MEGADOCK-GPU: Acceleration of Protein-Protein Docking Calculation on GPUs

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Outline

• Background

• MEGADOCK-GPU

• Evaluation of Performance

• Conclusion
Protein-Protein Interaction Network

• Protein-protein interaction (PPI)
  – Proteins interact with each other and make interaction network

• PPI network
  – Important for understanding of cell behaviors
  – Needs a lot of wet experiments
    • Computational prediction method is required

Protein-Protein Interaction Prediction

- Computational PPI prediction method
  - Sequence based method
  - Domain-domain interaction based method
  - Structure based method

- Structure based method
  - Molecular Dynamics (MD)
    - High-definition simulation but very slow
  - Rigid body protein-protein docking
    - Fast but low-definition calculation

References:

Protein-Protein Docking Software

• Protein-protein docking software
  – Non-FFT-based
    • PATCHDOCK  
      – Geometric hashing  

  – FFT-based
    • ZDOCK  
      – High precision docking  
      – Widely used  
    • PIPER  
    • MEGADOCK
MEGADOCK

• Protein-protein interaction prediction system
  – For large-scale PPI network
  – Using protein-protein docking

• Features
  – FFT-based
  – Fast
  – Open source
Which protein pair will interact with each other?

Perform docking calculation and PPI decision for all combinations of proteins.

Docking calculation

PPI decision

PPI\((i,j)\) True / False

\[
PPI(i,j) = \begin{cases} 
\text{True} & \text{if } E > E^* \\
\text{False} & \text{otherwise}
\end{cases}
\]

\[
E = \frac{S_{Z_{R_1}} - \mu}{\sigma}
\]

\[
\text{Mean of } S \quad \mu \\
\text{S.D. of } S \quad \sigma
\]
Docking Calculation Algorithm

• Flow of docking calculation
  – Using voxel space

Fast Docking Calculation Using FFT

• Bottleneck: Score calculation
  – 3-D product & 3-D overlap pattern ⇒ $O(N^6)$
    • $N$ is voxel size (about 100 to 300)

• Fast Fourier Transform (FFT)
  – FFT reduces computational complexity ⇒ $O(N^3 \log N)$
Calculation Time

• MEGADOCK compresses 3 energy terms into only one time FFT calculation
  – 1. Shape complementarity
  – 2. Hydrophobic interaction
  – 3. Electrostatic interaction

• Other docking software needs many time FFT calculation
  – ZDOCK needs 8 times FFT
  – PIPER needs 22 times FFT
Problems: Large calculation time

• Application example
  – Apoptosis pathway dataset
    • Includes 158 proteins
    • Combination of proteins: $158 \times 158 = 24,964$ pairs
    • Average docking time of 1 pair in 1 CPU core: 12.5 mins
    • Runtime: 12.5 mins $\times$ 24,964 pairs = 217 days

• Faster calculation method is required

Research Purpose

• Purpose
  – Acceleration of protein-protein docking calculation of MEGADOCK

• Approaches
  – Acceleration by GPU
    1. GPU Implementation of main processes
    2. Optimization of FFT size
    3. Using full computing resources in a node
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Graphics Processing Unit

- GPU (Graphics Processing Unit)
  - Processors for Graphics processing
  - Computational performance of GPUs overtakes that of CPUs
  - High efficiency

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<tr>
<td>GPU</td>
<td>NVIDIA Tesla M2050</td>
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<tr>
<td>CPU</td>
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<td>70</td>
<td>95</td>
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- CUDA (Compute Unified Device Architecture)
  - Development platform for GPU programming
Related Works

• GPU-accelerated bioinformatics software

• FFT-based protein-protein docking software
  – All processes were not on GPUs
Bottlenecks in MEGADOCK CPU Version

Workflow of MEGADOCK

Profile of CPU version

FFT part occupies 85%
Approach (① GPU Implementation of main processes

- P5, P7: Forward FFT & Inverse FFT
  - Accelerated by using NVIDIA CUFFT library

- P6: Modulation
  - Modulation: complex conjugates and multiplication
    \[ \text{FFT}[R]^* \times \text{FFT}[L] \]
  - Parallelized by voxel element
ApproachGPU Implementation of main processes

- P5, P6, P7: Forward FFT, Modulation, Inverse FFT Processes are performed on GPUs

- However large temporary data should be transferred
① GPU Implementation of main processes

• P4: Ligand voxelization
  – Voxelization: assigning a value to each voxel based on atom radius
  – Parallelized by atom

• P8: Finding the best solutions
  – Using reduction method

• All processes (P4) – (P8) are performed on GPU
  ➔ avoid to transfer large temporary data
② Optimization of FFT Size

- FFT size is decided based on the protein size
- FFT runtime seems to be proportional to FFT size
- However, CUFFT library may drastically slow down on some FFT sizes
  - Original MEGADOCK uses FFTW library and the influence of this problem is small

- According to the manual, CUFFT library shows the best performance on condition that:

\[
\text{FFT size } N = 2^a \times 3^b \times 5^c \times 7^d
\]
Approach② Optimization of FFT Size

• Relation between FFT size and runtime

Select FFT size from only FFT sizes that CUFFT library can process efficiently.
③ Using full computing resources in a node

- Our computing systems TSUBAME 2.0
  - Multiple CPU cores and GPUs

- TSUBAME 2.0 thin node: 12 CPU cores and 3 GPUs
  - Assign decomposed works to multiple CPU cores and GPUs dynamically
    - 3 CPU cores & 3 GPUs: used as GPU version
    - 9 CPU cores: used as CPU version
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Experiment Environment

- **Computation Environment**
  
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<tr>
<th>Tokyo Tech TSUBAME 2.0 Thin Node</th>
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<tr>
<td>CPU</td>
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<td>GPU</td>
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<tr>
<td>Memory</td>
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<td>FFT library</td>
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- **Dataset**
  - Protein-Protein Docking Benchmark 4.0
    - Typical benchmark for protein-protein docking problem
    - 352 protein pairs

- **Measurement**
  - Total docking calculation time of 352 protein pairs
Comparison of each process (1 CPU core vs. 1 CPU core and 1 GPU)

- Comparison of CPU version and GPU version
  1. FFT, Modulation: 20-30-fold faster
  2. Voxelization,
     Finding the best solutions: 2-6-fold faster
  3. Only initialization process slows down because of GPU initialization
Comparison of total docking runtime

- Comparison of CPU version and GPU version

![Graph showing comparison of docking runtime for different configurations.
1CPU core: 73.5 hours
1CPU core & 1GPU: 5.3 hours
12CPU cores: 8.2 hours
12CPU cores & 3GPUs: 2.0 hours]
Conclusion

• We have accelerated docking calculation of MEGADOCK
  – 1 CPU core & 1 GPU: 13.9-fold acceleration
  – 12 CPU cores & 3 GPUs: 37.0-fold acceleration

• Ex.) Prediction for an apoptosis pathway
  – Runtime in 1 CPU core: 217 days
  – Runtime in 12 CPU cores & 3 GPUs: 6 days

MEGADOCK-GPU is freely available at www.bi.cs.titech.ac.jp/megadock/gpu/