The ubiquity of directional motion in nonmotor proteins

# Introduction

## The evolution of molecular motors

Molecular motors transform chemical energy into mechanical work through the catalysis of cellular energy stores. The most common mechanism is the rotation of an amino acid torsion angle leading to the relative movement of protein domains. In contrast, many enzymes catalyze ATP and it does not lead to significant conformational changes. Proteins such as myosin move along a track, while others such as the F1 ATPase and those found in flagella have circular motion. There is a huge range of design, efficiency, and capability of molecular motors. They are very ancient.

But, in principle, biological machines do not need to transform chemical energy (in the form of ATP hydrolysis, for example) into mechanical work. Rather, they can rectify thermal motions for an out of equilibrium system {Kay:2006dn}.

## Directionality in motion

What is the nature of asymmetry? In 1894, Pierre Curie stated “the symmetries of the causes are to be found in the effects.” {Curie:1894vj}.

Asymmetry means time-reversal symmetry is broken.

## Theoretical models for molecular motors

## Synthetic molecular motors

# Methods

## Data

Discrete population histograms of amino acid torsion angles (phi, psi, and chi) are determined from long time simulations of protein kinase A.

## Model setup

Discrete population histograms of amino acid torsion angles (phi, psi, and chi) are converted to chemical potentials. The chemical potentials are offset to matched the experimental bound and unbound populations determined from the KD. Rate constants for moving along each surface separately are calculated using the Boltzmann ratio so that detailed balance is satisfied

between adjacent bins. Rate constants for moving between the bound and unbound surface are given by

|  |  |  |
| --- | --- | --- |
|  |  | (1) |

and

|  |  |  |
| --- | --- | --- |
|  |  | (2) |

so the ratio is

|  |  |  |
| --- | --- | --- |
|  |  | (3) |

whereas rate constants for moving between the unbound and bound surface at bin are

given by

|  |  |  |
| --- | --- | --- |
|  |  | (4) |

The rate constants for moving from bound to unbound include the effects of catalysis:

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  | (5) |

So that the ratio between these is

|  |  |  |
| --- | --- | --- |
|  |  | (6) |

…which, in the absence of catalysis and with the concentration of ATP equal to 30 mM, is

|  |  |  |
| --- | --- | --- |
|  |  | (7) |

The bound to unbound transition rates are increased by a catalytic rate,

which is determined from the literature to be the amount of time spent in the bound and unbound states (Adams, 2001).

## Model parameters and estimates

There are five free parameters in our model. Three of these can be determined directly from experimental data on PKA and the other two can be determined from computational studies.

We build a Markov transition matrix with these rate constants and solve for

the eigenvalues and eigenvectors.

The prefactor for intrasurface transitions was determined from a simulation

of butane in the absence of any rotational energy barriers.

The prefactor for intersurface transitions was determined from the [Adams,

Biochemistry].

# Results

* There is no net flux without asymmetry in the populations.
* Net flux depends upon the catalytic rate, the offset between surfaces, and the ATP concentration.
* The individual amino acids act as microscopic molecular motors.
* The stall force is very small for these microscopic motors.
* What is the efficiency of the motors? Is the duty ratio given by the time spent undergoing directional motion relative to the time spent sloshing or simply going back and forth?
* Any system that exists in two states – and can be driven between them – is capable of exhibiting this behavior. Motors are a (necessary) consequence of being out of equilibrium.

Adams, J.A. (2001). Kinetic and catalytic mechanisms of protein kinases. Chemical Reviews *101*, 2271–2290.

# Relationship of our model to the Smoluchowski equation

# The relationship of our model to the Smulochowski equation