Computational Genomics (0382.3102) Lecture 5

Multiple Sequence Alignment:

Hueristics; A 2–Approximation Algorithm

Prof. Benny Chor School of Computer Science Tel-Aviv University

Based in part on MSA sections in Gusfield's book, and chapter 3 in Kanehisa's book

• Input: Sequences $S_1, S_2, \ldots, S_k, k \geq 3$.

- Input: Sequences $S_1, S_2, \ldots, S_k, k \geq 3$.
- Typical sequences' lengths $n_1, n_2, \ldots, n_k \approx a$ few hundreds for AAs, 1000-2000 bp for DNA sequences.

- Input: Sequences $S_1, S_2, \ldots, S_k, k \geq 3$.
- Typical sequences' lengths $n_1, n_2, \ldots, n_k \approx a$ few hundreds for AAs, 1000-2000 bp for DNA sequences.
- DP on the full k-dim box of volume $n_1 \times n_2 \times \ldots \times n_k$ takes $O(n_1 \cdot n_2 \cdot \ldots \cdot n_k \cdot 2^k)$.

- Input: Sequences $S_1, S_2, \ldots, S_k, k \geq 3$.
- Typical sequences' lengths $n_1, n_2, \ldots, n_k \approx a$ few hundreds for AAs, 1000-2000 bp for DNA sequences.
- DP on the full k-dim box of volume $n_1 \times n_2 \times \ldots \times n_k$ takes $O(n_1 \cdot n_2 \cdot \ldots \cdot n_k \cdot 2^k)$.
- Such running time is very slow even for k = 3, and totally infeasible for $k \ge 6$.

- Input: Sequences $S_1, S_2, \ldots, S_k, k \geq 3$.
- Typical sequences' lengths $n_1, n_2, \ldots, n_k \approx a$ few hundreds for AAs, 1000-2000 bp for DNA sequences.
- DP on the full k-dim box of volume $n_1 \times n_2 \times \ldots \times n_k$ takes $O(n_1 \cdot n_2 \cdot \ldots \cdot n_k \cdot 2^k)$.
- Such running time is very slow even for k = 3, and totally infeasible for $k \ge 6$.
- Certain versions of MSA are known to be NPH, so an exact poly time (poly in what?) is unlikely.

• Several (of many) approaches:

- Several (of many) approaches:
- Hueristics.

- Several (of many) approaches:
- Hueristics.
- Fixed parameter complexity.

- Several (of many) approaches:
- Hueristics.
- Fixed parameter complexity.
- Poly time approximation algorithms.

• Several (of many) approaches:

- Several (of many) approaches:
- Searching only a promising subset of the k-dim box (used by Carillo-Lipman).

- Several (of many) approaches:
- Searching only a promising subset of the k-dim box (used by Carillo-Lipman).
- Progressive pairwise alignment (used in CLUSTALW, a very popular package.

- Several (of many) approaches:
- Searching only a promising subset of the k-dim box (used by Carillo-Lipman).
- Progressive pairwise alignment (used in CLUSTALW, a very popular package.

Fixed Parameter Complexity

• Is MSA in FTP?

Approximation Algorithms

• Gusfield 2-approximation algorithm.

Approximation Algorithms

- Gusfield 2-approximation algorithm.
- Setting: Sum of pairs. Distance Measure.

• Four Sequences: S_1, S_2, S_3, S_4 .

- Four Sequences: S_1, S_2, S_3, S_4 .
- d(mismatch) = 3, d(indel) = 2(triangle inequality holds).

- Four Sequences: S_1, S_2, S_3, S_4 .
- d(mismatch) = 3, d(indel) = 2(triangle inequality holds).

- Four Sequences: S_1, S_2, S_3, S_4 .
- d(mismatch) = 3, d(indel) = 2(triangle inequality holds).

- Four Sequences: S_1, S_2, S_3, S_4 .
- d(mismatch) = 3, d(indel) = 2(triangle inequality holds).
- $d(S_1, S_i) = 3$, $d(S_i, S_j) = 4$.

General Analysis of MSA Quality

• Denote $D(S_i, S_j) = MSA$ -induced distance of S_i, S_j .

General Analysis of MSA Quality

- Denote $D(S_i, S_j) = MSA$ -induced distance of S_i, S_j .
- Denote $d(S_i, S_j)$ = optimal (pairwise-induced) distance of S_i, S_j .

General Analysis of MSA Quality

- Denote $D(S_i, S_j) = MSA$ -induced distance of S_i, S_j .
- Denote $d(S_i, S_j)$ = optimal (pairwise-induced) distance of S_i, S_j .
- By algorithm, $D(S_1, S_j) = d(S_1, S_j)$.

• By triangle inequality,

$$D(S_i, S_j) \le D(S_i, S_1) + D(S_1, S_j)$$

= $d(S_i, S_1) + d(S_1, S_j)$

By triangle inequality,

$$D(S_i, S_j) \le D(S_i, S_1) + D(S_1, S_j)$$

= $d(S_i, S_1) + d(S_1, S_j)$

Thus

$$\sum_{i=1}^{k} \sum_{j=i+1}^{k} D(S_{i}, S_{j})$$

$$\leq \sum_{i=1}^{k} \sum_{j=i+1}^{k} d(S_{i}, S_{1})$$

$$+ \sum_{i=1}^{k} \sum_{j=i+1}^{k} d(S_{1}, S_{j})$$

By triangle inequality,

$$D(S_{i}, S_{j}) \leq D(S_{i}, S_{1}) + D(S_{1}, S_{j})$$

= $d(S_{i}, S_{1}) + d(S_{1}, S_{j})$

Thus

$$\sum_{i=1}^{k} \sum_{j=i+1}^{k} D(S_{i}, S_{j})$$

$$\leq \sum_{i=1}^{k} \sum_{j=i+1}^{k} d(S_{i}, S_{1})$$

$$+ \sum_{i=1}^{k} \sum_{j=i+1}^{k} d(S_{1}, S_{j})$$

• Standard arithmetic now implies 2 approx. ratio (in fact 2 - 1/k).

By triangle inequality,

$$D(S_i, S_j) \le D(S_i, S_1) + D(S_1, S_j)$$

= $d(S_i, S_1) + d(S_1, S_j)$

Thus

$$\sum_{i=1}^{k} \sum_{j=i+1}^{k} D(S_{i}, S_{j})$$

$$\leq \sum_{i=1}^{k} \sum_{j=i+1}^{k} d(S_{i}, S_{1})$$

$$+ \sum_{i=1}^{k} \sum_{j=i+1}^{k} d(S_{1}, S_{j})$$

- Standard arithmetic now implies 2 approx. ratio (in fact 2 1/k).
- See Gusfield for full details.