

**Source:**

## 1 | Preliminary Research

### 1.1 | Sources

<https://www.frontiersin.org/articles/10.3389/fchem.2019.00540/full>

### 1.2 | Notes

#### 1.2.1 | Target Processes

1. Enzyme catalysis
  - catalyzing reactions with actions
2. Protein-ligand binding
  - neurotransmitters (dopamine), protein is dopamine receptor how does the ligand bind the proper site to open the channel?
    - ligand: how to pronounce?
3. signal transduction
  - bind to other protein to trigger chain of actions
    - release calcium from intercellular stores
4. allosteric regulation
  - a reason why knowing the structure and pockets is important
  - predict allosteric sites
    - similar to non-competitive inhibition?
    - but for dna binding proteins, like the dna transcription inhibitor
  - ligand binds allosteric site and activates the protein

#### 1.2.2 | Folding Simulation Methods

1. all-atom molecular dynamics (MD)
  - Obtains all desired information regarding the kinetics and thermodynamics
- (a) Time scale bottleneck
  - very slow (supercomputers -> microseconds of simulation)
  - require microsecond to millisecond time scales
- i. optimizations
  - A. conformational sampling?
    - retains atomistic representation of the system
  - B. overcome kinetic trapping and thorough sampling of conformational space techniques
    - umbrella sampling
    - multicanonical algorithms
    - simulated tempering

- transition path sampling
- targeted molecular dynamics
- replica exchange method molecular dynamics (REMD)
- accelerated molecular dynamics (AMD)
  - see below

## 2. Accelerated molecular dynamics (AMD)

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## 1.3 | Meetings

### 1.3.1 | 12 oct 2020

- computational prediction modeling
  - trying to predict the crystal structure
    - why?
      - to analyze would this fit?
      - does it work with this target
- solving the structure
  - xray cristologyraphy
    - gold standard
    - now got the structure
      - what does that mean?
      - can we simulate how it interacts?
      - can you then do modeling on that to see if drug molecules work? are useful
- look at some concrete examples?
- tell a biological story alongside with computational relevance piece

## 1. protien synthase

not as much simulation stuff

## 2. neurotransmitters

dopamine sodium rushes in, electrochemical and concentration gradient recharge gradient by releasing potassium

- nerst equation
  - electrochemical gradient as battery
- goldman-katz equation
  - applied to neuro
  - ions?

## 3. Case study

- why do we care? why is this useful
- knowing the structure can lead to some useful information
- how did it lead to some sort of accelerated understanding?

## 4. prions

- how to pronounce?