Molecular docking

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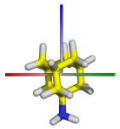
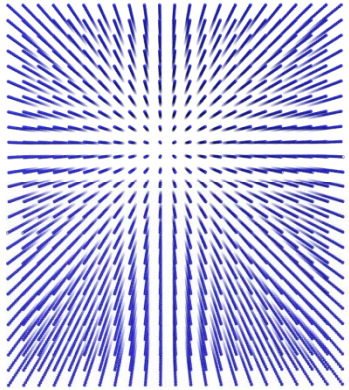
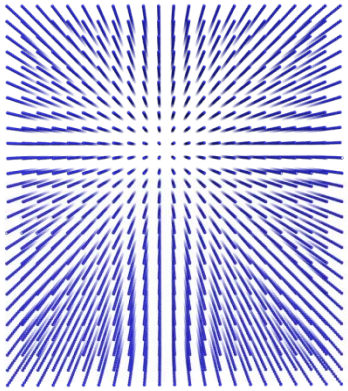
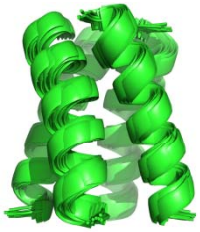
Small molecule docking

- Used as a tool for structure-based drug design
  - M2 proton channel
  - Helix ‘interceptors’
- Active field with many software packages (both academic and commercial)
- Our current implementation allows us to rigidly dock (i.e., no torsional degrees of freedom) 10,000 compounds in about 15 hours on a single workstation







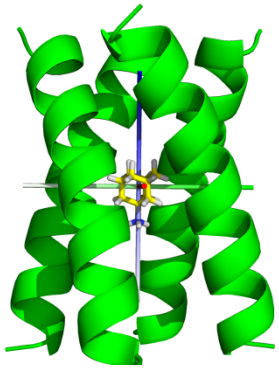


‘Correlate’ values at grid points

$$Score(\alpha,\beta,\gamma)=\sum_{l,m,n} R_P(l,m,n)\cdot L_P(l+\alpha,m+\beta,n+\gamma)$$

3D FFT

Rank the poses



M2 proton channel

Brett Hannigan

What are the problems?

1. Current class of compounds has between 8-32 torsional degrees of freedom for the ligand (Rotations reduce to a set of matrix multiplications—serial)
    1. Rotation of $atom_{n+1}$ may be dependent on $atom_n$
2. During each rotation, the feasibility of the conformation needs to be checked (non bonded calculations).

Goals for GPU implementation

- Since I can separate sampling of ligand degrees of freedom from docking, I can explore more conformational space
  - Current CPU approach—use an exhaustive enumeration of different conformations followed by filtering
  - Possible GPU approach—use a depth-first-search and perform filtering on the fly

Impact of work

- Organic/medicinal chemists would like to carry out docking on their Windows driven laptops that can make use GPU technology
  - My laptop has a NVIDIA GeForce 8400 M GS card

- Useful as a tool for testing different scoring functions and backbone *relaxation* protocols

Amount of parallelism available

- Filtering (i.e, nonbonded) calculations can be parallelized
- Can I parallelize the matrix multiplication calculations?
- Any thoughts on DFS?

Challenges…

- Reducing the amount of interfacing with CPU-driven routines (i.e., side chain repacking)
- Some ‘ligands’ are small peptides (torsional degrees of freedom can > 40)
- For side chains implement some sort of *table search* that can be implemented within the GPU framework