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), protien is dopamine receptor how does the ligand bind the proper site to open the channel?

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 cites
     - similar to non-competative inhibiton?
     - but for dna binding protiens, like the dna transcription inhibitor
   - ligand binds allosteric site and activates the protien

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 milisecond time scales

   i. optimizations

   A. conformational sampling?

   - retains atomistic representation of the system

   B. overcome kinetic trapping and thourough 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)

   -

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 cristolography
    - 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

   (a) nerst equation
   electrochemical gradient as battery

   (b) 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