High Throughput Convolution for Protein Docking

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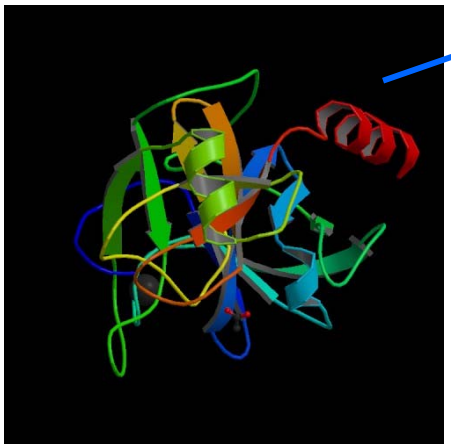
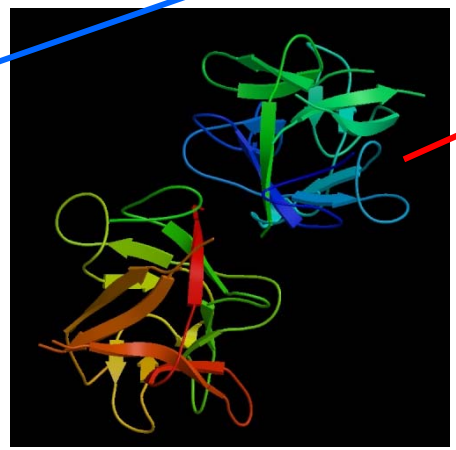
Protein Docking

- **>30,000 protein structures are in PDB database.**
  - Interactions among them are determined by experiments.
    - Yeast two-hybrid essay, mass spectrometry, etc.
- **Structure of a complex in 3D-space**
  - Experiments
    - X-ray crystallography, NMR, etc.
    - Difficult to determine.

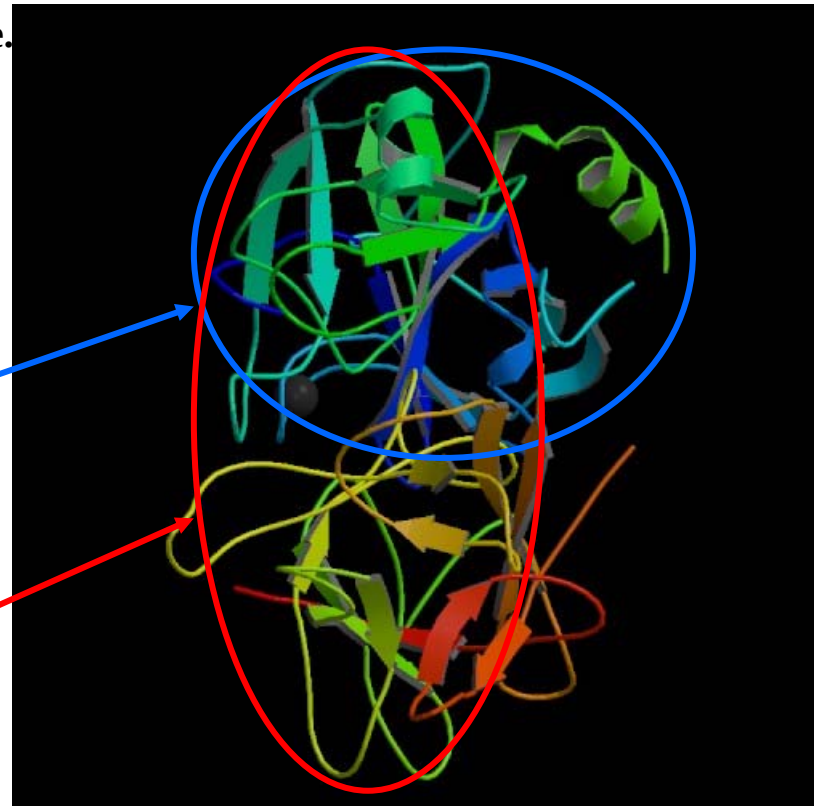
By computation



Porcine trypsin
(1qqu)



Soybean trypsin inhibitor
(1ba7)

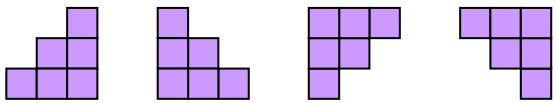


Complex (1avx)

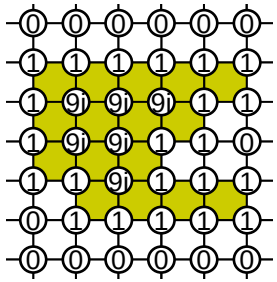
make a complex without destroying original structures.

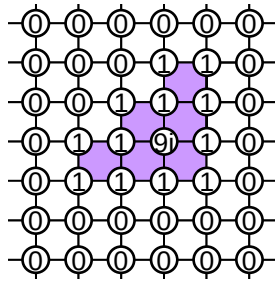
Shape Complementary Search

- Shape complementary search is the first step from computational approach.
- Evaluation of docking orientation
  - Proteins are discretized to NxNxN cubic grids assuming proteins have rigid body.
  - Score functions are based on shape complementarity, desolvation energy, and electrostatics. [FtDock, ZDock]
- Search
  - Exhaustively to avoid overlooking.
    - Scores by translational move is computed by complex (or real number) convolution.
    - Search is iterated for multiple angles.
      - e.g. angle steps in 3D vs. #non-isomorphic rotational moves
        - Δ=15° → 3600 rot.
        - Δ=6° → 54000 rot.



Rotation Δ=90° in 2D





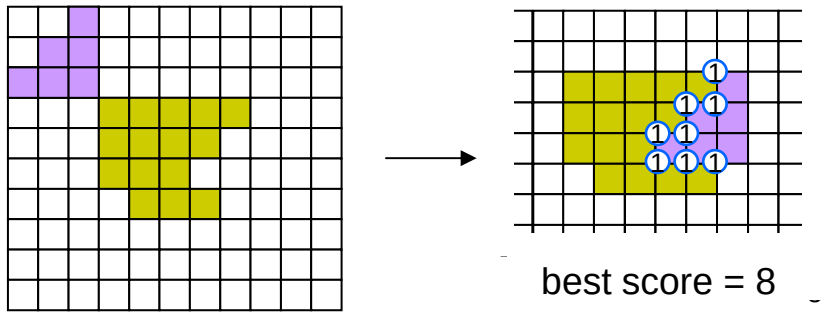
Local match score:

core – core = 9i × 9i = -81

surface – surface = 1 × 1 = +1

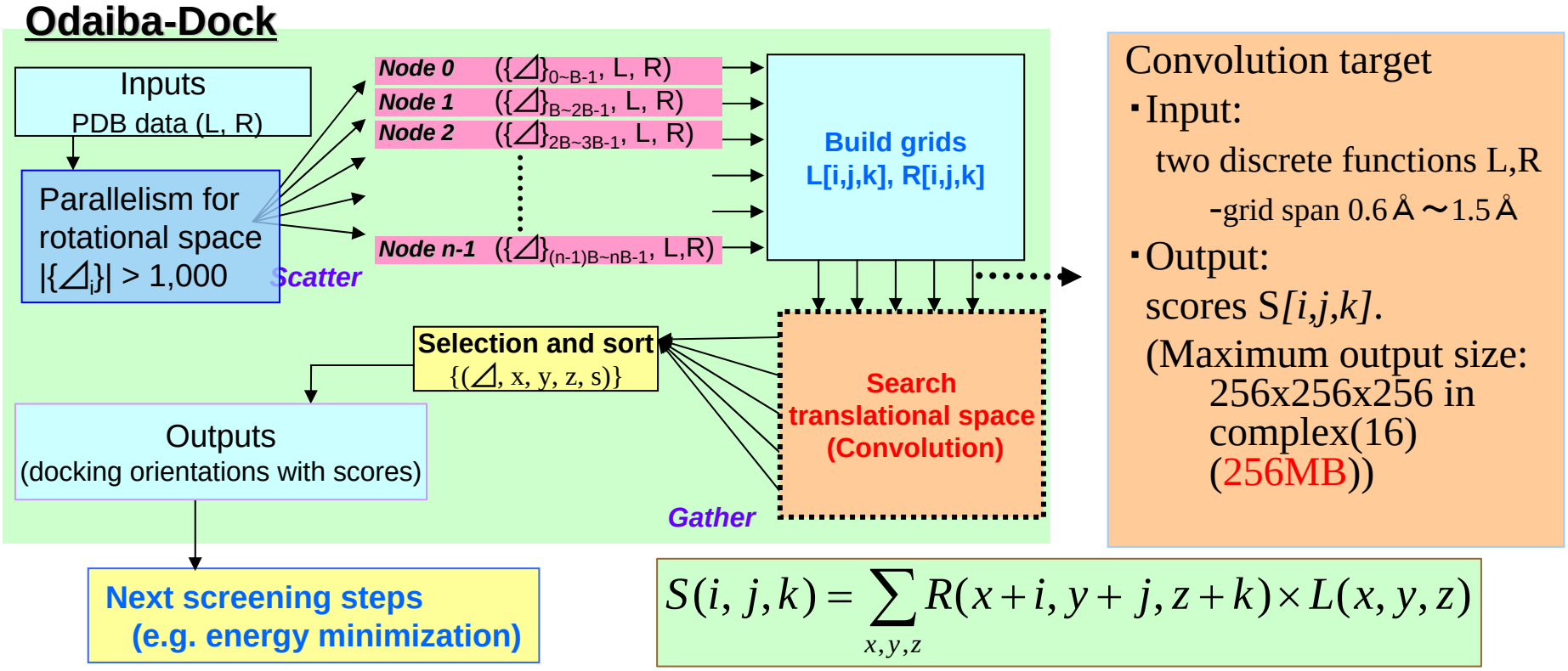
$$S(k,l) = \sum_{i,j} R(i,j) \times L(i+k, j+l)$$

convolution (correlation)



Example of translational search in 2D

OdaibaDock: Target Problem & Strategy



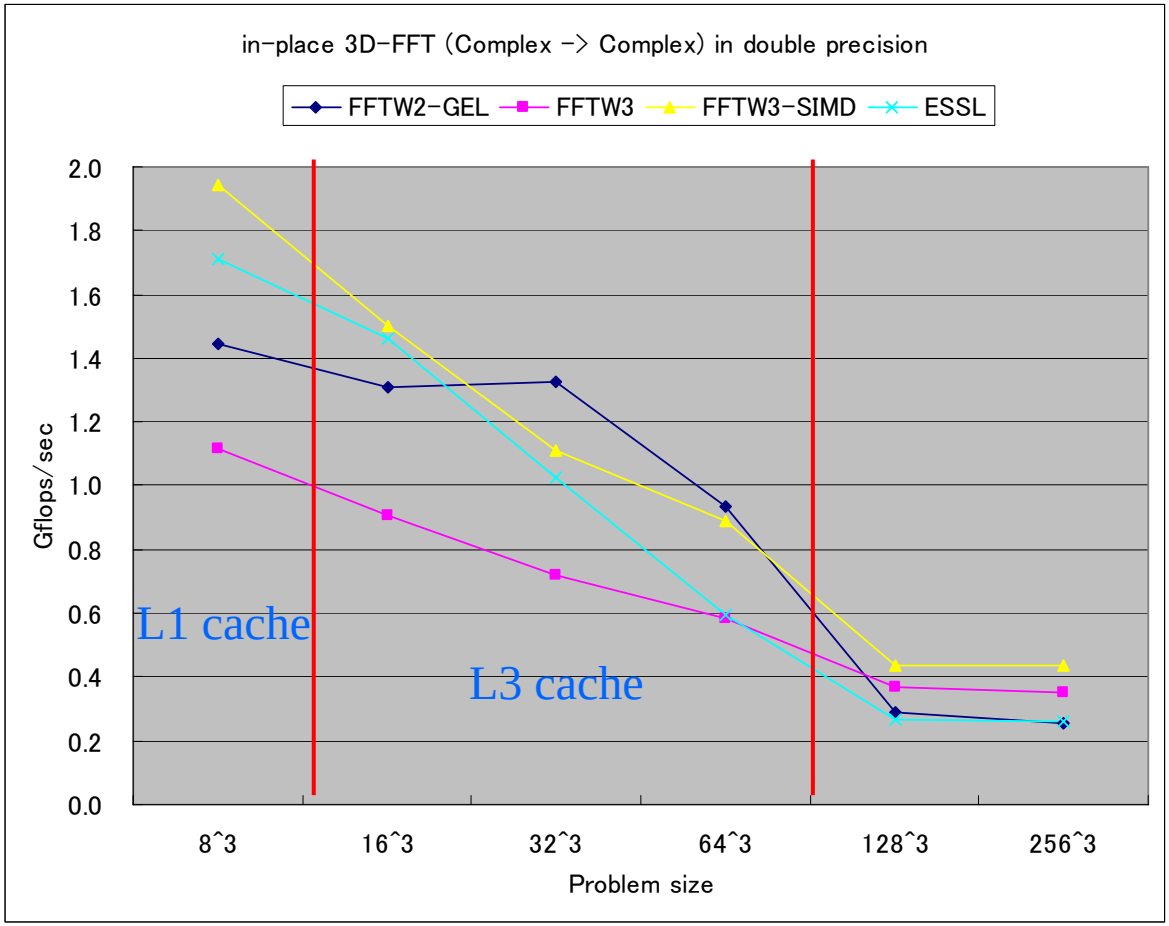
$$S(i,j,k) = \sum_{x,y,z} R(x+i, y+j, z+k) \times L(x,y,z)$$

Time complexity

Direct : $O(N^6)$

FFT : $O(N^3 \log N)$

3D-FFT Performance (fftw, essl)



Output Size 8KB 64KB 512KB 4MB 32MB 256MB

- fftw-gel:
  fftw-gel.2.1.5 provided by Stefan Kral (Vienna Univ.) and Bob Walkup (IBM Watson)
- ESSL:
  The benchmark results are provided by people at IBM Japan.
- fftw3:
  fftw 3.1 with compiler optimization for Double Hummer (xlc)
- fftw3-simd:
  modified fftw-3.1 [-enable-sse2] (SSE2 instructions are replaced with Double Hummer intrinsic functions.)

Improved memory access in 3D-FFT

Not open to the public
for the time being

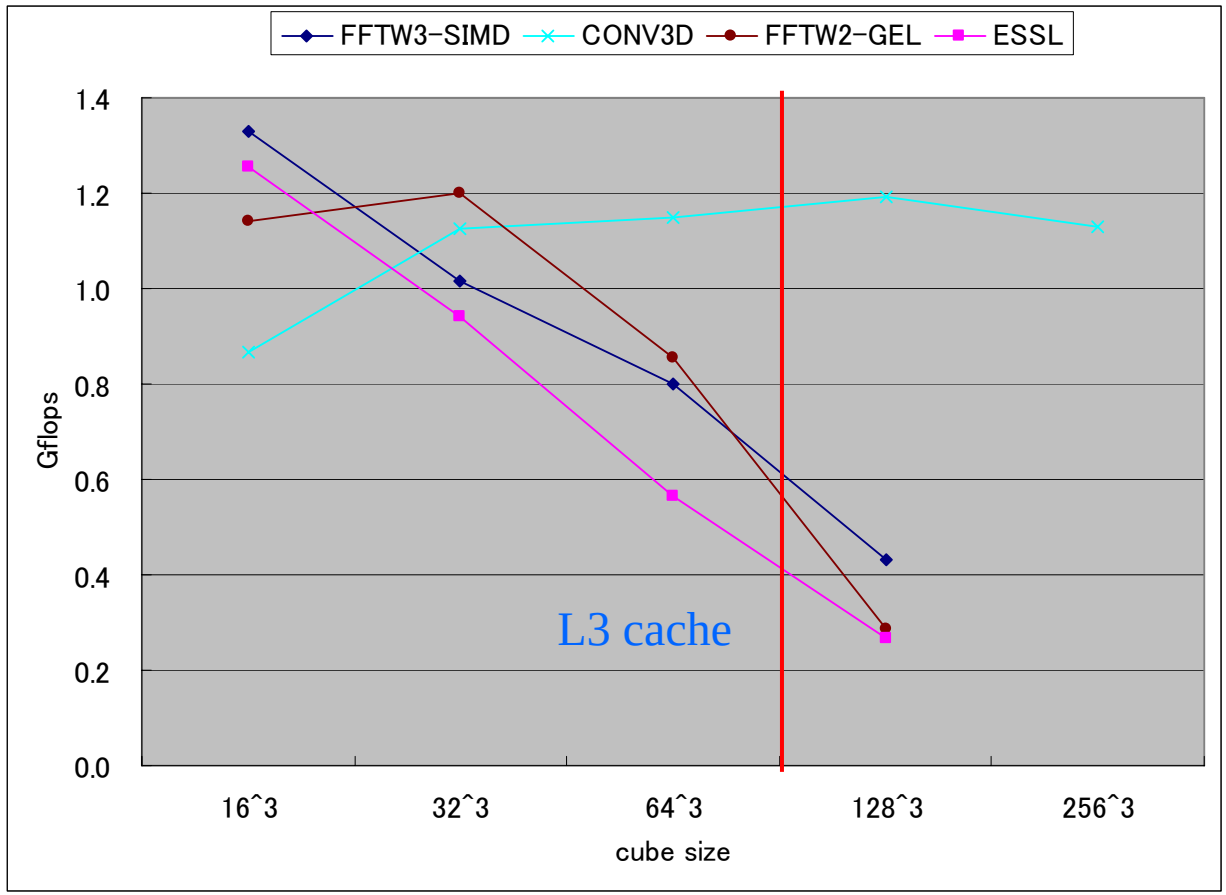
1D-FFT kernel for 3D-Convolution

Complex → Complex (Double Precision)

Not open to the public
for the time being

3D-Convolution Performance

(Complex → Complex)



Output Size	64KB	512KB	4MB	32MB	256MB

Why CONV3D fast?

Not open to the public
for the time being

Summary

Not open to the public
for the time being