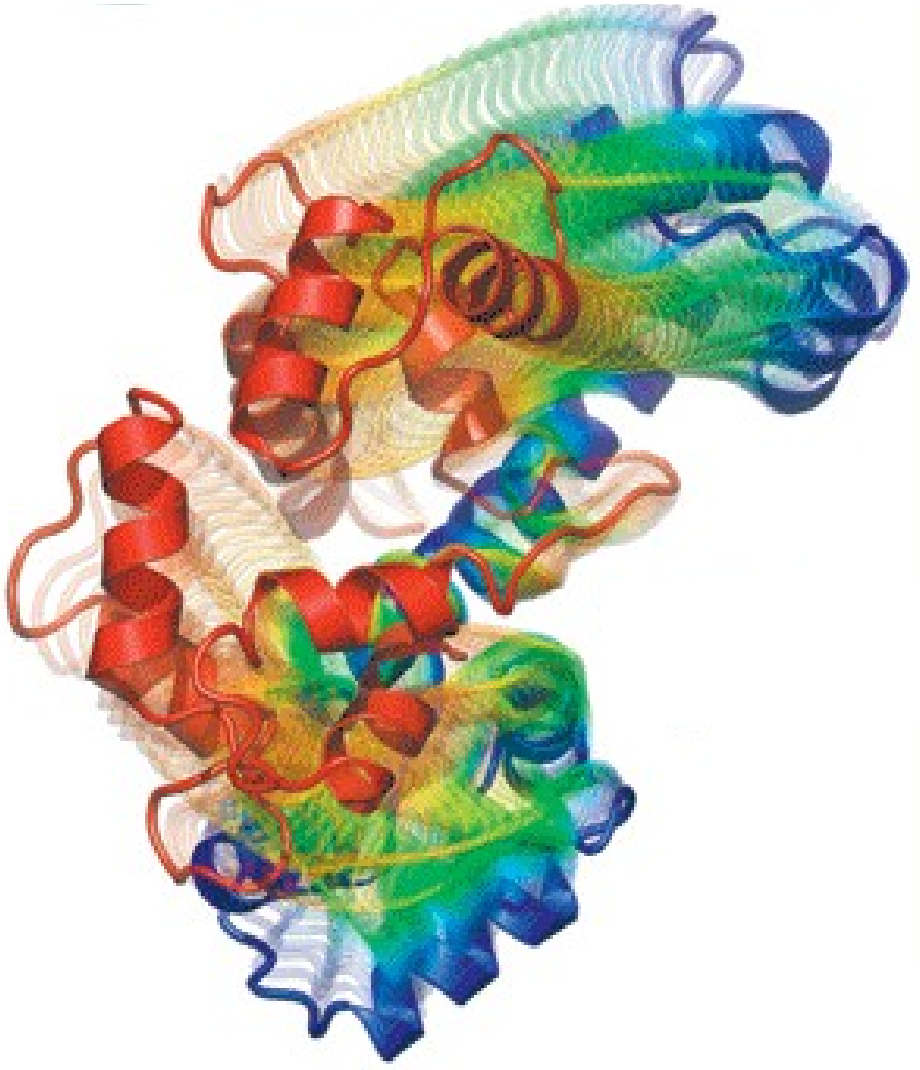
Normal Mode Analysis



Maina Bitar and Markus Meier

Introduction

- What are they?
- What are they good for?
- How are they calculated?

Harmonic Oscillators

- Single
- Coupled

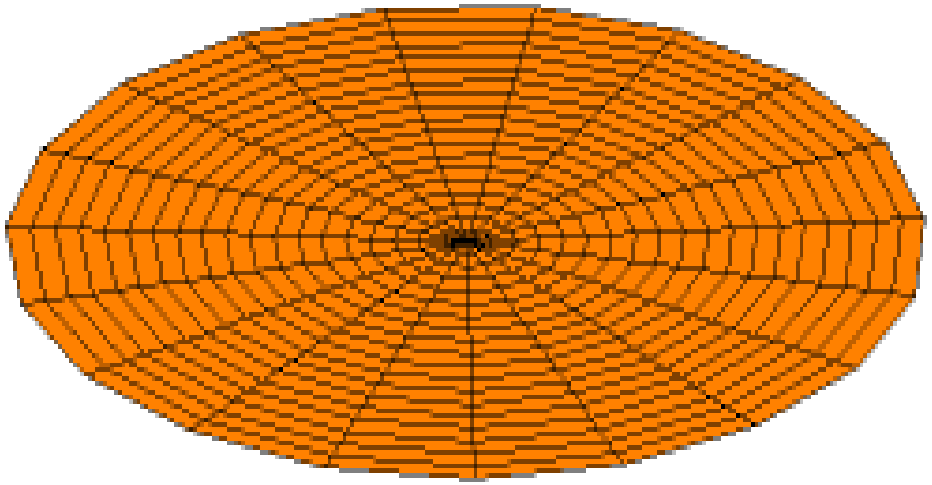
Example

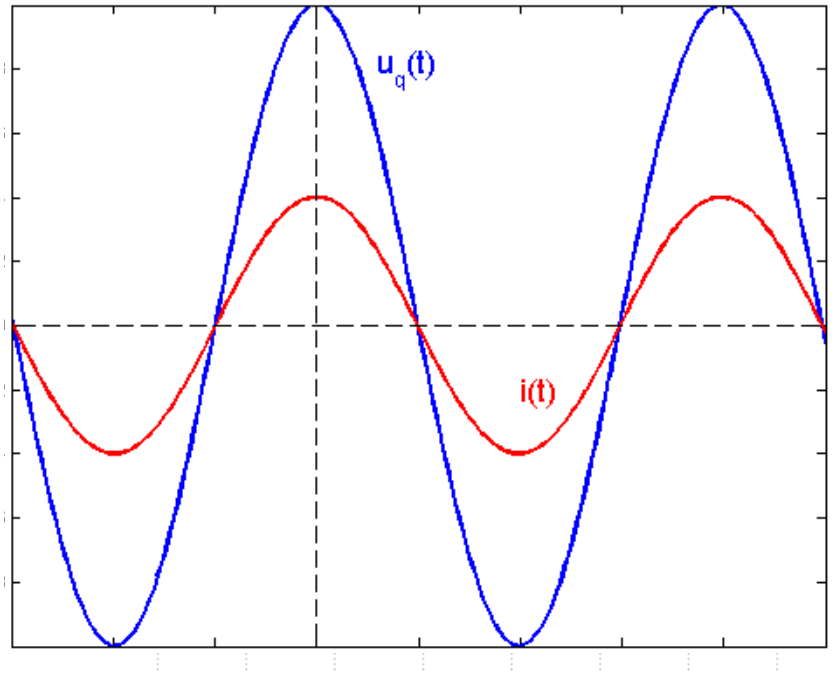
Methods

- All-atom
- Elastic Network

Introduction

What are they?



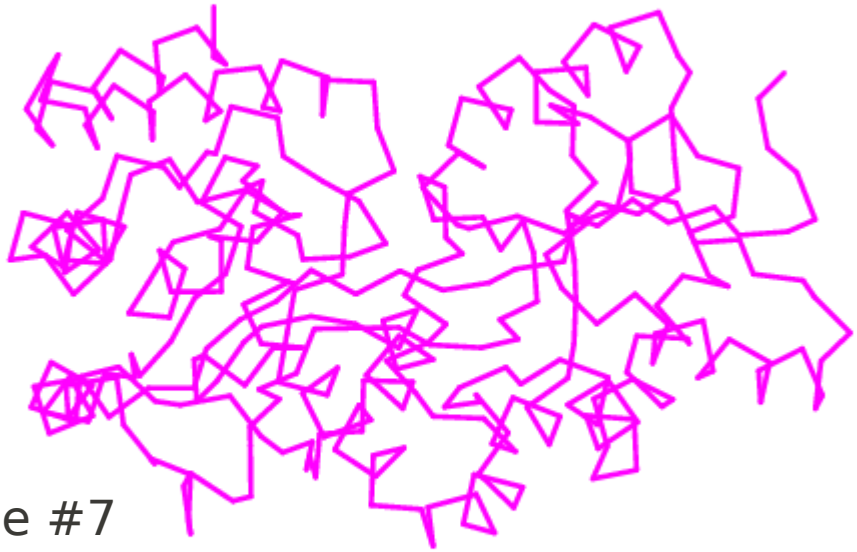


A normal mode of an oscillating system is a pattern of motion in which *all* parts of the system move with the same frequency and in phase. [Wikipedia, The Free Encyclopedia]

Introduction

What are they good for?

Processes that involve the correlated motion of large masses must be slower than localized vibrations. [Levitt and Stern, 1985]



Citrate Synthase, normal mode #7

[ttp://lorentz.immstr.pasteur.fr]

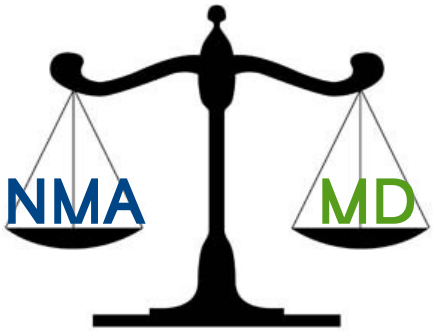
Normal modes analysis is better suited to study large structural rearrangement than molecular dynamics. [Skjaerven, Reuter et. al. 2009]

Introduction

What are they good for?

Normal Mode Analysis:

- Previous energy minimization has to be carried out with care.
- There is a high demand on computer memory.
- Larger molecular movements are more easily handled.
- There is no time variable involved.



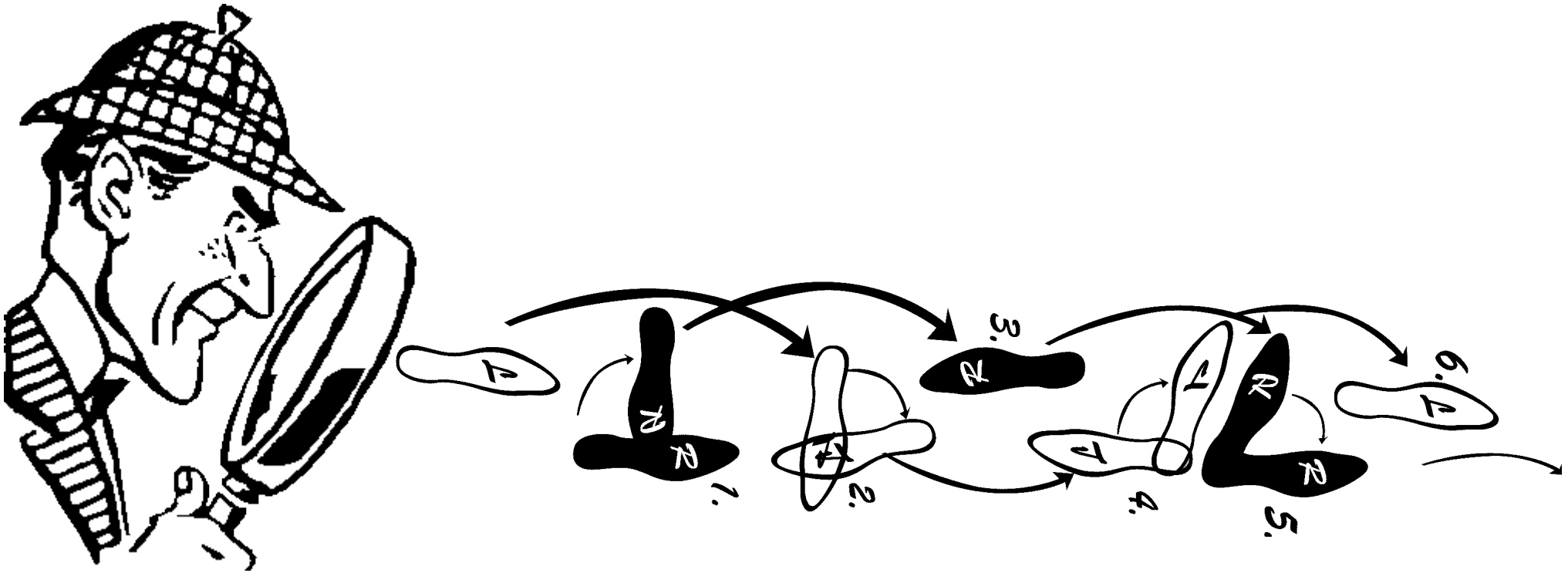
Molecular Dynamics:

- The global/local minima are accessed through the simulation.
- There is a high demand for CPU time.
- Larger molecular movements are hard to access.
- The simulations are in respect to time steps.

Introduction

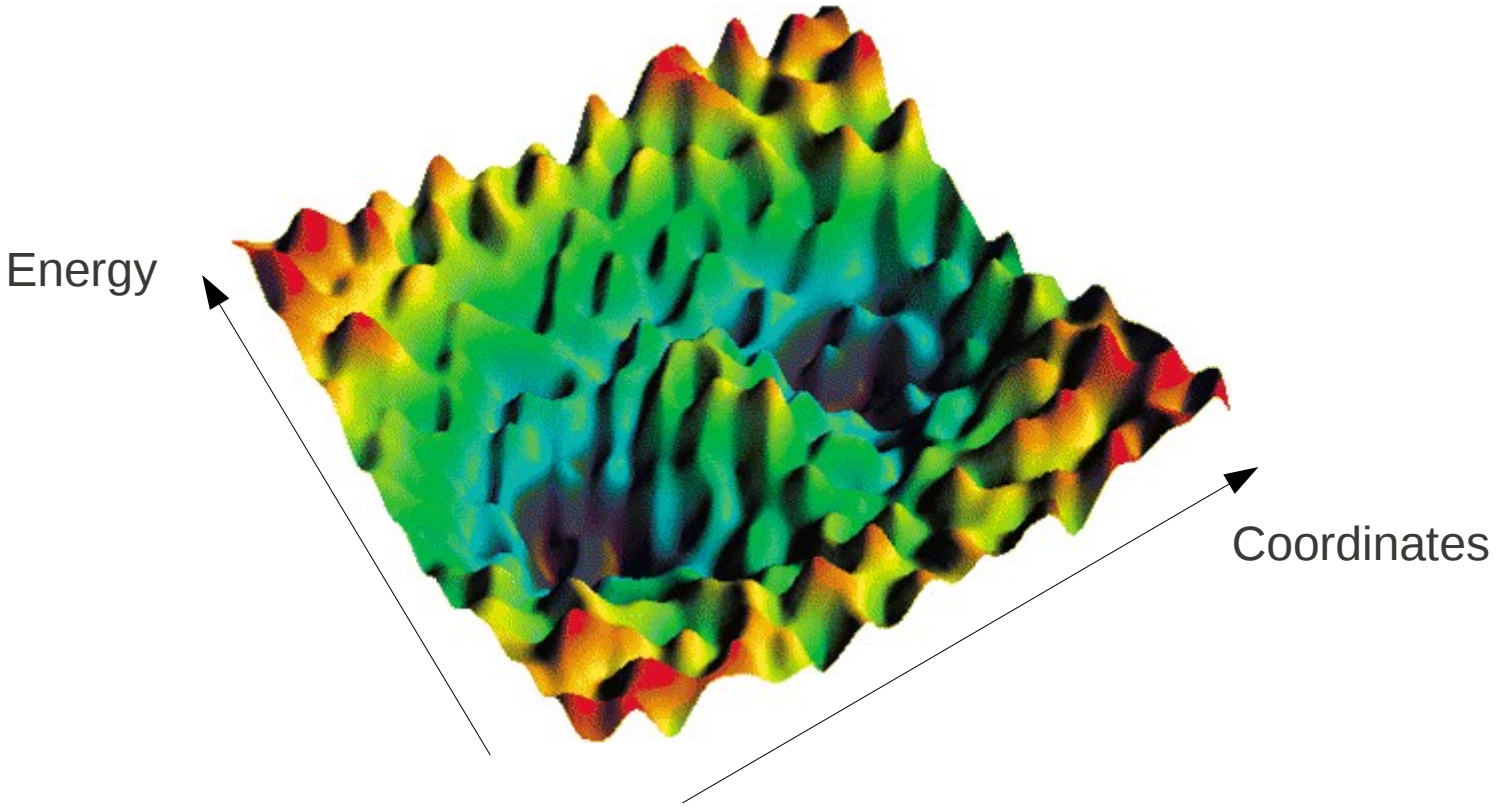
How are they calculated?

To calculate Molecular Normal Modes, we can follow simple steps.



Introduction

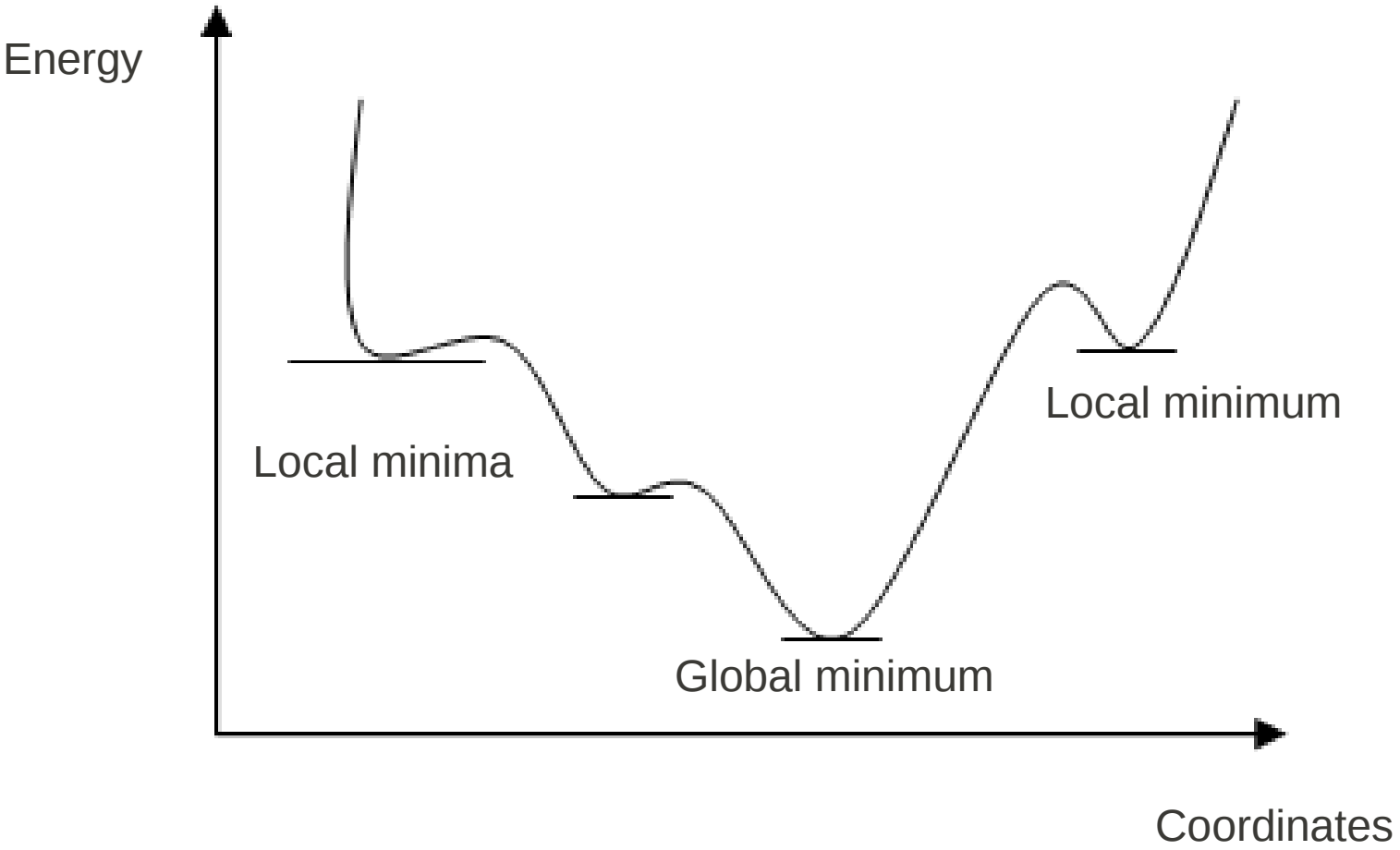
How are they calculated?



Energy surface for a complex molecule.

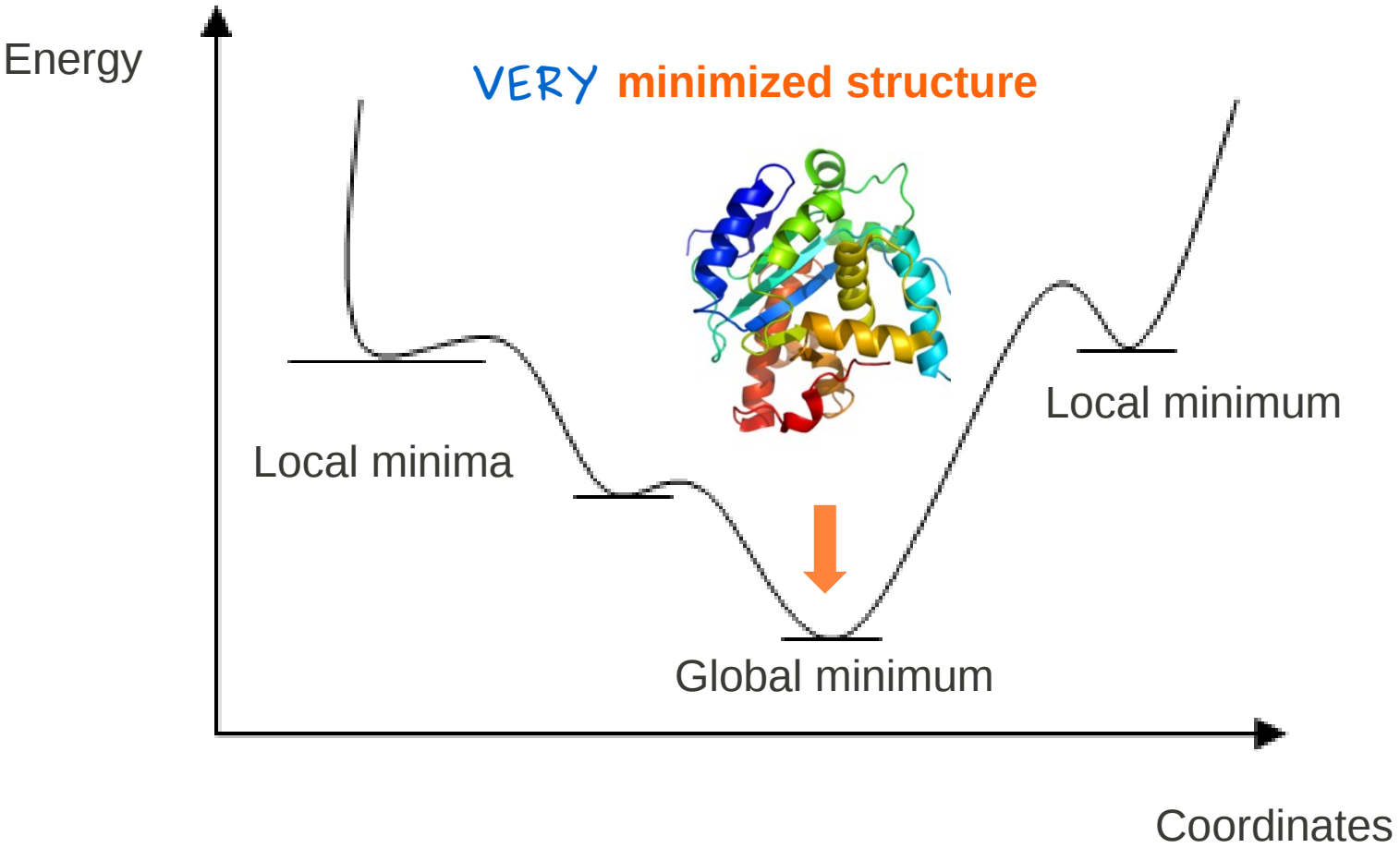
Introduction

How are they calculated?



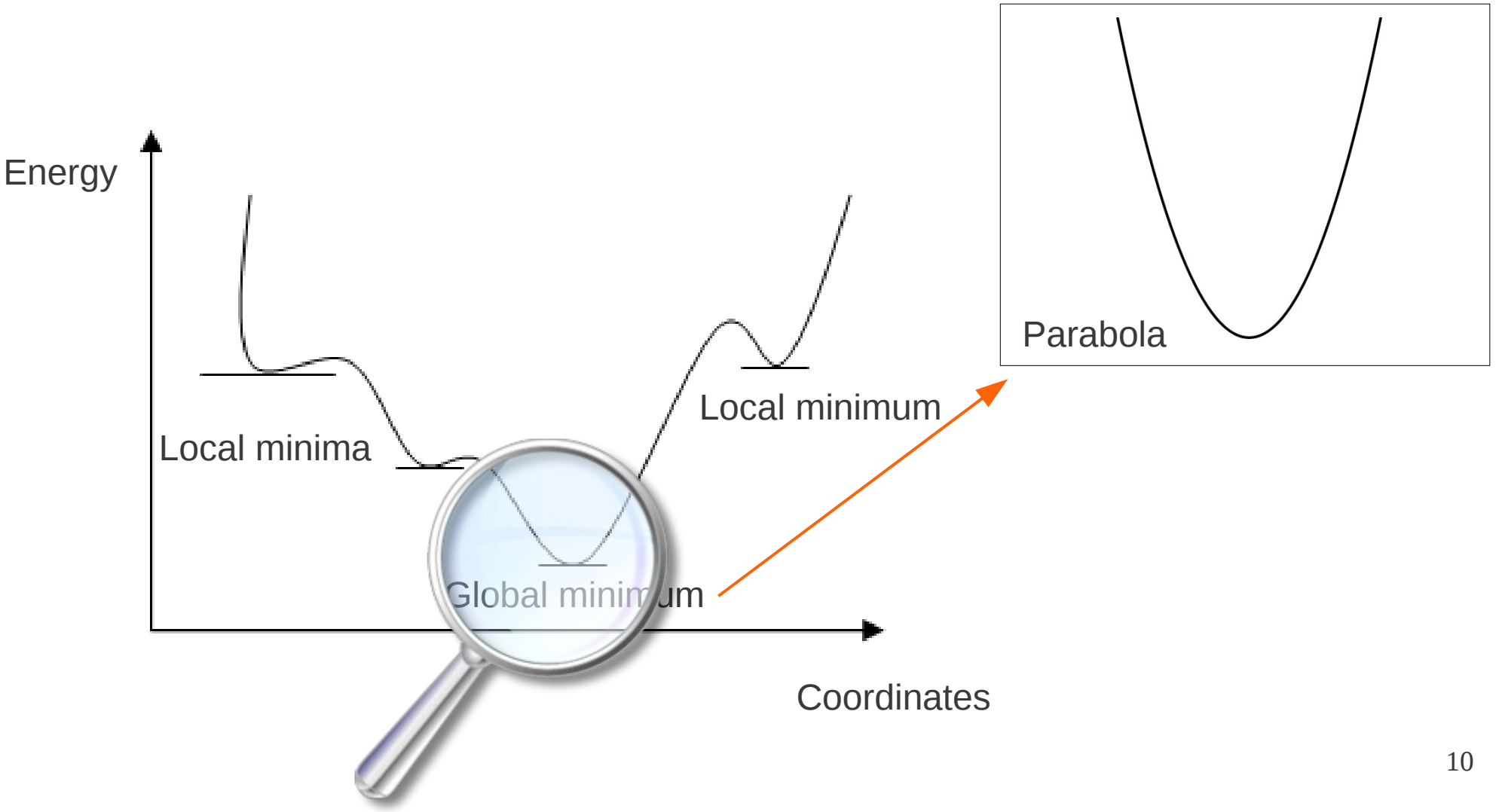
Introduction

How are they calculated?



Introduction

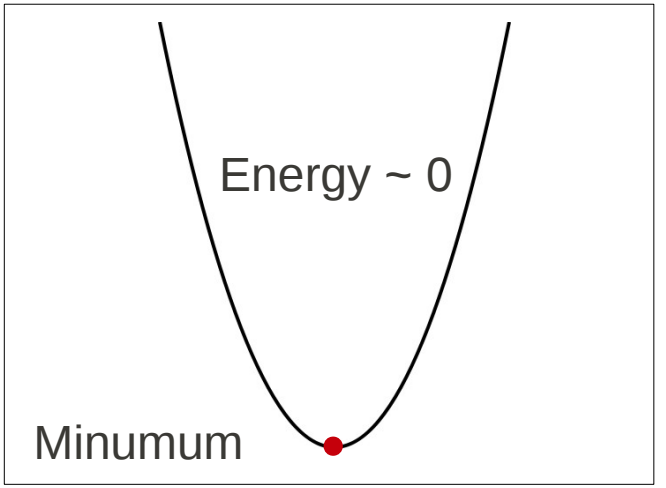
How are they calculated?



Introduction

How are they calculated?

Taylor expansion of a function around a defined point. In this case the Global minimum, where the potential energy is approximately zero.



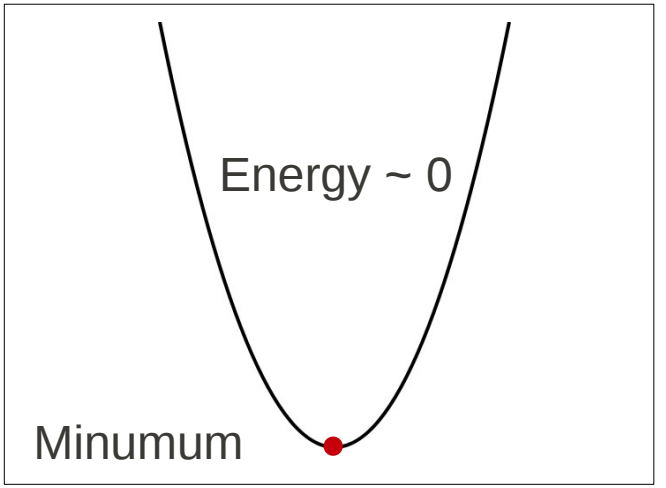
$$V(x) = V(0) + \frac{V'(0)}{1!}(x-0) + \frac{V''(0)}{2!}(x-0)^2 + \ldots$$

Introduction

How are they calculated?

zero zero ignored

$$V(x) = V(0) + \frac{V'(0)}{1!}(x-0) + \frac{V''(0)}{2!}(x-0)^2 + \ldots$$

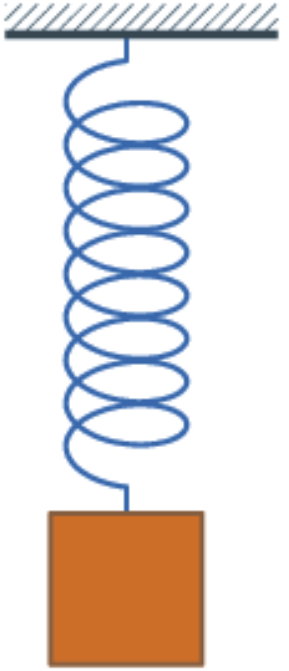


Very near to the Global minimum, the energy surface is a multidimensional parabola. [Go, Nishikawa et al. 1983]

$$V(x) = \frac{V''(0)}{2!}(x-0)^2 = \frac{1}{2}\,V''(0)\,x^2 = \frac{1}{2}kx^2$$

Introduction

How are they calculated?



Classical harmonic oscillator. $V(x) = \frac{1}{2}kx^2$

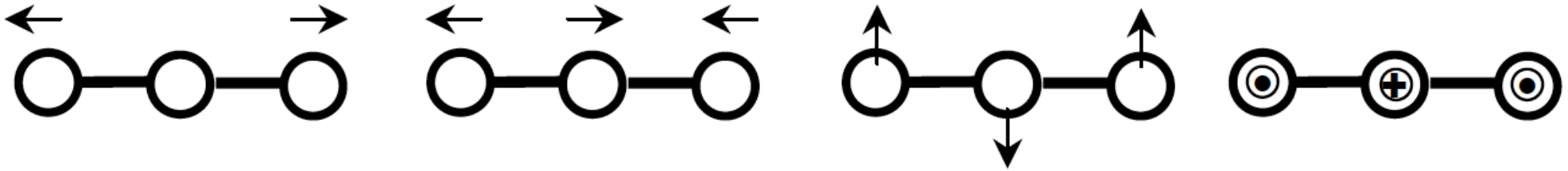
The potential energy function can therefore be approximated according to the Hooke's law for a classical harmonic oscillator.

Introduction

What are they?

The vibrations of a molecule are given by its normal modes.

$$CO_2 \rightarrow O = C = O$$

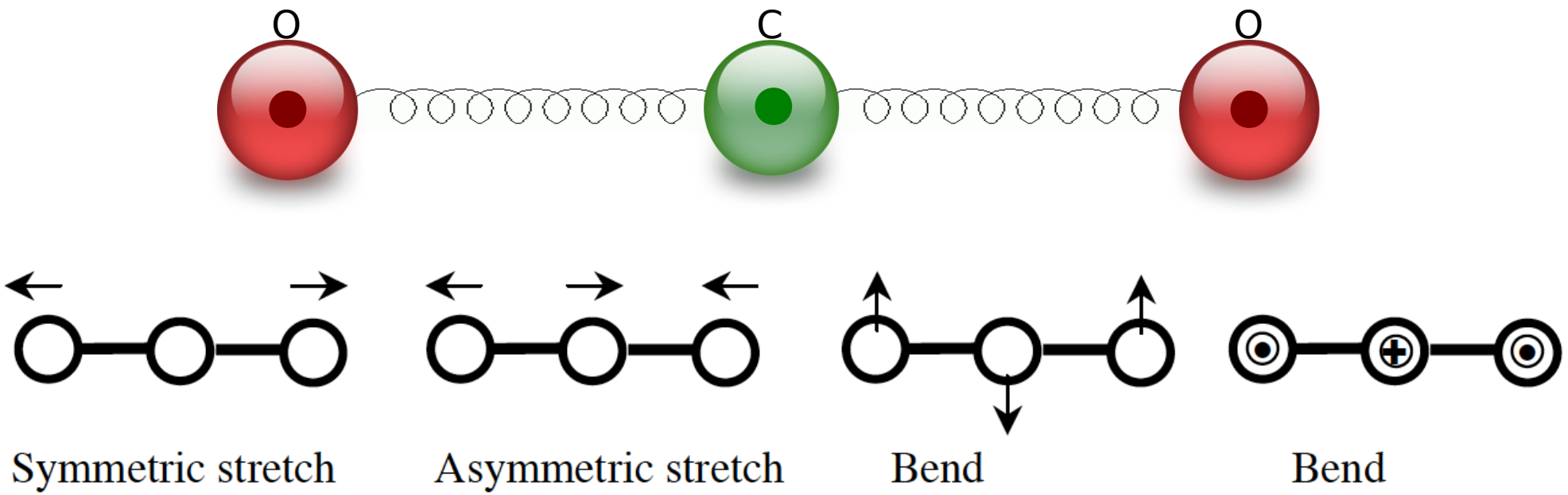


Normal Modes for a linear triatomic molecule. [Classical Normal Mode Analysis: Harmonic Approximation (lecturenote)]

Introduction

What are they?

The vibrations of a molecule are given by its normal modes.



Normal Modes for a linear triatomic molecule. [Classical Normal Mode Analysis: Harmonic Approximation (lecturenote)]

All-Atom NMA

Main advantage:

- It is more realistic.

Main disadvantage:

- It is more consuming.

For a 400 residues protein:

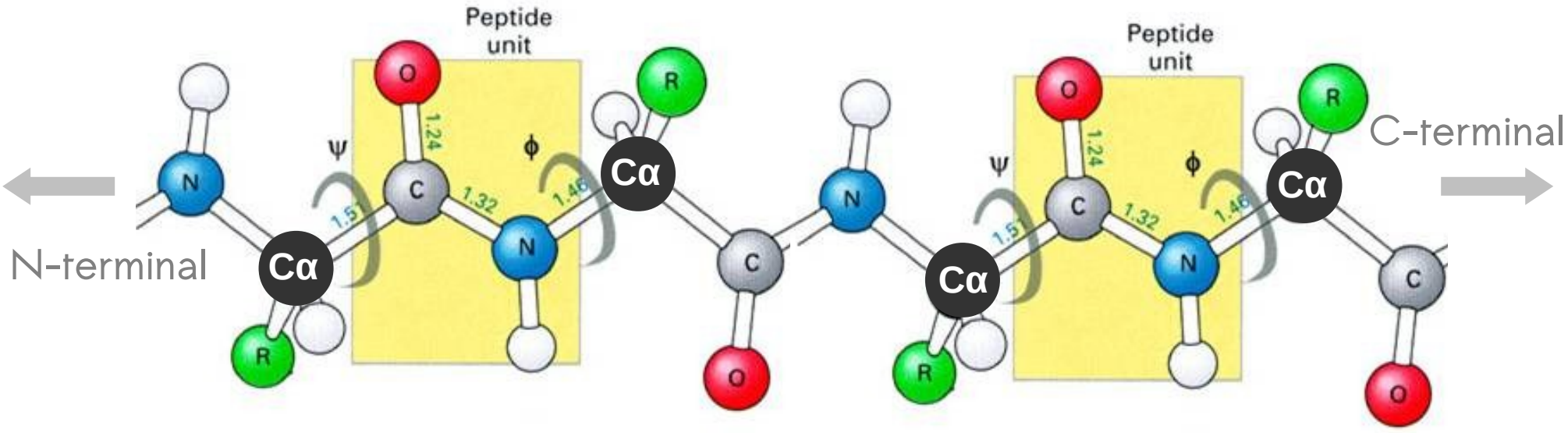
Approximately 4,000 atoms.

A 12,000 x 12,000 Hessian matrix to be diagonalized.

More than 2.5 Gb of memory for storage.

All-Atom NMA

"All-atom" ball-and-spring model



All-Atom NMA

Approximations