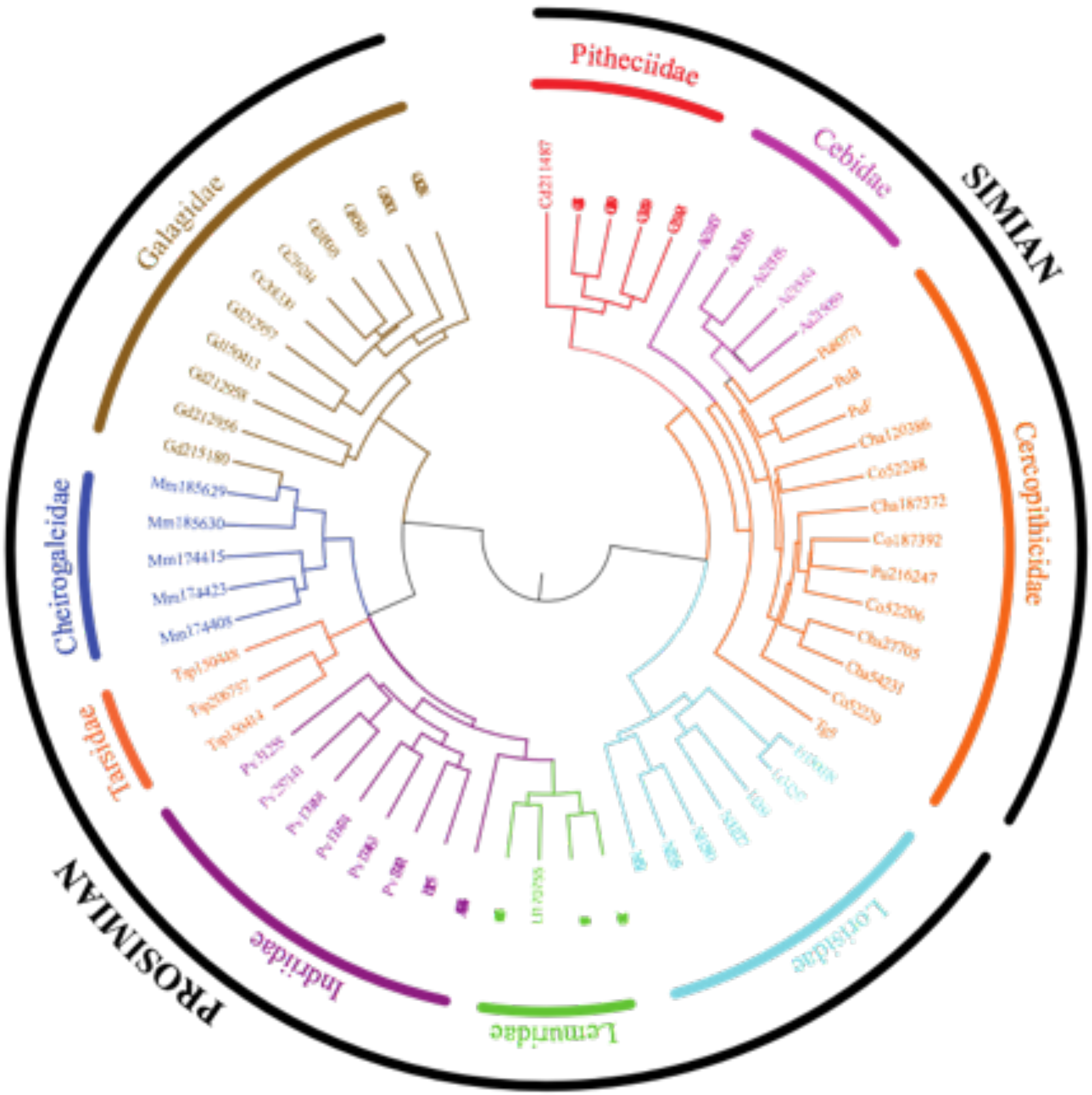


Simian:
White eared titi
(new world)

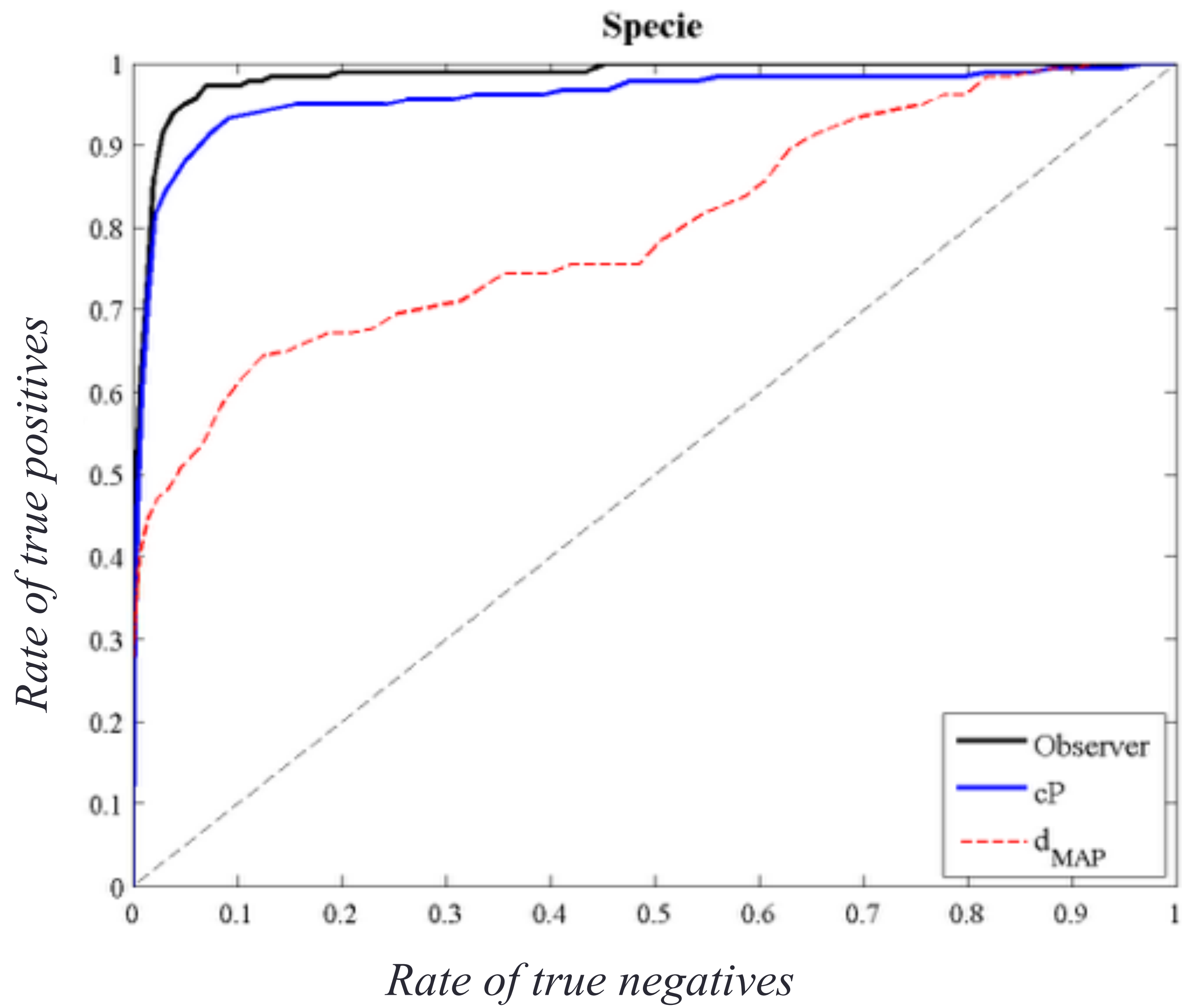
Analysis of anatomical data



Analysis of anatomical data

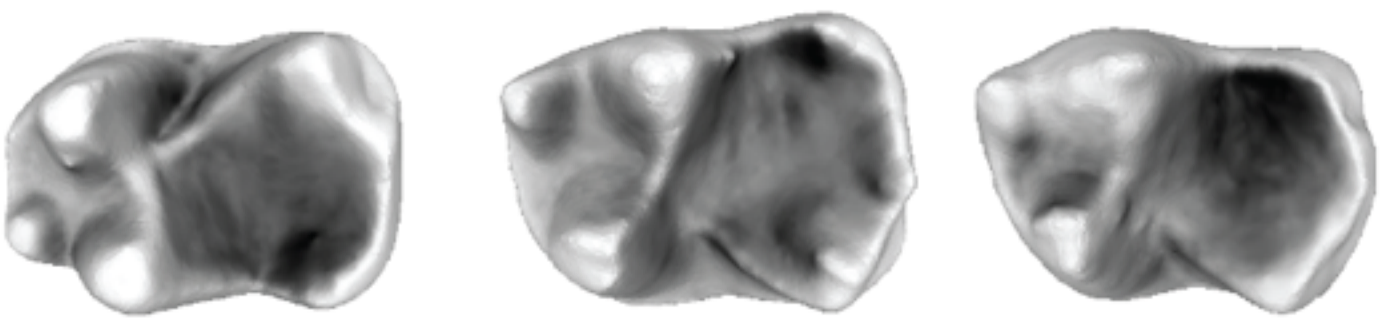


Comparing lower molars from primates



Comparing lower molars from primates:

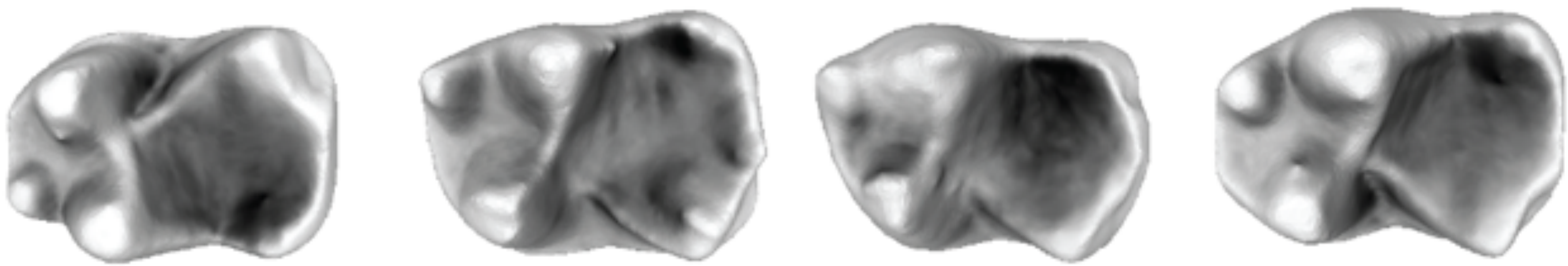
A10-A13: same order, same family
Q06 : same order, different family



	A10	A13	Q06
A10	0.0	**0.38**	**0.30**

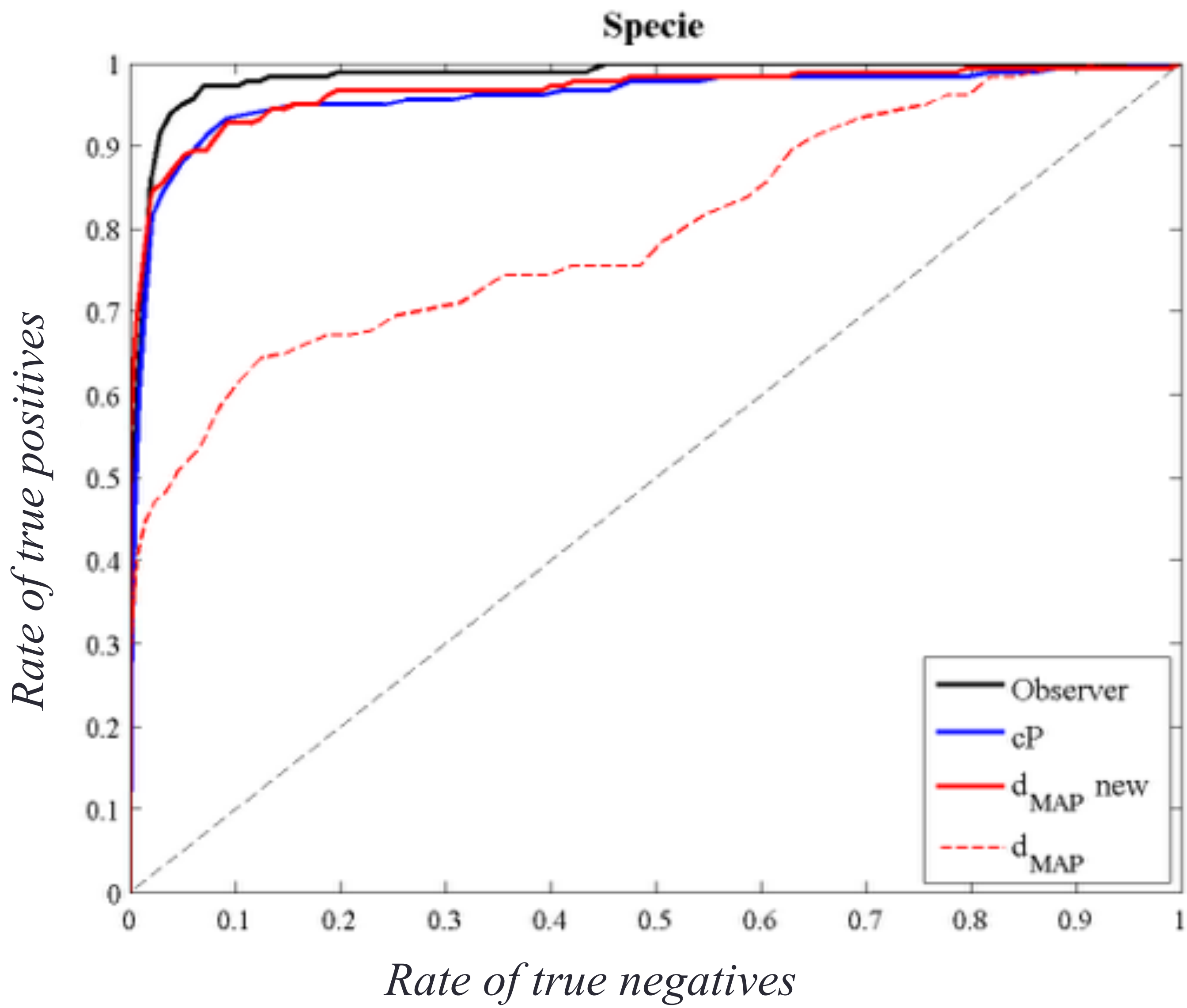
Comparing lower molars from primates:

A10-A13: same order, same family
Q06   : same order, different family



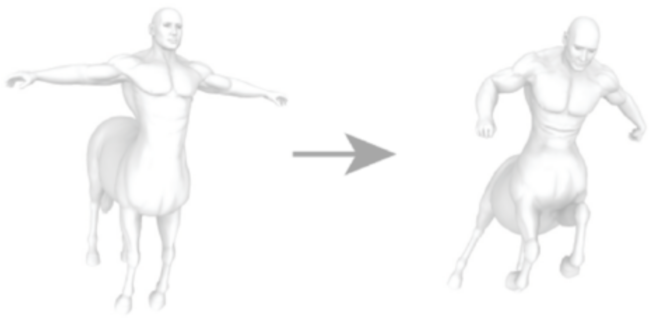
	A10	A13	Q06	A10R
A10	0.0	**0.38**	**0.30**	**0.36**
A10R	**0.36**	**0.18**	**0.22**	**0.0**

Comparing lower molars from primates



Comparing (biological) shapes

Part I: Optimal diffeomorphism



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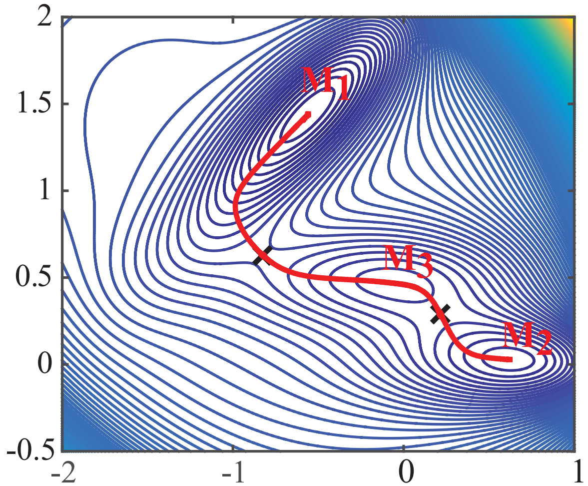


Minimum Action Paths and Shape Similarity

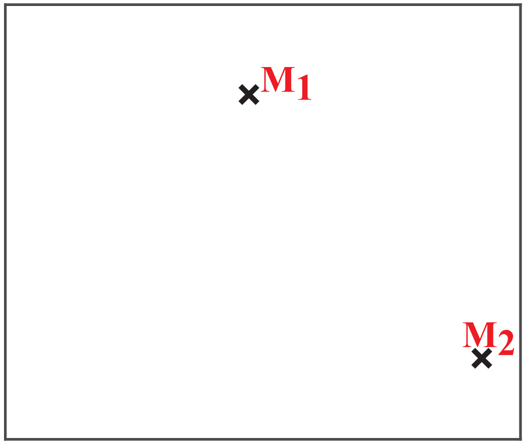
1. Defining a (geodesic) distance between shapes

2. Applications to simple 2D potentials

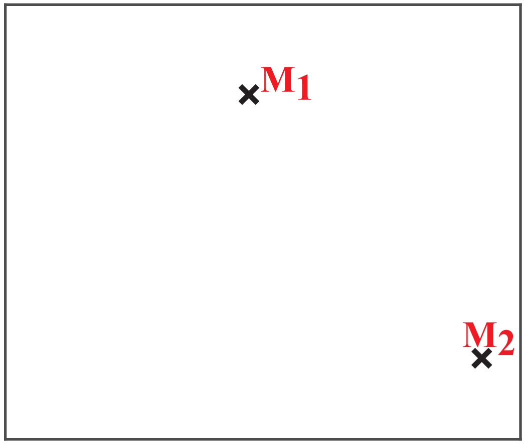
3. Applications to proteins: a simplified potential

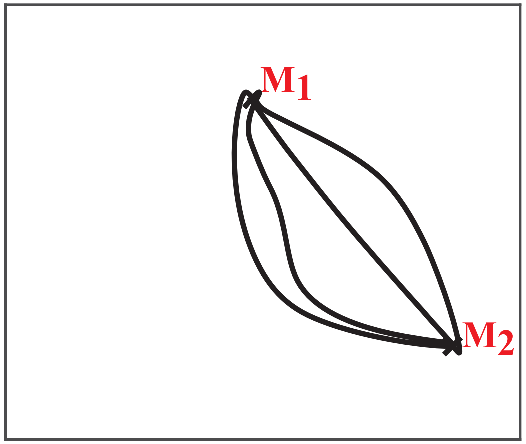
4. Applications to large shapes: more simplifications

Distance between Shapes…

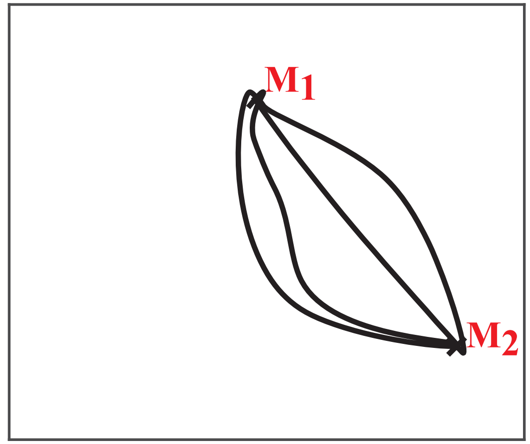


$$D = \sqrt{\left(x_1 - x_2\right)^2 + \left(y_1 - y_2\right)^2}$$





$$D = \sqrt{\left(x_1 - x_2\right)^2 + \left(y_1 - y_2\right)^2}$$



$$L = \sqrt{\left(\frac{dX}{dt}\right)^2}$$

$$\frac{\partial L}{\partial X} = \frac{d}{dt}\left(\frac{\partial L}{\partial \dot{X}}\right)$$

$$D = \sqrt{\left(x_1 - x_2\right)^2 + \left(y_1 - y_2\right)^2}$$

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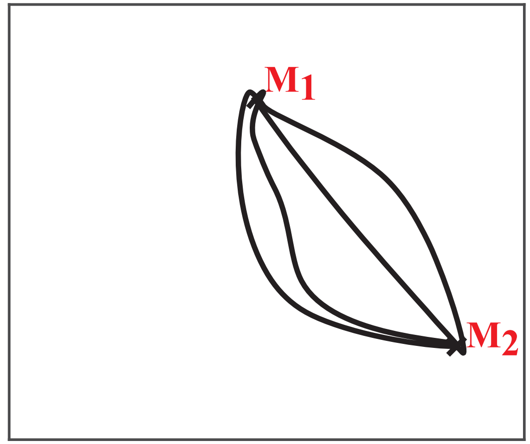

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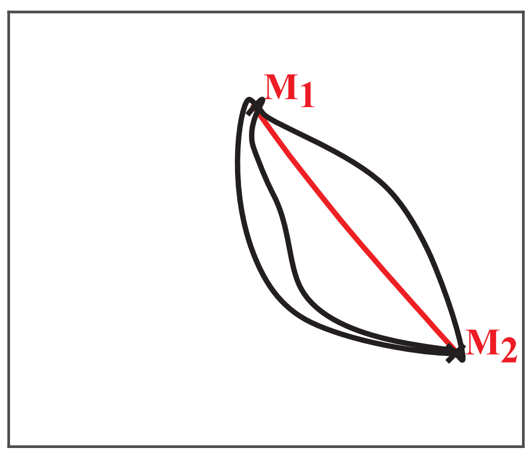
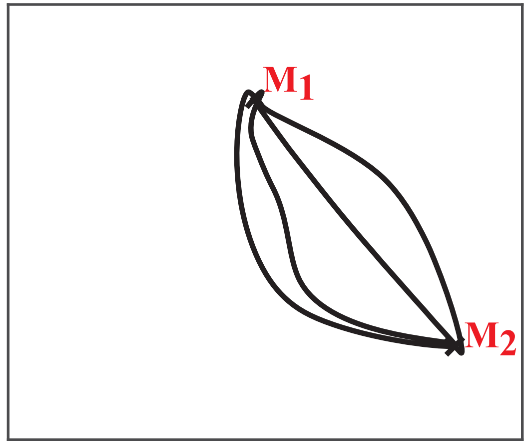


$$S = \int_0^T L\,dt = \sqrt{\left(x_1 - x_2\right)^2 + \left(y_1 - y_2\right)^2}$$

$$D = \sqrt{\left(x_1 - x_2\right)^2 + \left(y_1 - y_2\right)^2}$$



$$L = \sqrt{\left(\frac{dX}{dt}\right)^2}$$

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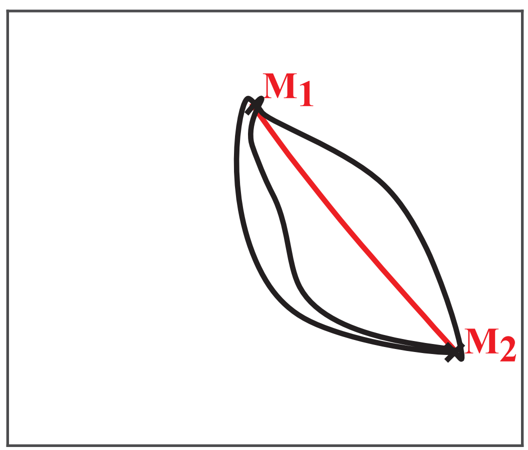
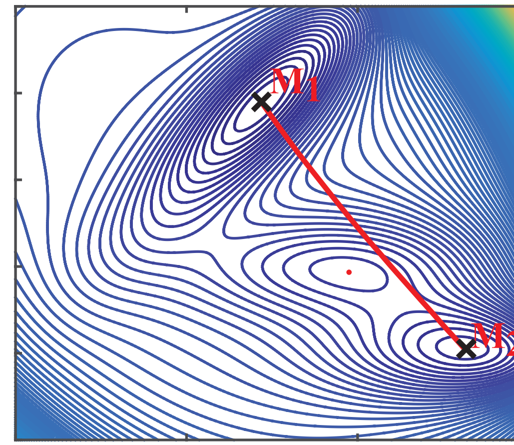


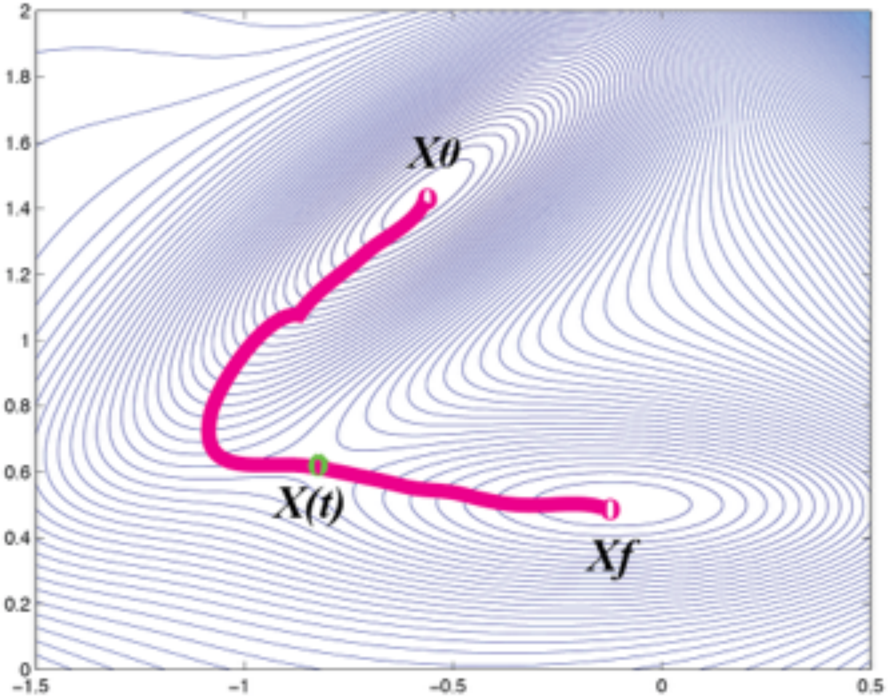
$$S = \int_0^T L\,dt = \sqrt{\left(x_1 - x_2\right)^2 + \left(y_1 - y_2\right)^2}$$



Diffusive form of Langevin Equation:

$$\eta M \frac{dX}{dt} = -\nabla U(X) + B$$

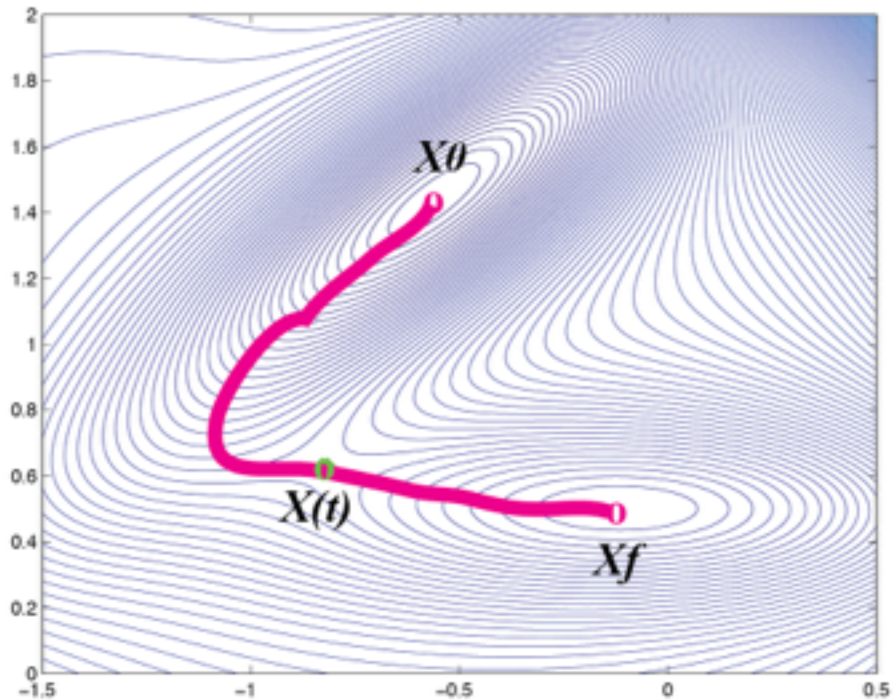
η: *friction*
M: diagonal mass matrix
U: potential energy
B: random force



For a trajectory

$$X(0) \rightarrow X(t) \rightarrow X_f(T_f)$$

$$P\left(X(0) \rightarrow X_f(T_f)\right) \propto \exp\left(-\frac{S}{k_B T}\right)$$



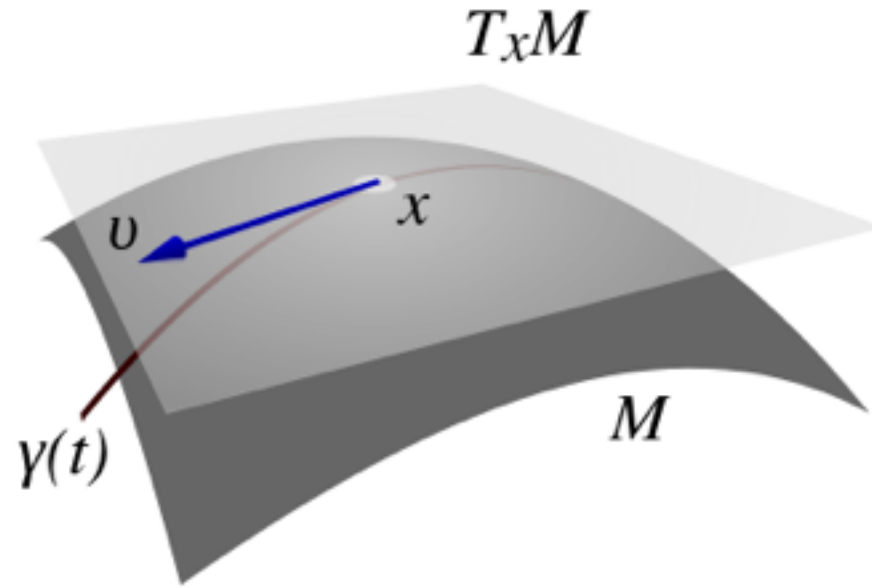
where the action, S, is given by (Onsager and Machlup, 1953):

$$S = \frac{1}{2\eta}\int_0^{Tf}\left(\eta M \frac{dX}{dt} + \nabla U(X)\right)^2 dt$$

Corresponding Lagrangian: $$L = \left(\eta M \frac{dX}{dt} + \nabla U(X)\right)^2$$

Let M be a (smooth) manifold and

E a function from (M,TM) то [0,∞);



Let X_0 and X_F be two points on M. Then

$$d(X,Y) = \inf\left\{ \int_0^T E(\gamma(t),\dot{\gamma}(t))\,dt \;\middle|\; \gamma \in C^1([0,T],M), \gamma(0) = X_0, \gamma(T) = X_F \right\}$$

defines an intrinsic quasi-metric on M.

There always exist length minimizing curves on (M,E). Such curves can always be reparametrized to be geodesics, and any geodesic must satisfy the Euler-Lagrange equation for F(γ):

$$F(\gamma)=\int_{X_0}^{X_F} L(\gamma(t),\dot{\gamma}(t))dt=\int_{X_0}^{X_F}\left[E(\gamma(t),\dot{\gamma}(t))\right]^2 dt$$

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$$F(\gamma) = \int_{X_0}^{X_F} L(\gamma(t), \dot{\gamma}(t))dt = \int_{X_0}^{X_F} \left[E(\gamma(t), \dot{\gamma}(t)) \right]^2 dt$$

Onsager and Machlup (1953) action:

$$S = \frac{1}{2\eta} \int_0^{Tf} \left(\eta M \frac{dX}{dt} + \nabla U(X) \right)^2 dt$$

Corresponding Lagrangian:

$$L = \left(\eta M \frac{dX}{dt} + \nabla U(X) \right)^2$$

Lagrangian:

$$L = \left(\eta M \frac{dX}{dt} + \nabla U(X) \right)^2$$

Euler Lagrange equations:

$$\frac{\partial L}{\partial X} = \frac{d}{dt}\left(\frac{\partial L}{\partial \dot{X}} \right)$$

$$\frac{d^2 X}{dt^2} = \nabla\nabla U(X) \nabla U(X)$$

Boundary conditions:

$$X(0) = X_0 \qquad X(T_f) = X_f$$

Minimum Action Paths and Shape Similarity

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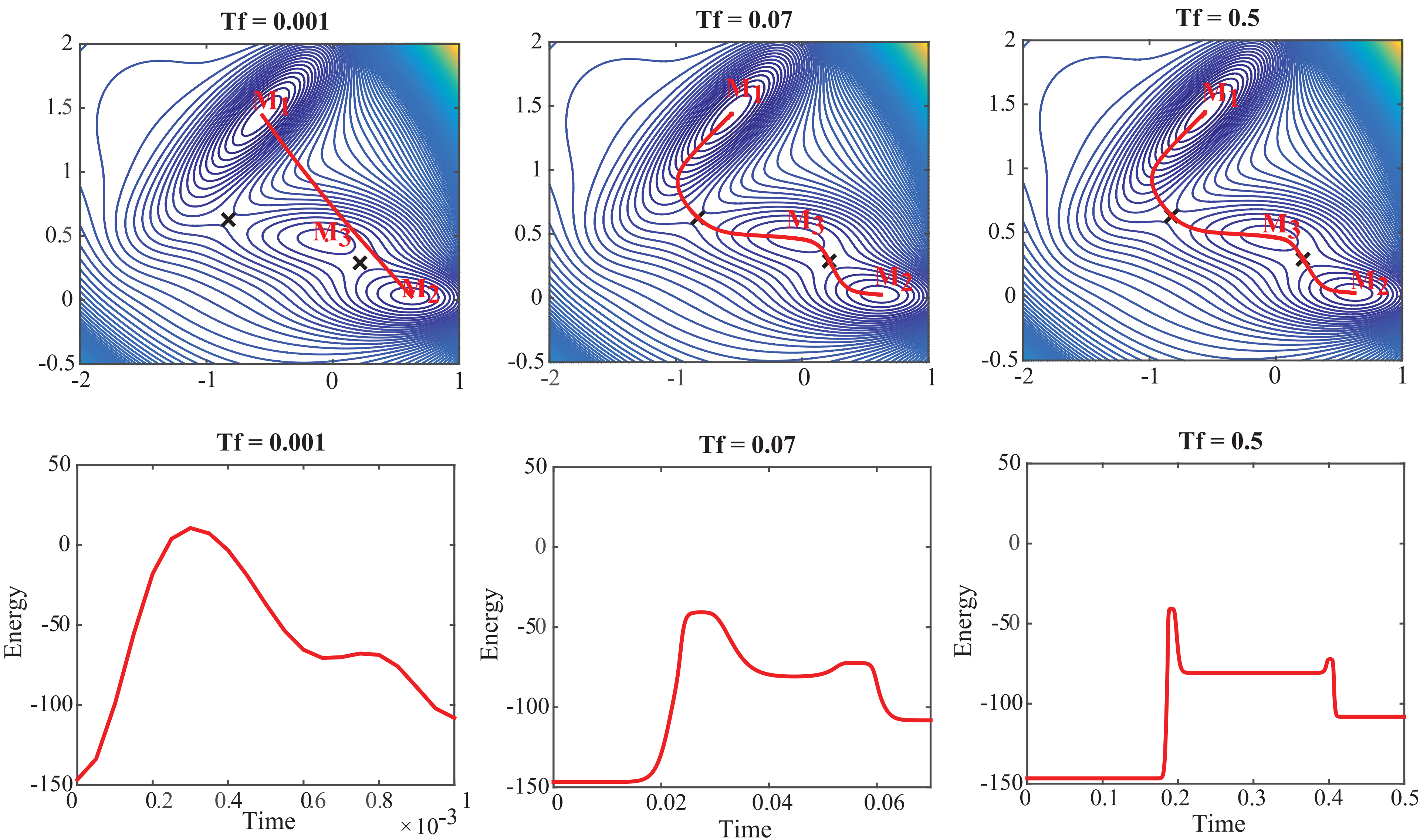
3. Applications to proteins: a simplified potential

4. Applications to large shapes: more simplifications



Tf = 0.001
Tf = 0.07
Tf = 0.5
M1
M2
M3
Energy
Time
×10-3

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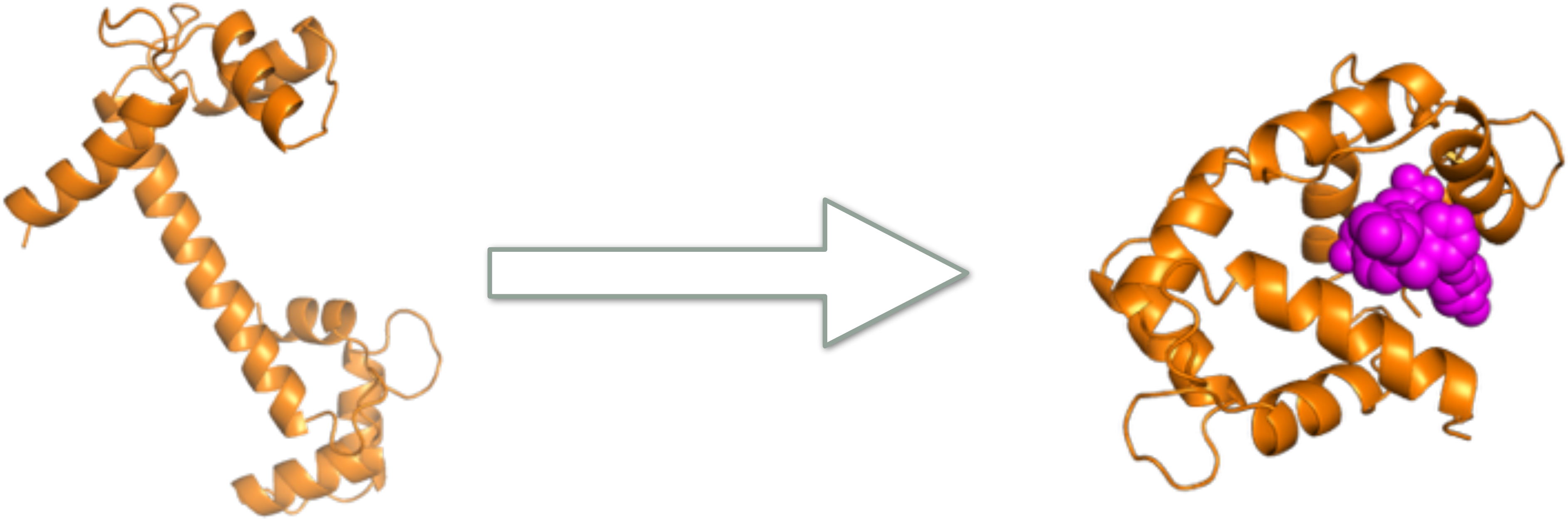
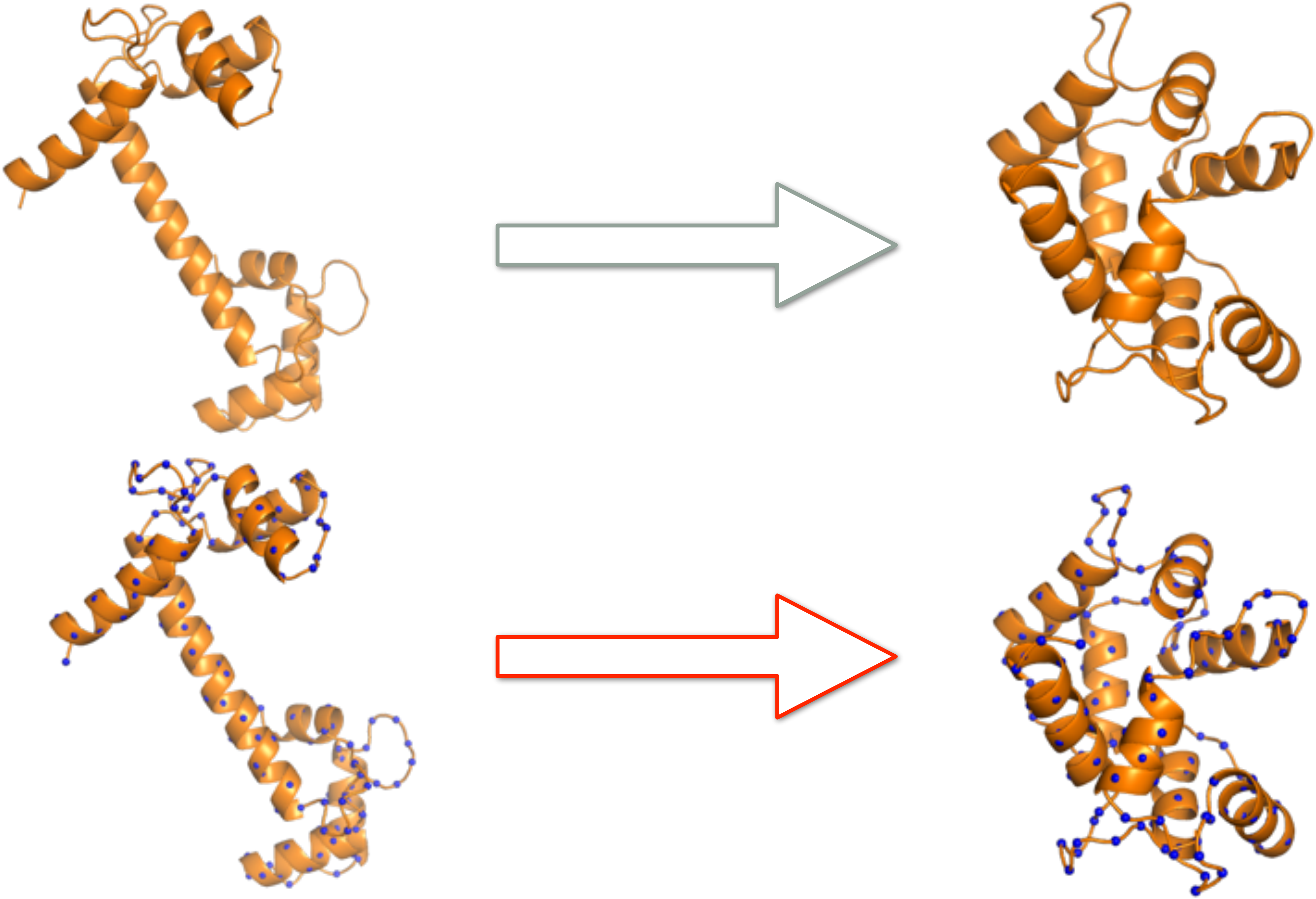
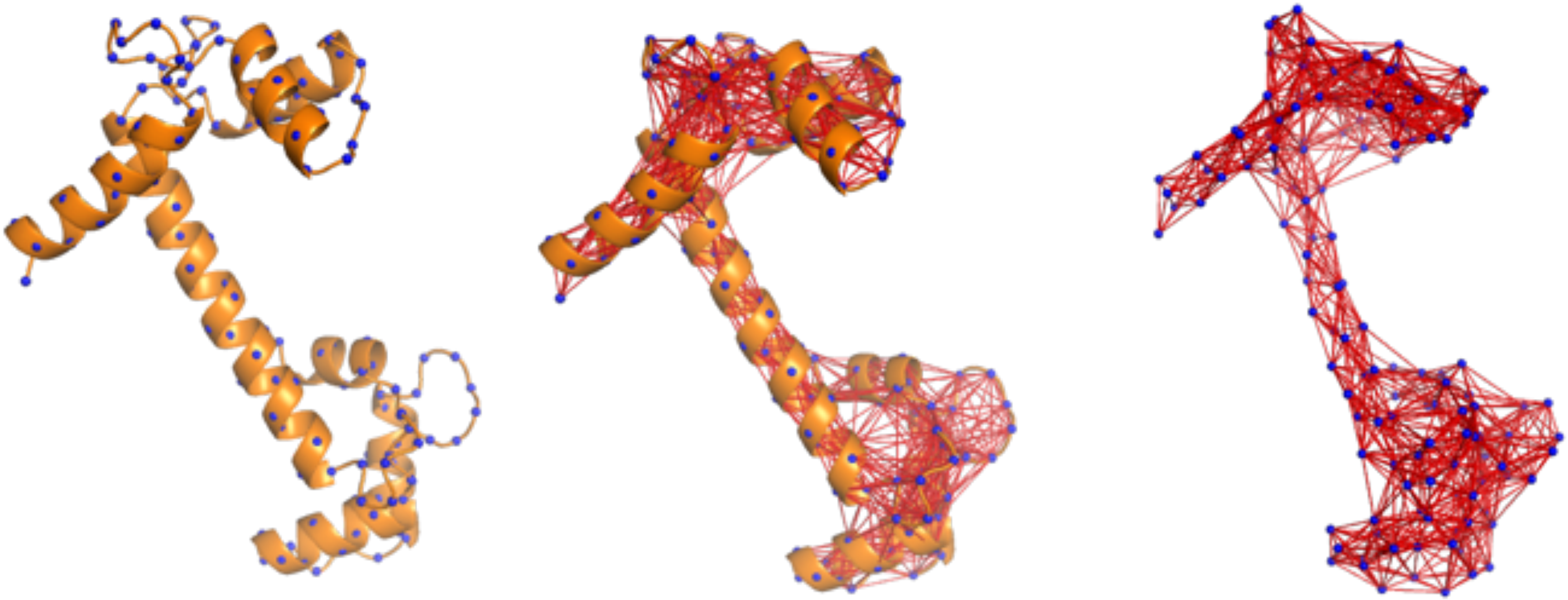




Elastic network for biomolecules:



Elastic network for biomolecules:

Elastic potential:

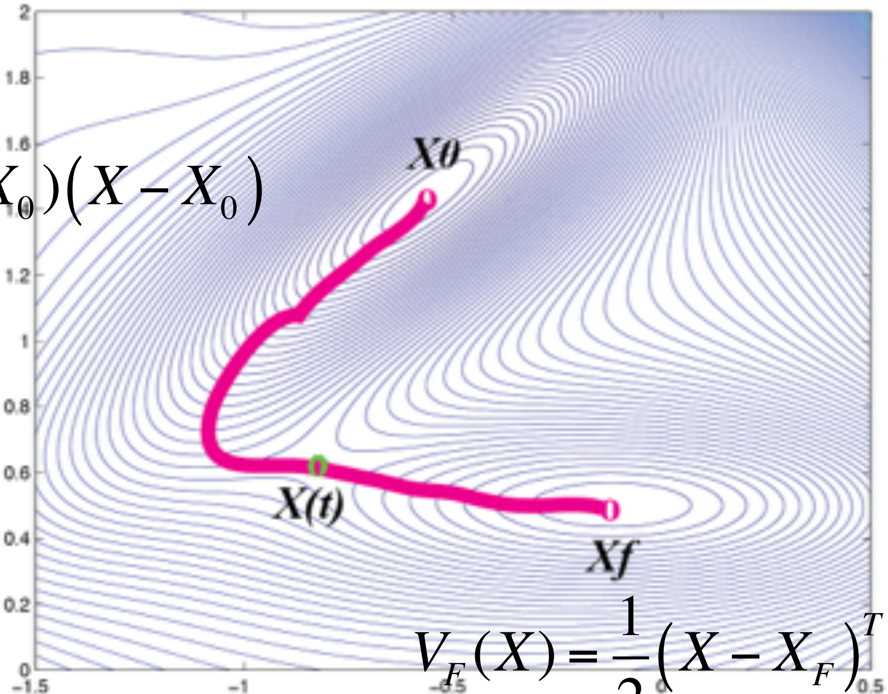
$$V_{ENM}(X) = \frac{1}{2}\sum_{i=1}^{N}\sum_{j>i} k_{ij}(r_{ij} - r_{ij}^{0})^2$$

2nd order Taylor expansion:

$$V_{ENM}(X) \approx V_{ENM}(X^0) + \nabla V_{ENM}(X^0)^T(X - X^0) + \frac{1}{2}(X - X^0)^T H(X - X^0)$$

$$V_{ENM}(X) \approx \frac{1}{2}(X - X^0)^T H(X - X^0)$$

Mixing potential for transition path:



$$V_0(X) = \frac{1}{2}\left(X - X_0\right)^T H(X_0)\left(X - X_0\right)$$

$$V_F(X) = \frac{1}{2}\left(X - X_F\right)^T H(X_F)\left(X - X_F\right)$$

Mixing potential:

$$U(X) = -\log\left(e^{-V_0(X)} + e^{-V_F(X)}\right)$$

Solve:

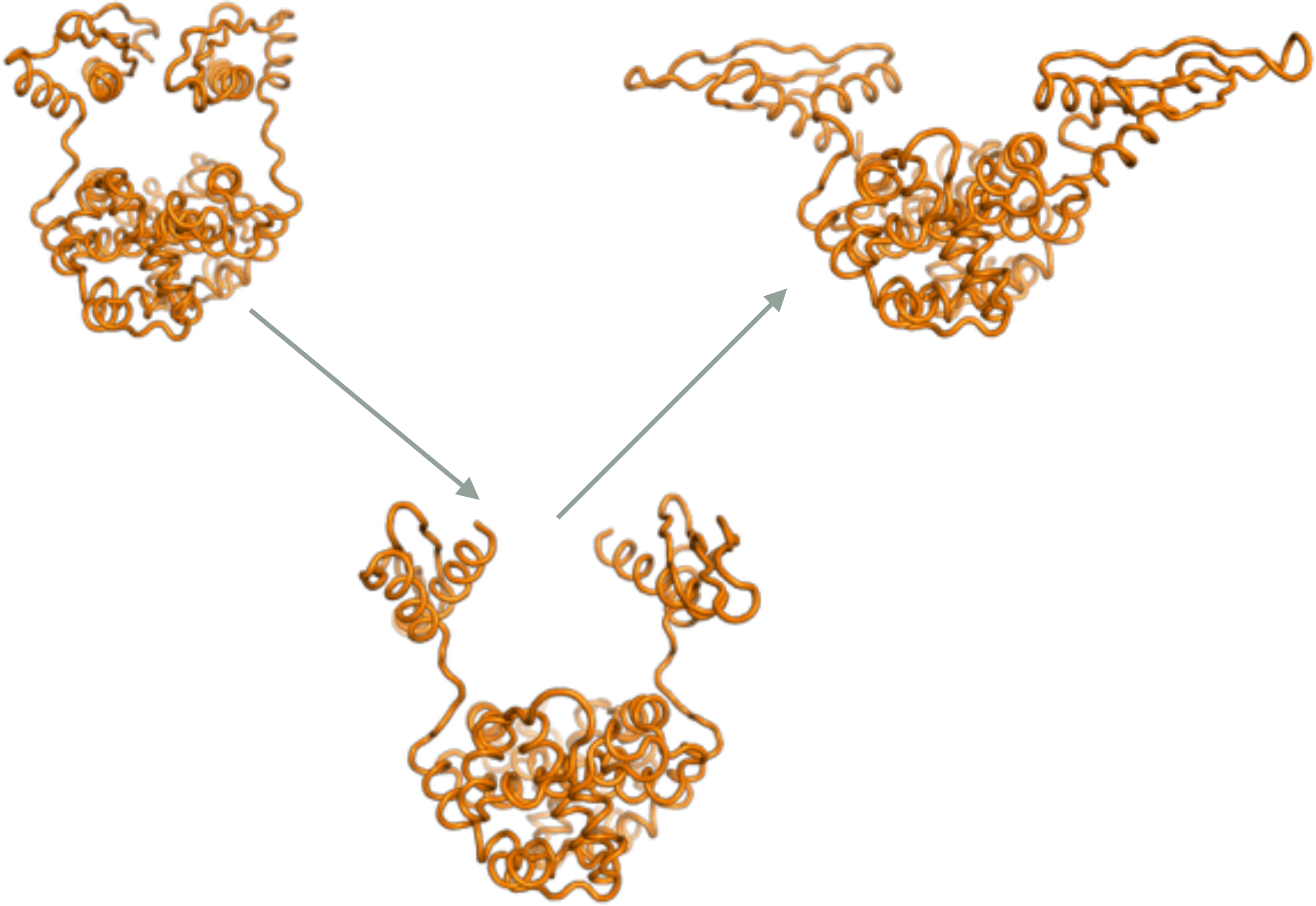
$$\frac{d^2X}{dt^2} = \nabla\nabla U(X)\nabla U(X)$$

with boundary conditions:

$$X(0) = X_0 \qquad X(T_f) = X_f$$

using a relaxation method.

Transition Path for a Ribonuclease III



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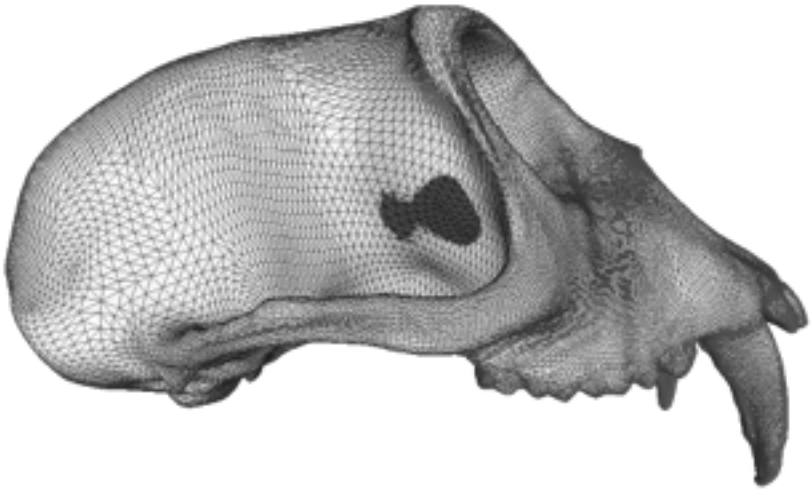
An elastic model for shapes

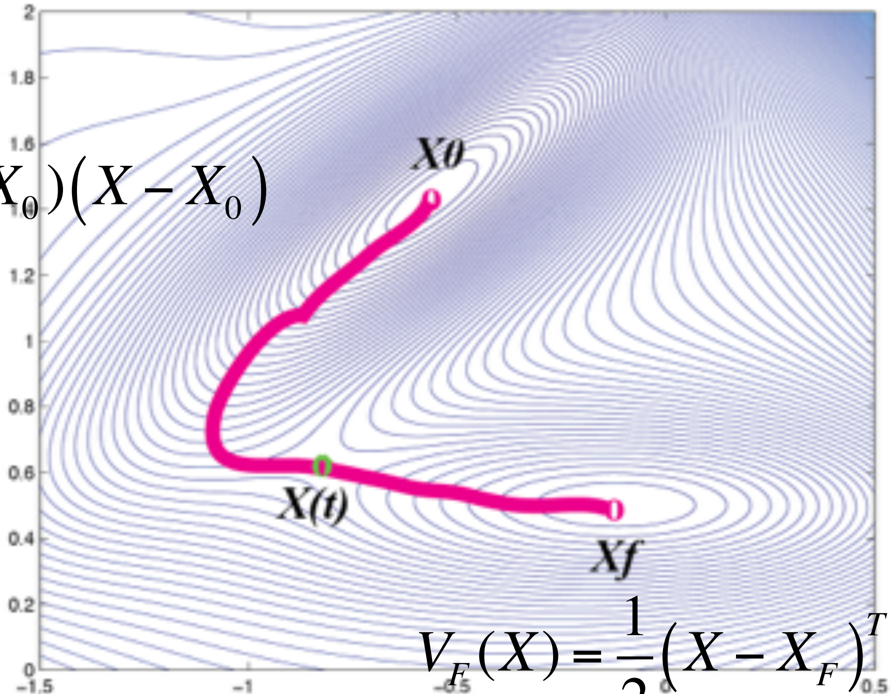


$$U_1(X) = \sum_{edges(i,j)} \left(d_{ij}(X) - d_{ij}(X_0) \right)^2$$

$$\begin{aligned} U(X) &\approx E(X_0) + \nabla E(X_0)^T + \frac{1}{2}\left(X(t) - X_0\right)^T H(X_0)\left(X(t) - X_0\right) \\ &= \frac{1}{2}\left(X(t) - X_0\right)^T H(X_0)\left(X(t) - X_0\right) \end{aligned}$$

Mixing potential for transition path:

$$V_0(X) = \frac{1}{2}\left(X - X_0\right)^T H(X_0)\left(X - X_0\right)$$



$$V_F(X) = \frac{1}{2}\left(X - X_F\right)^T H(X_F)\left(X - X_F\right)$$

Mixing potential:

$$U(X) = \min\left(V_0(X), V_1(X)\right)$$

Euler-Lagrange equations for stationary action:

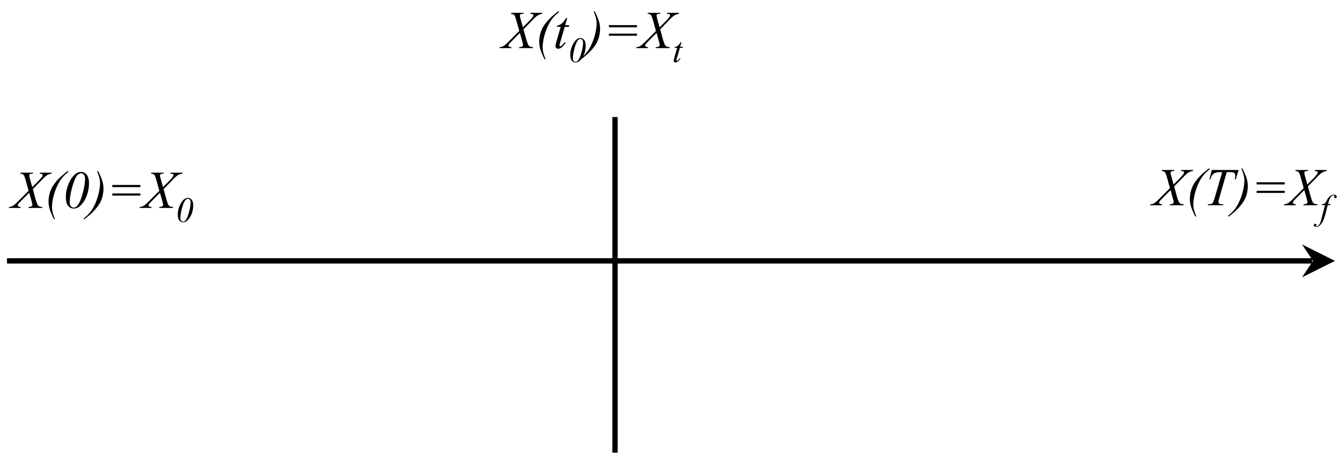
$$\frac{\partial L}{\partial X} = \frac{d}{dt}\left(\frac{\partial L}{\partial \dot{X}}\right) \Rightarrow \begin{cases} \ddot{X} = H(X_0)^T H(X_0)(X - X_0) & t \leq t_0 \\ \ddot{X} = P(X_f)^T P(X_f)(X - X_f) & t \geq t_0 \end{cases}$$

$$X(t \rightarrow t_0) = X_t = X(t_0 \leftarrow t)$$

$$\dot{X}(t \rightarrow t_0) = \dot{X}(t_0 \leftarrow t)$$

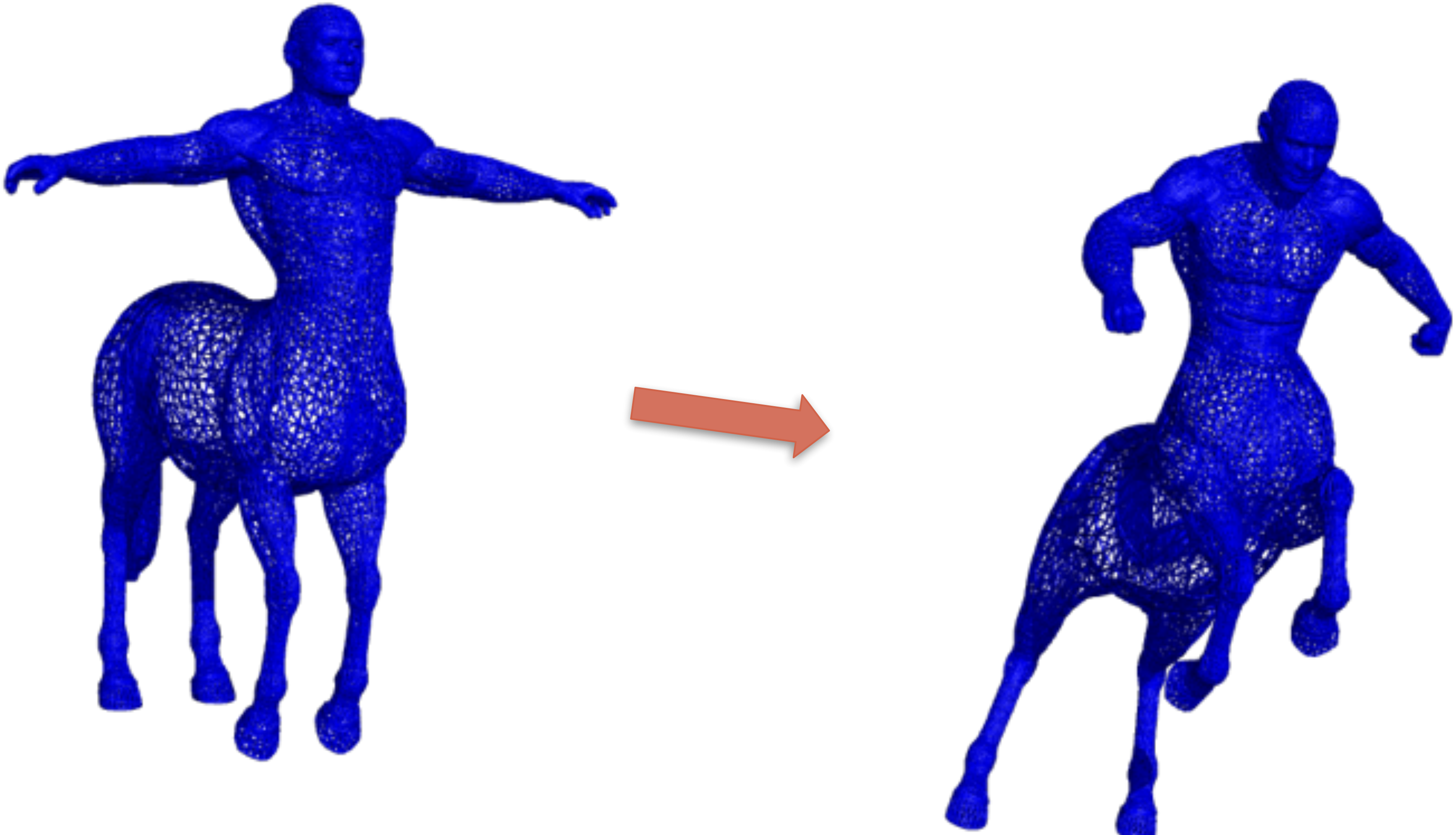
$$U(X(t \rightarrow t_0)) = U(X(t_0 \leftarrow t))$$

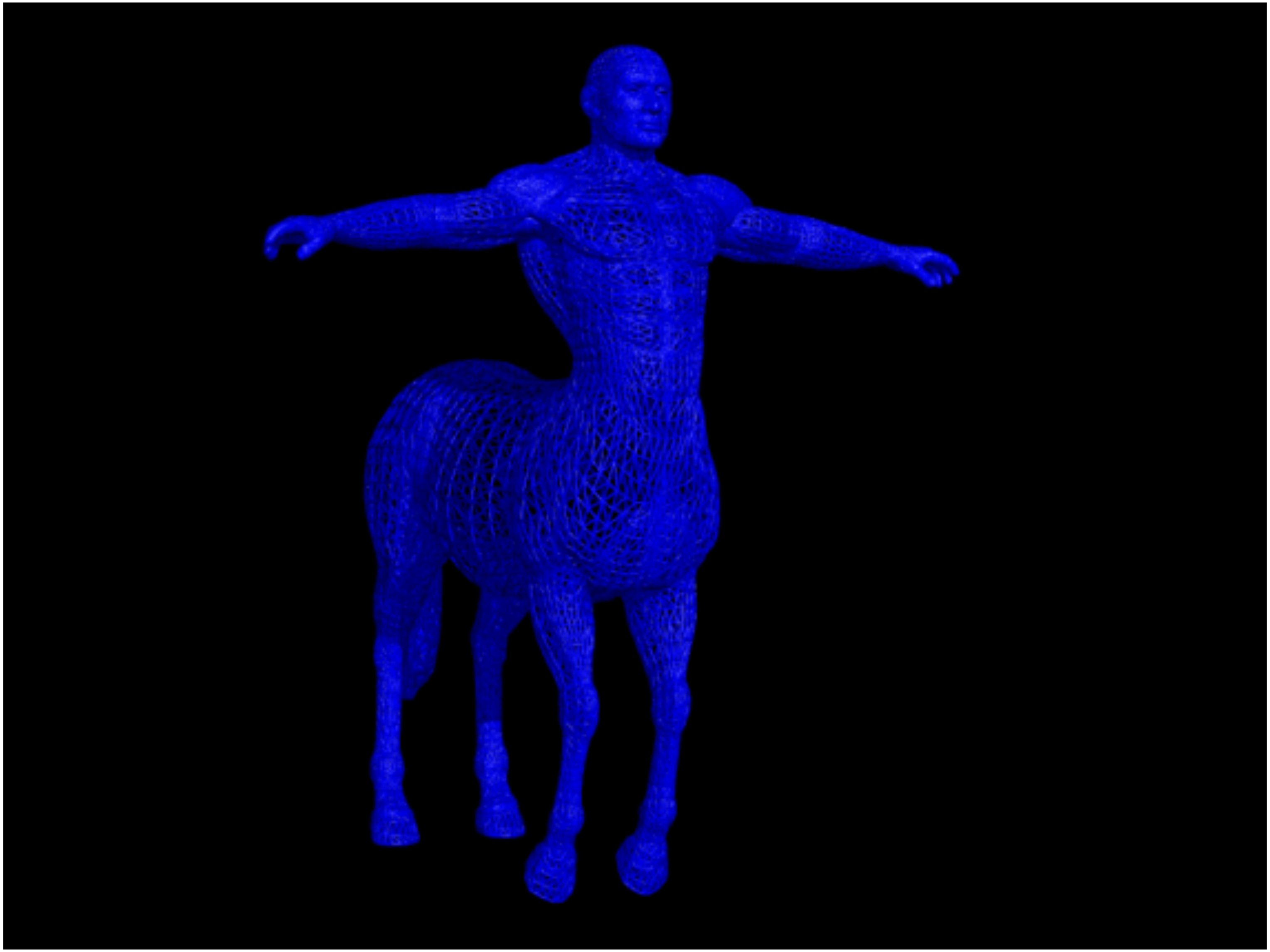
Transitions between two states



$$X(t) = \sinh(Ht)\operatorname{csch}(Ht_0)(X_t - X_0) + X_0$$

$$X(t) = \sinh(P(t-T))\operatorname{csch}(P(T-t_0))(X_f - X_t) + X_f$$



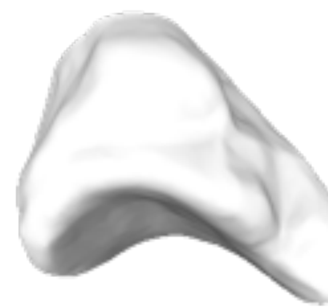


Analysis of anatomical data

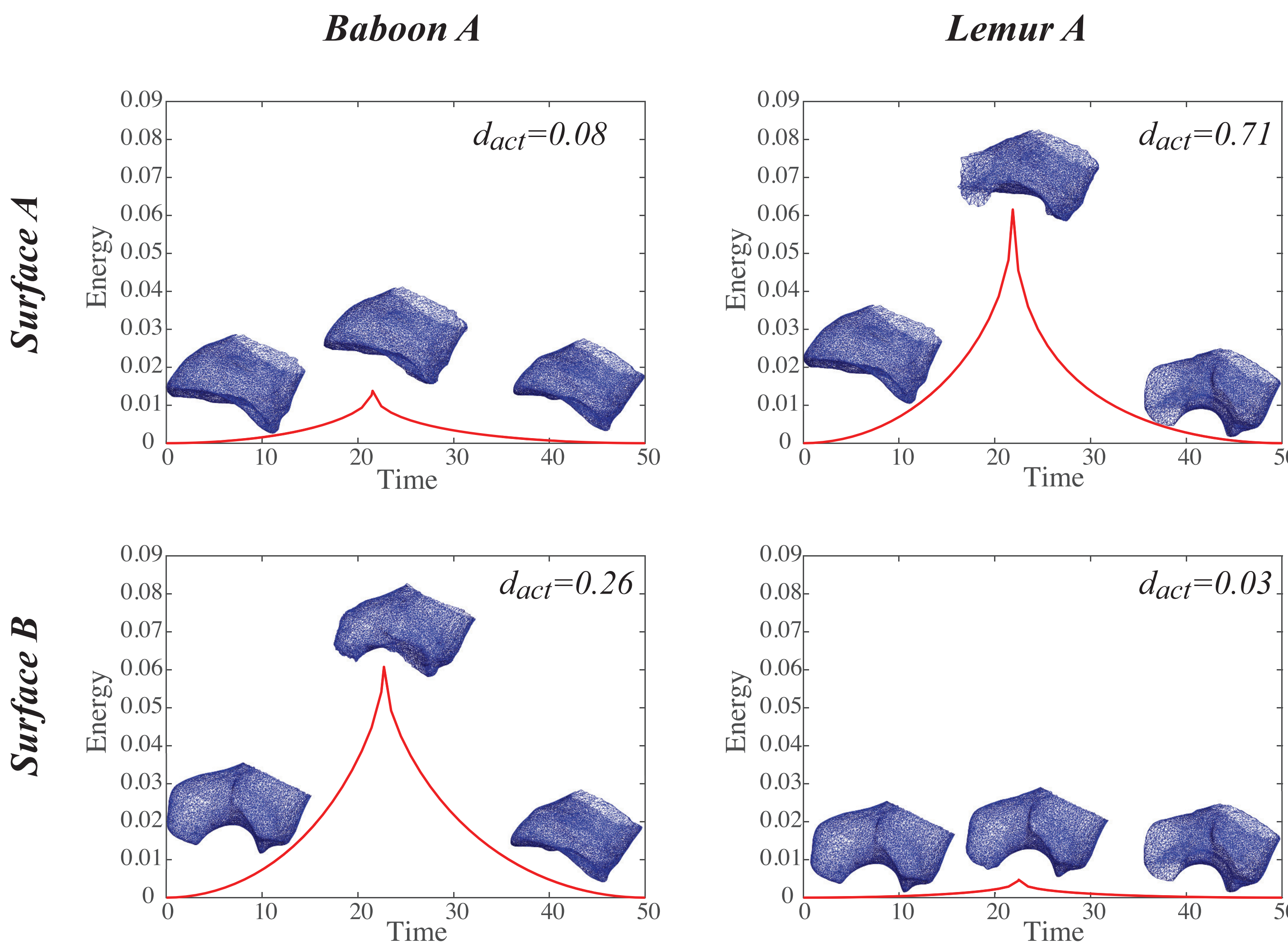
Dataset of proximal first metatarsals from 38 prosimian primates, and 23 New and Old World monkeys

Prosimian:
lemur

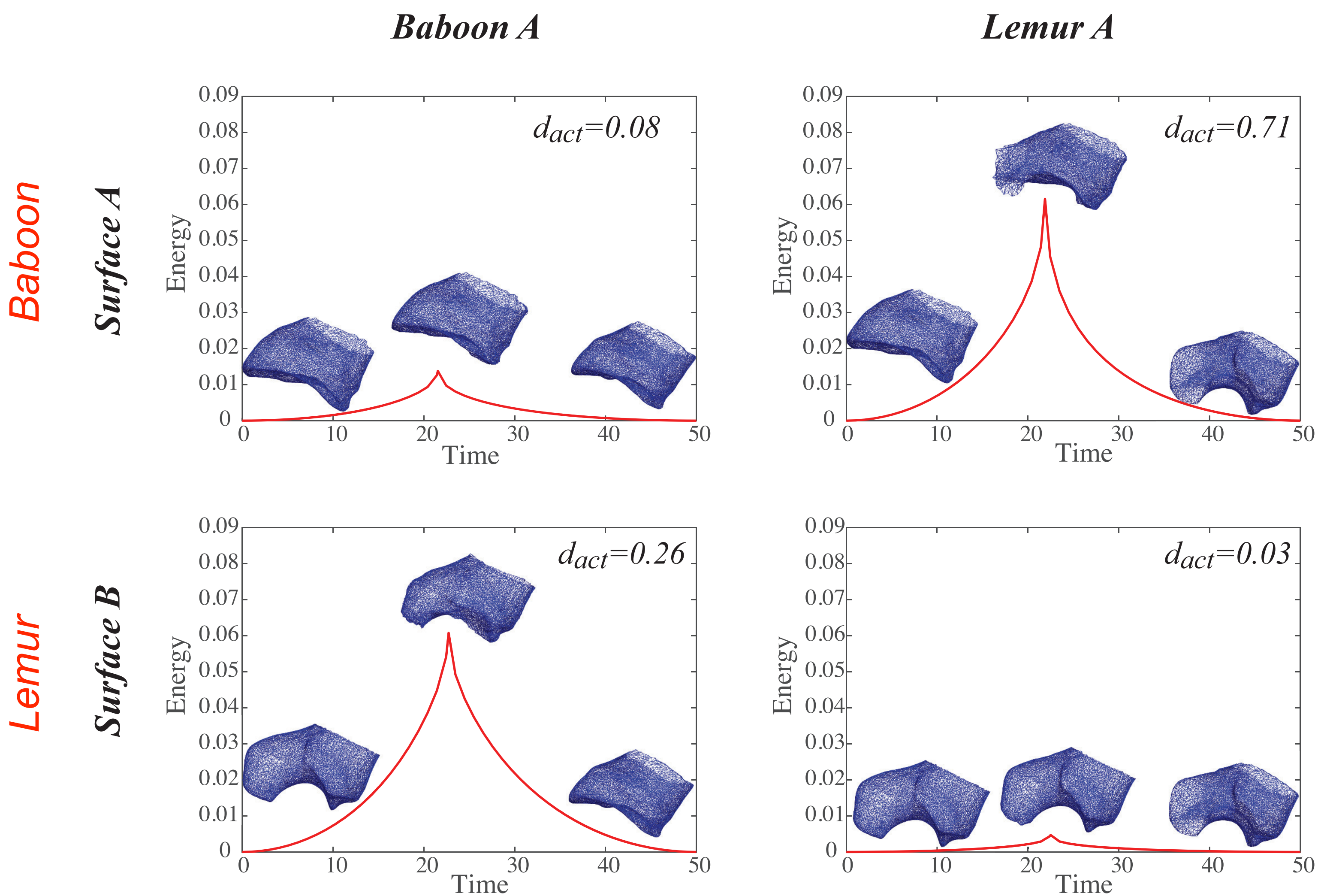
Simian:
Cape baboon
(old world)



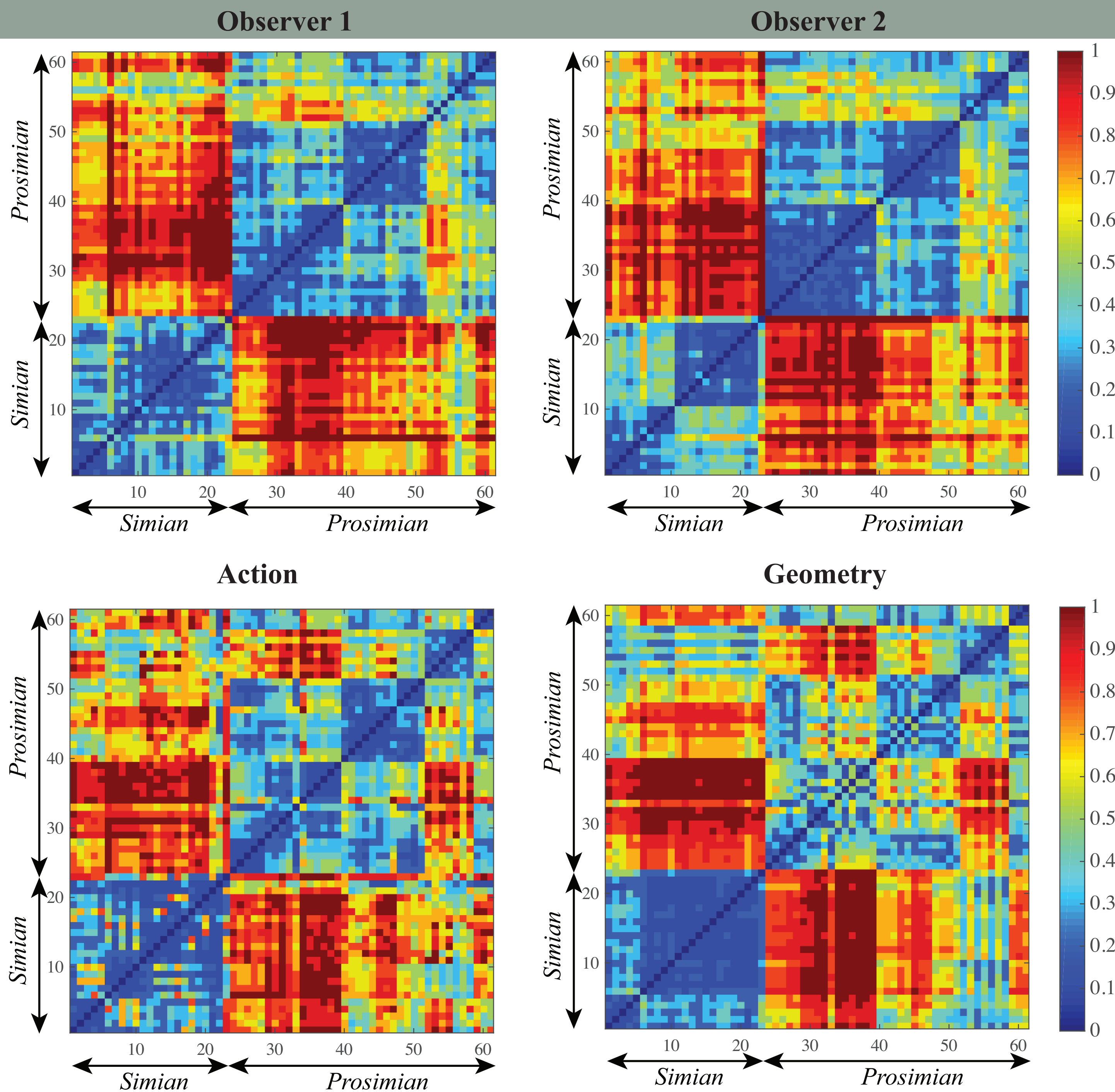
Simian:
White eared titi
(new world)



Baboon A
Lemur A
Surface A
Surface B
Energy
Time
d_act=0.08
d_act=0.71
d_act=0.26
d_act=0.03

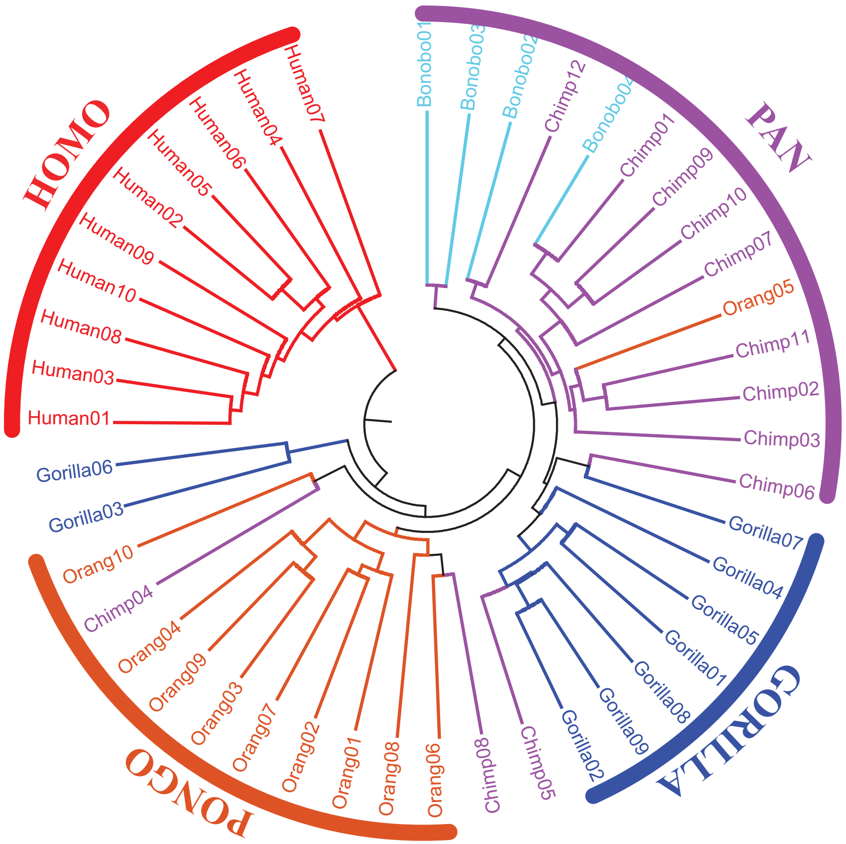


Baboon A
Lemur A
Baboon
Surface A
Lemur
Surface B
d_{act}=0.08
d_{act}=0.71
d_{act}=0.26
d_{act}=0.03
Energy
Time

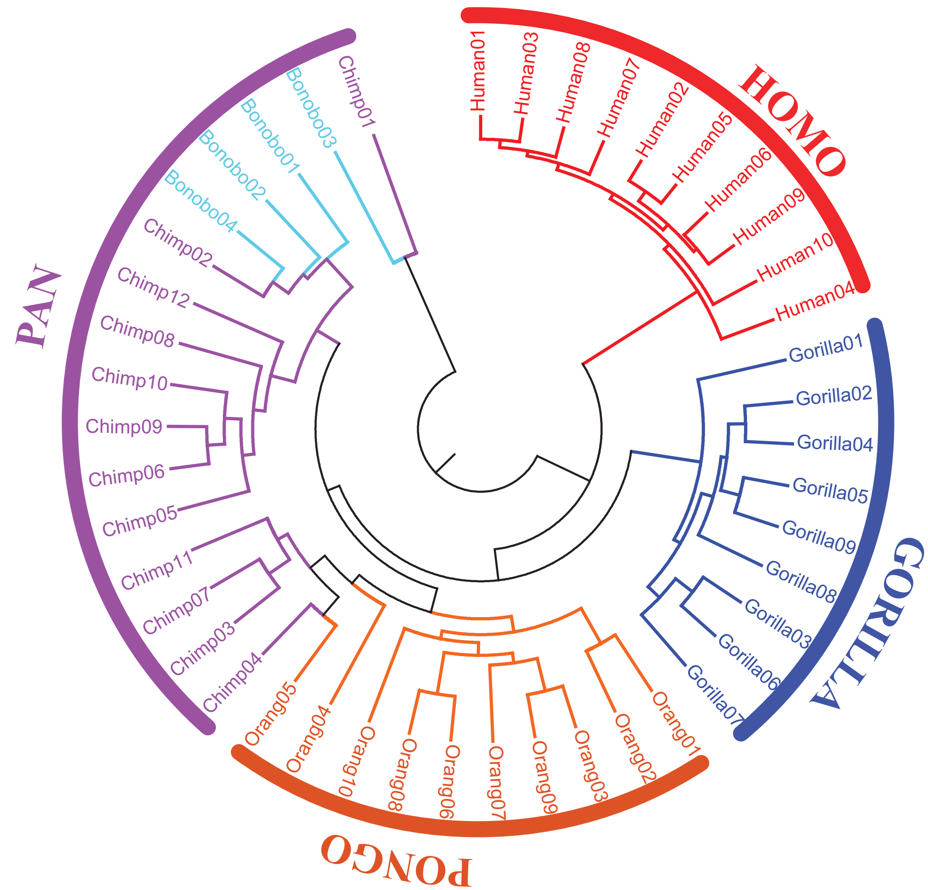


Observer 1
Observer 2
Action
Geometry
Prosimian
Simian
Prosimian
Simian
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
10
20
30
40
50
60

Trained morphometrist



Variational distance



Thank You

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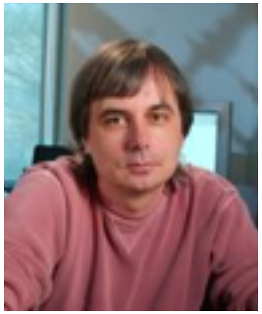

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