PROJECT ACA

Project Code: P25

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Project Supervisor: Stefano Cherubin

Reference Course: Advanced Computer Architectures

Academic Year: 2016-2017

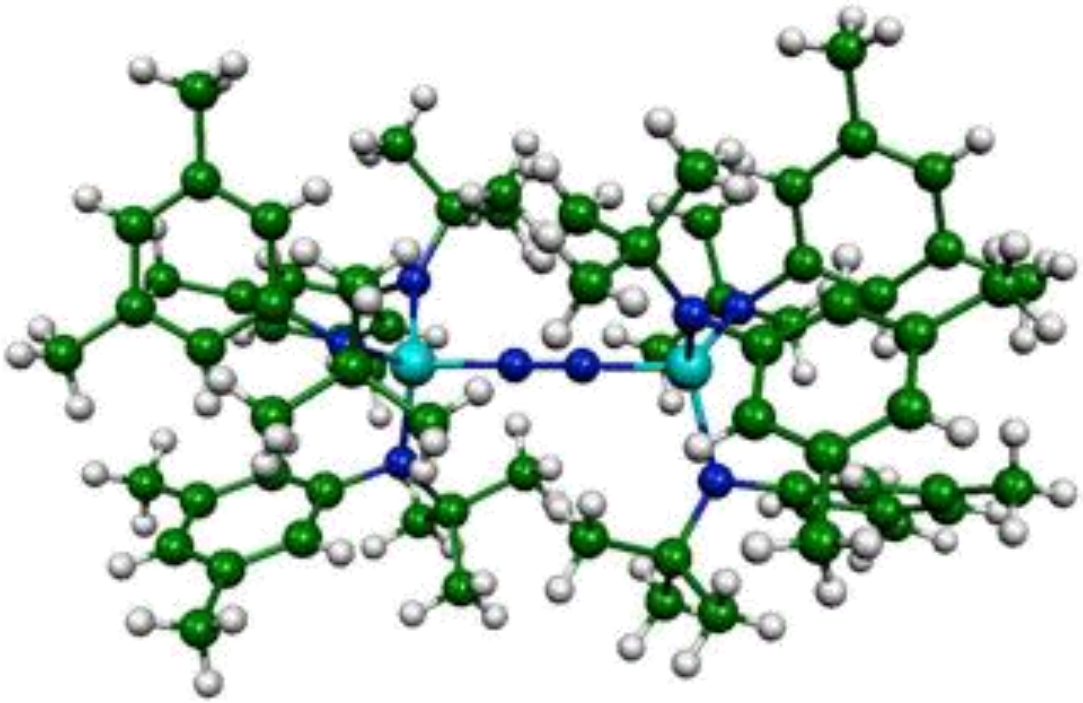
Assignment description

Set of Molecules (ligands)

Pocket

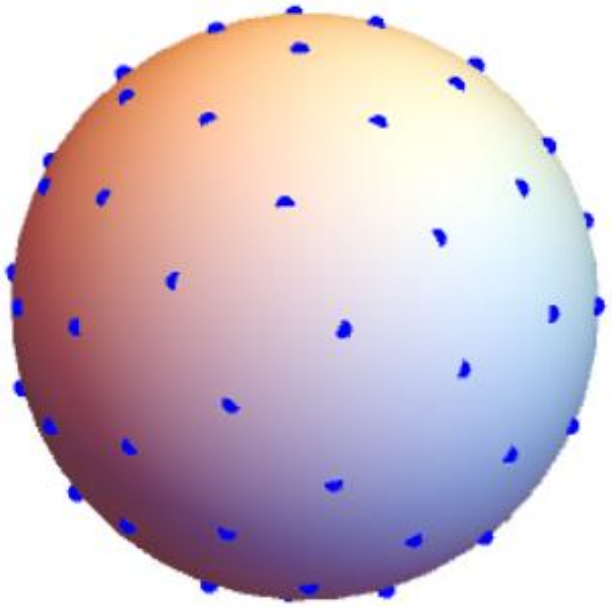
Apply transformations to the ligands in order to find the ligand that best fits in the pocket

Ligand



- Mol2: format used to represents molecule
  - List of atoms (3D coordinates)
    - Graph (adjacency list)

Pocket



- List of atoms (3d points) belonging to a spere
- (Domain symplification)

- Obtained from a list of 2D coordinates mapped to a spere

- Parameter:
  - ✓ number of atoms
  - ✓ distance between atoms

Centre the molecule

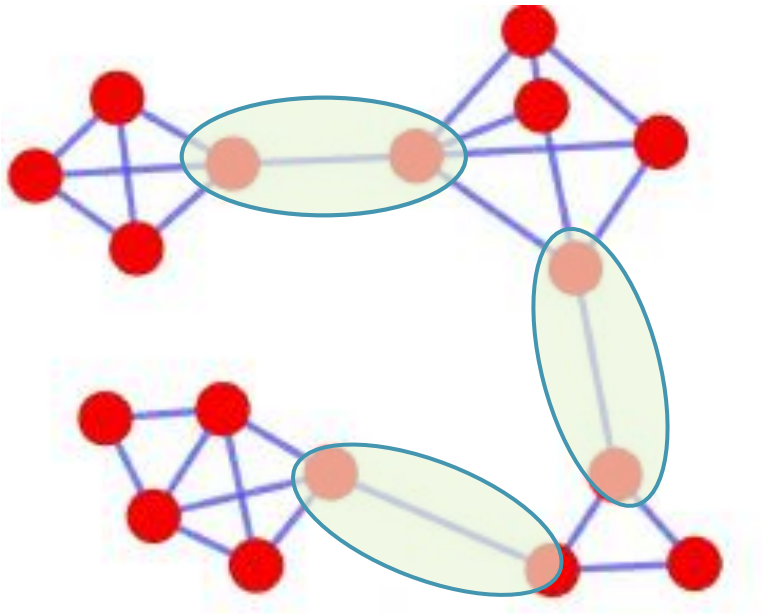
First of all it is necessary to translate the ligand to the center of mass

Translation matrix

$$\begin{bmatrix} 1 & 0 & 0 & dx \\ 0 & 1 & 0 & dy \\ 0 & 0 & 1 & dz \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} x \\ y \\ z \\ 1 \end{bmatrix} = \begin{bmatrix} x + dx \\ y + dy \\ z + dz \\ 1 \end{bmatrix}$$

$$dx = - X_{cm}$$
$$dy = - Y_{cm}$$
$$dz = - Z_{cm}$$

Rotable bond



Links:
- Not terminal
- Not belonging to a cycle

Axis of the rotations

For each rotable bond:

1) finds points on the right of the rotable bond
2) rotate them and for each rotation calculate the score
3) take the best one
4) do the same thing with the points on the left

How to perform rotation?

Use a matrix that represent the transformation

$$P' = M * P$$

Rotation of a point in 3D dimensional space by theta about an arbitrary axes:

1) translate so that the rotation passes through the origin
2) rotate about x axis so that the rotation axis lies on xz plane
3) rotate about y axis so that the rotation axis lies along the z axis
4) perform the rotation
5) apply inverse trasformation of steps 3, 2, 1

$$\mathbf{M = T^{-1} R_x^{-1} R_y^{-1} R_z R_y R_x T}$$

Calculate score

```
Score = 0

For each atom of the ligand:
   -find the nearest atom of the spere
   -sum this distance to score

Return  number_of_atoms / score
```

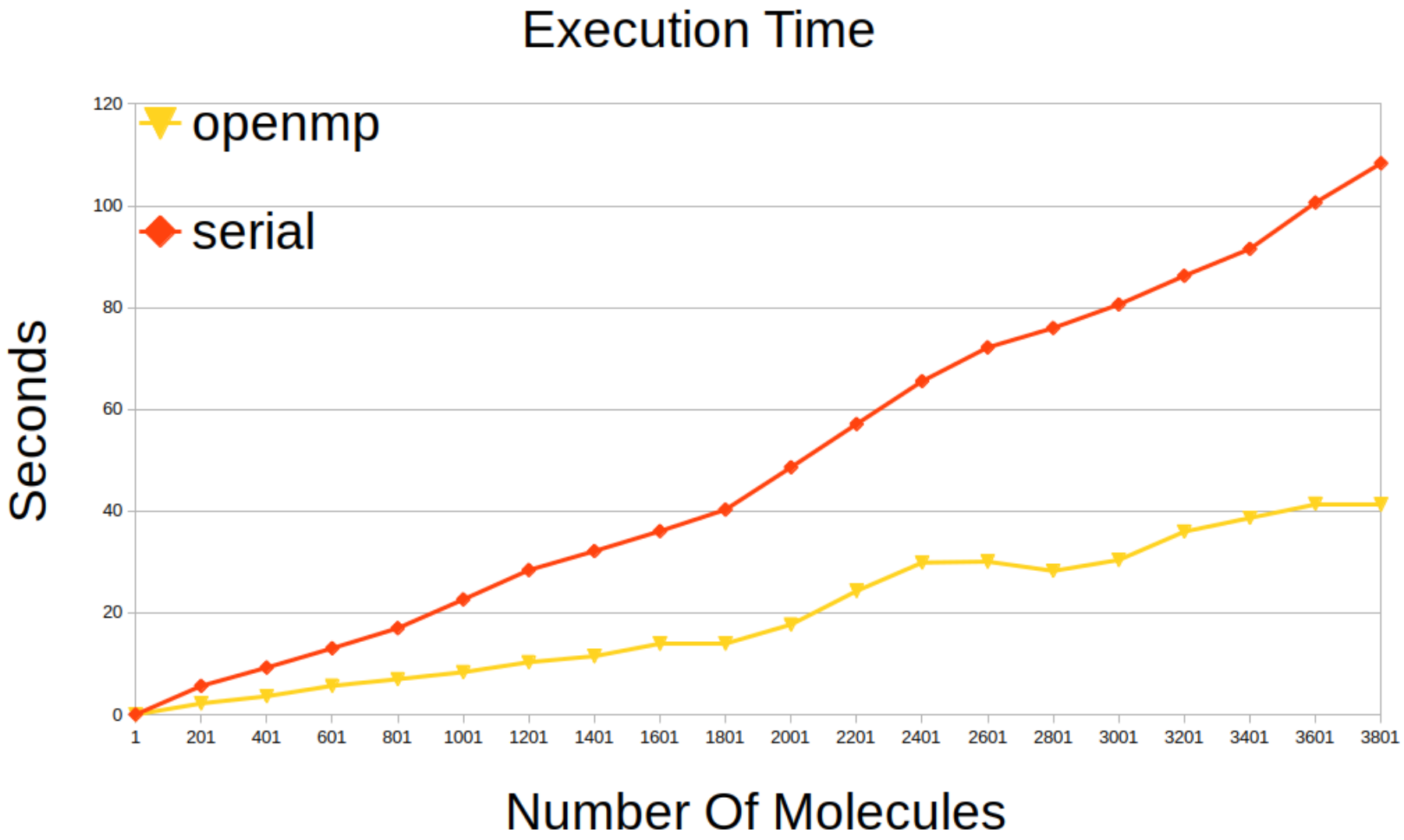
The score is a measure of the fitting of the ligand in the pocket

Pseudocode of the whole program

```
molecules = parseFile("db.mol2");
pocket = createPocket();

bestScore = 0;

for each molecule in molecules:
    centreMolecule(molecule);
    rotableBonds = calcolateRotableBonds(molecule);

    for each rotableBond in rotableBonds:
        for angle in range(0, 360, step): #step is parametric

            rotationMatrix = createRotationMatrix(molecule, rotableBond, angle);
            moleculeRotated = trasformMolecule(molecule, rotationMatrix);
            score = calculateScore(moleculeRotated, pocket);

            if (score > bestScore)
                bestScore = score;
                bestMolecule = moleculeRotated;
```

Details about implementation

- Boost library for matrix to make efficient on computations about matrix
- Boost program options to pass parameters at the command line
- OpenMP to parallelize the code:
  - SIMD parallelism
  - Num_threads = 4
  - Each ligands is rotated by a different thread


Execution Time
openmp
serial
Seconds
120
100
80
60
40
20
0
1
201
401
601
801
1001
1201
1401
1601
1801
2001
2201
2401
2601
2801
3001
3201
3401
3601
3801
Number Of Molecules

Work organisation

- Parsing .mol2 file and creating structures

(1 week)*

- Recognise rotable bonds, rotation functions and function that calcolate score (2 week)*

- Optimizing the code: (2 week)
  - Using boost library to make matrix computation efficient
  - Parallelize the code with openMP

- Benchmark and testing (1 week)*

* Collaboration with group P26


Questions?