Pairwise Alignment

Mark Voorhies

3/29/2011

Review

- FASTA files

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>Name Free-form annotation
MGCLLIMKEGGPGRKHKLIVMLYLDENQ
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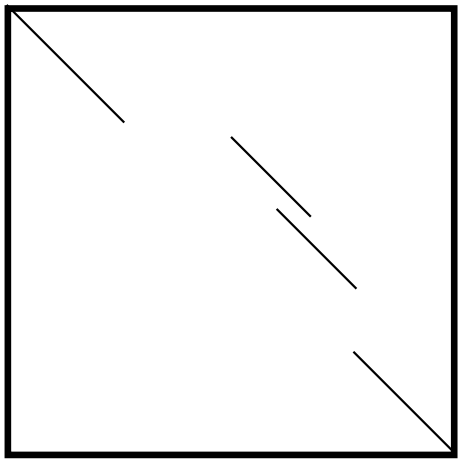
- Dotplots: unbiased plot of all possible ungapped alignments of two sequences.

Pairwise Alignment

How can we automate our dotplot protocol to find the "best" gapped alignment of our sequences?



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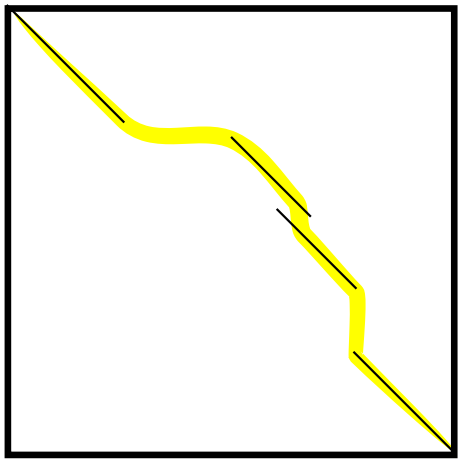

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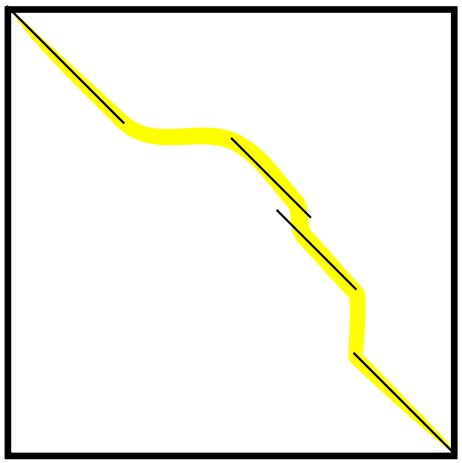

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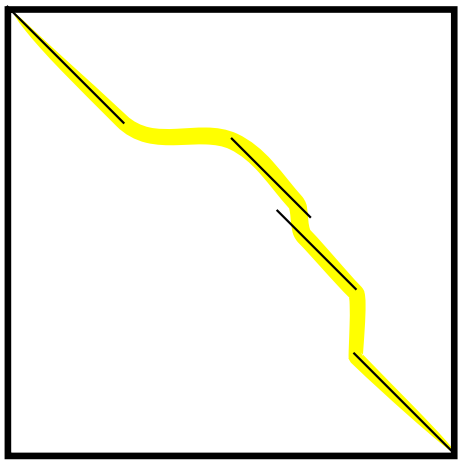

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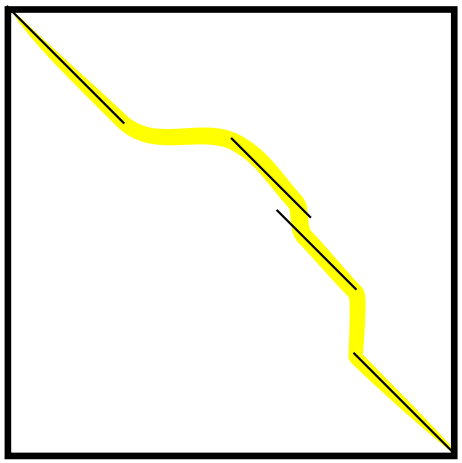

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- The sequence alignment maximizes a similarity function

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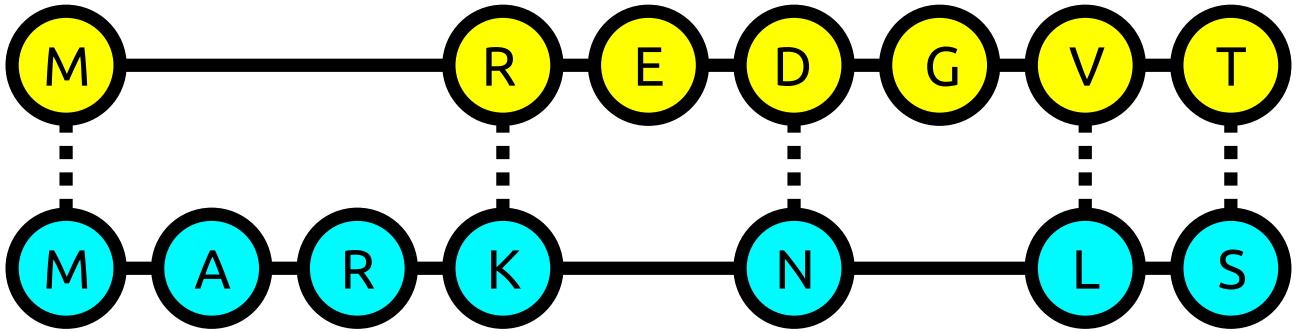

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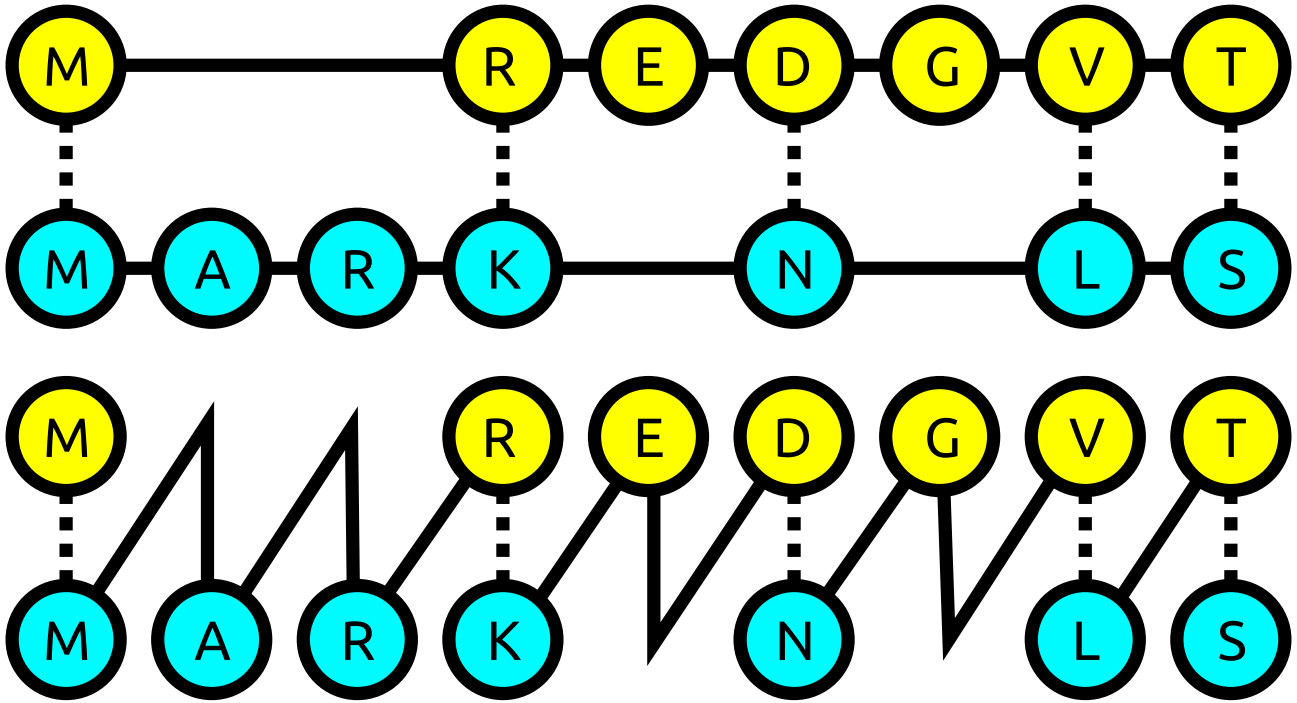

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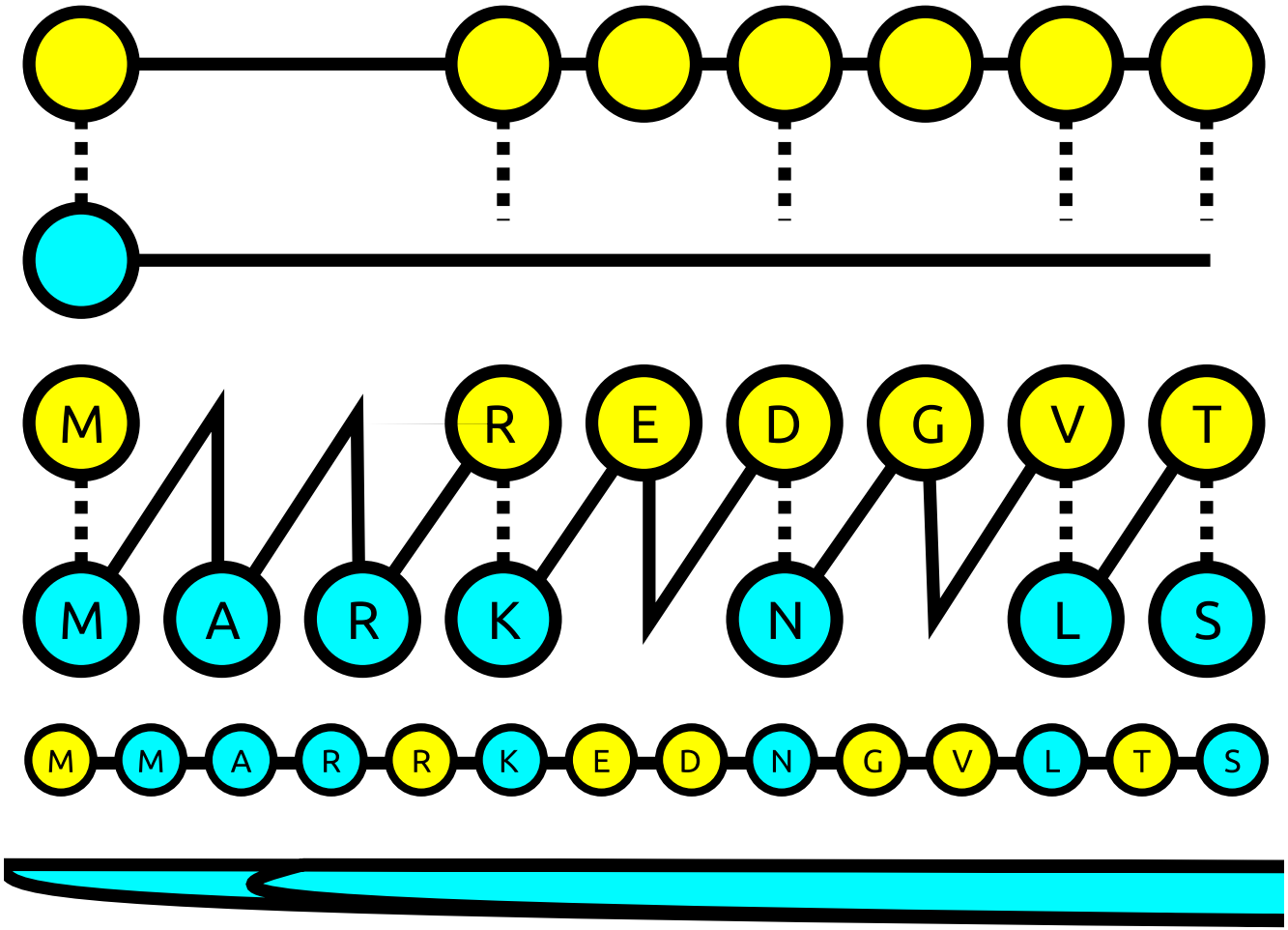

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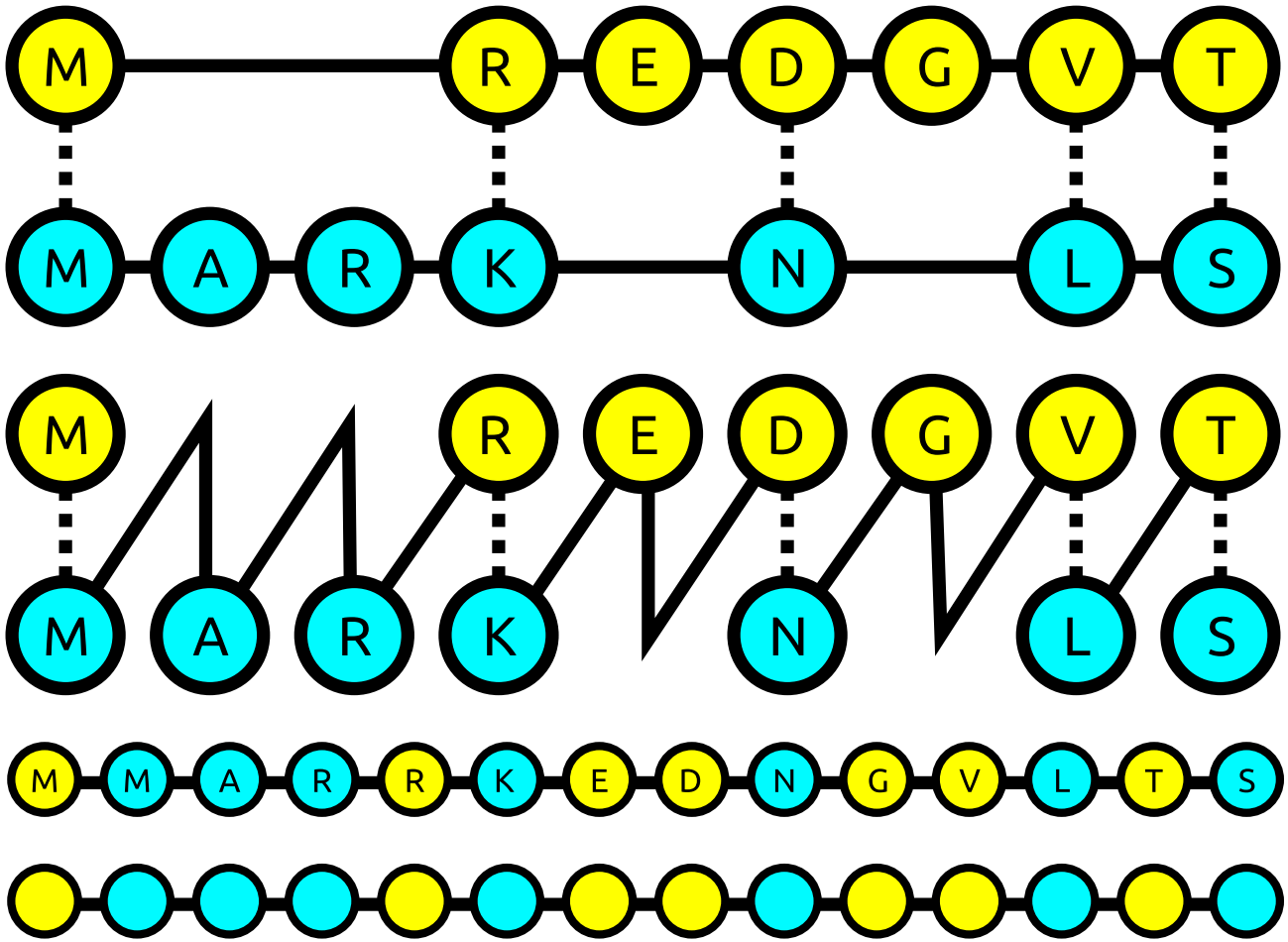

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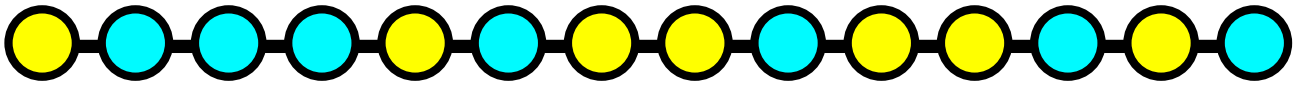

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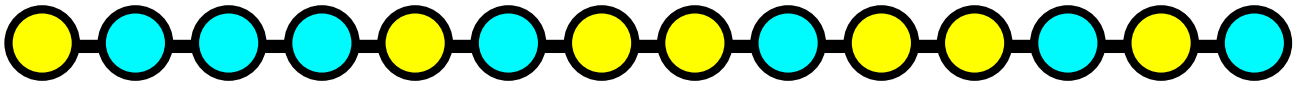

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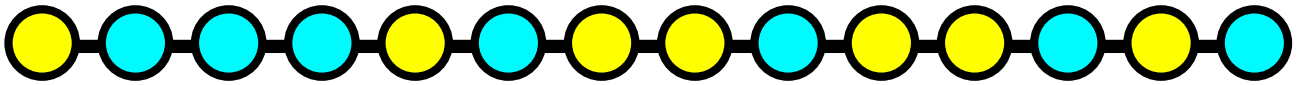

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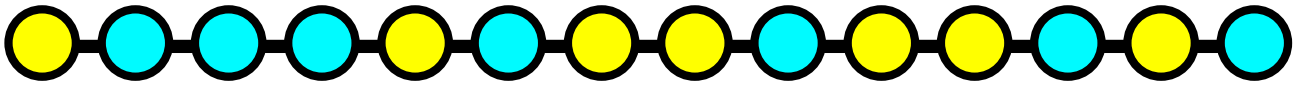

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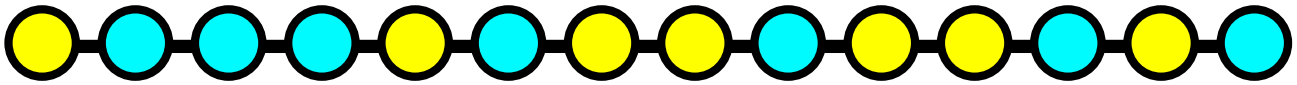

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Log odds (LOD) score:

$$s(i;j) = \log \frac{q_{ij}}{p_i p_j} \tag{9}$$

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- The BLOSUM matrices were determined from automatically generated ungapped alignments. Higher numbered BLOSUM matrices correspond to *smaller* evolutionary distances. BLOSUM62 is the default matrix for BLAST.

Fun with logarithms

In log space, multiplication and division become addition and subtraction:

$$\begin{aligned} \log(xy) &= \log(x) + \log(y) \\ \log(x{=}y) &= \log(x) - \log(y) \end{aligned}$$

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Also, we can change of the base of a logarithm like so:

$$\log_A(x) = \log(x){=}\log(A)$$

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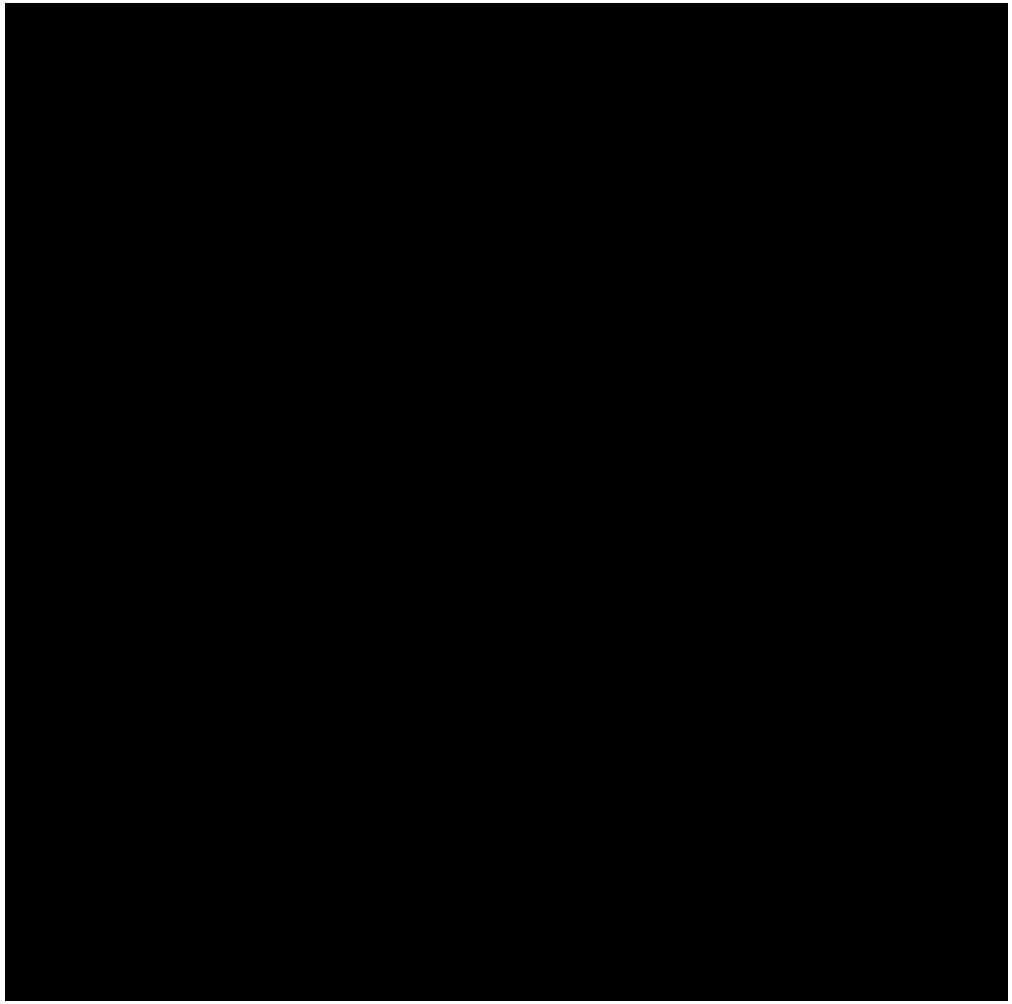
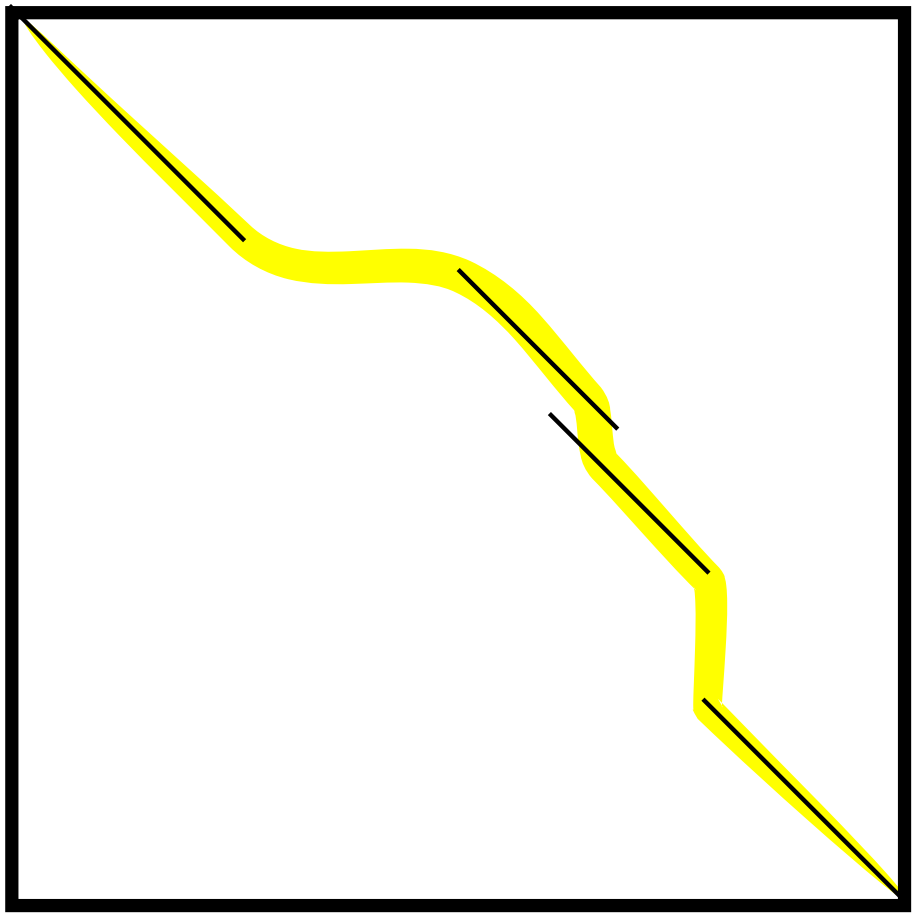
The best alignment of any pair of subsequences is independent of the global alignment.

Dynamic Programming



Needleman-Wunsch Global Alignment



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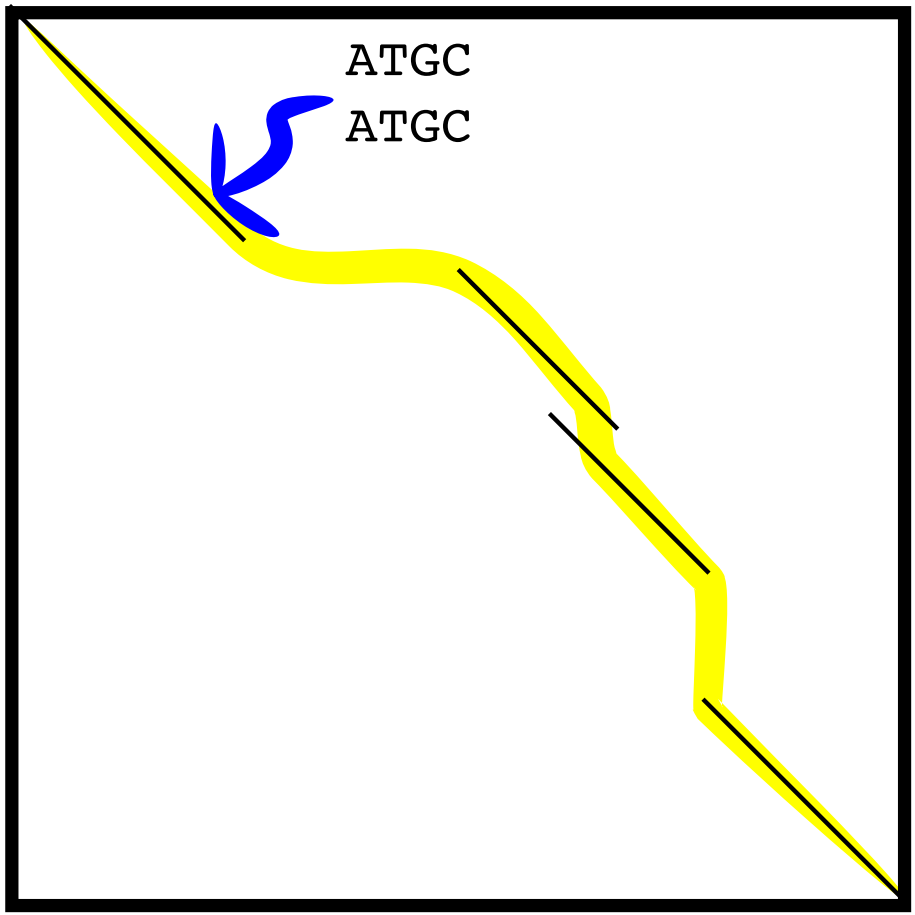

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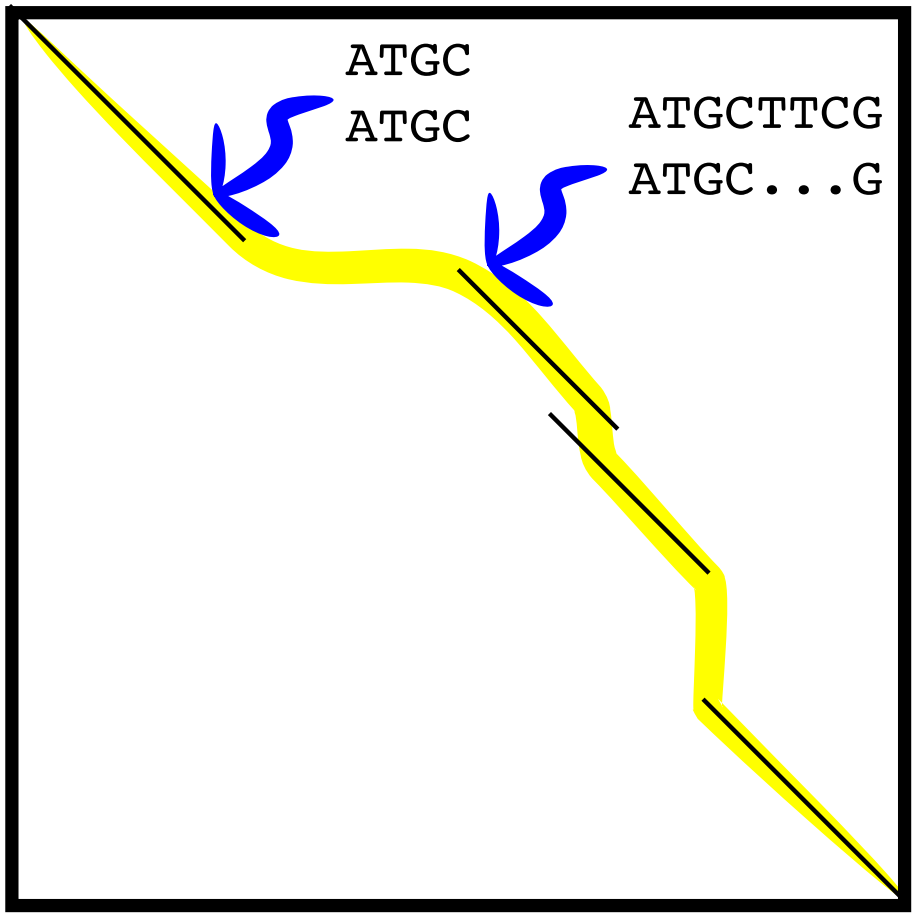

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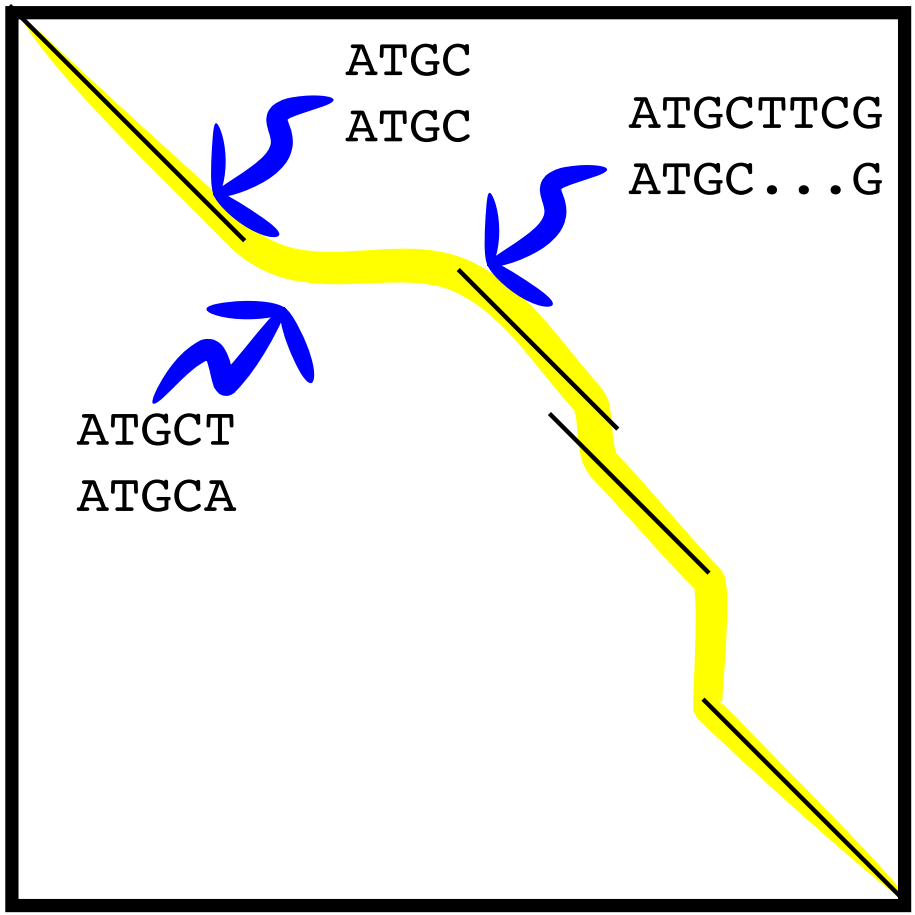

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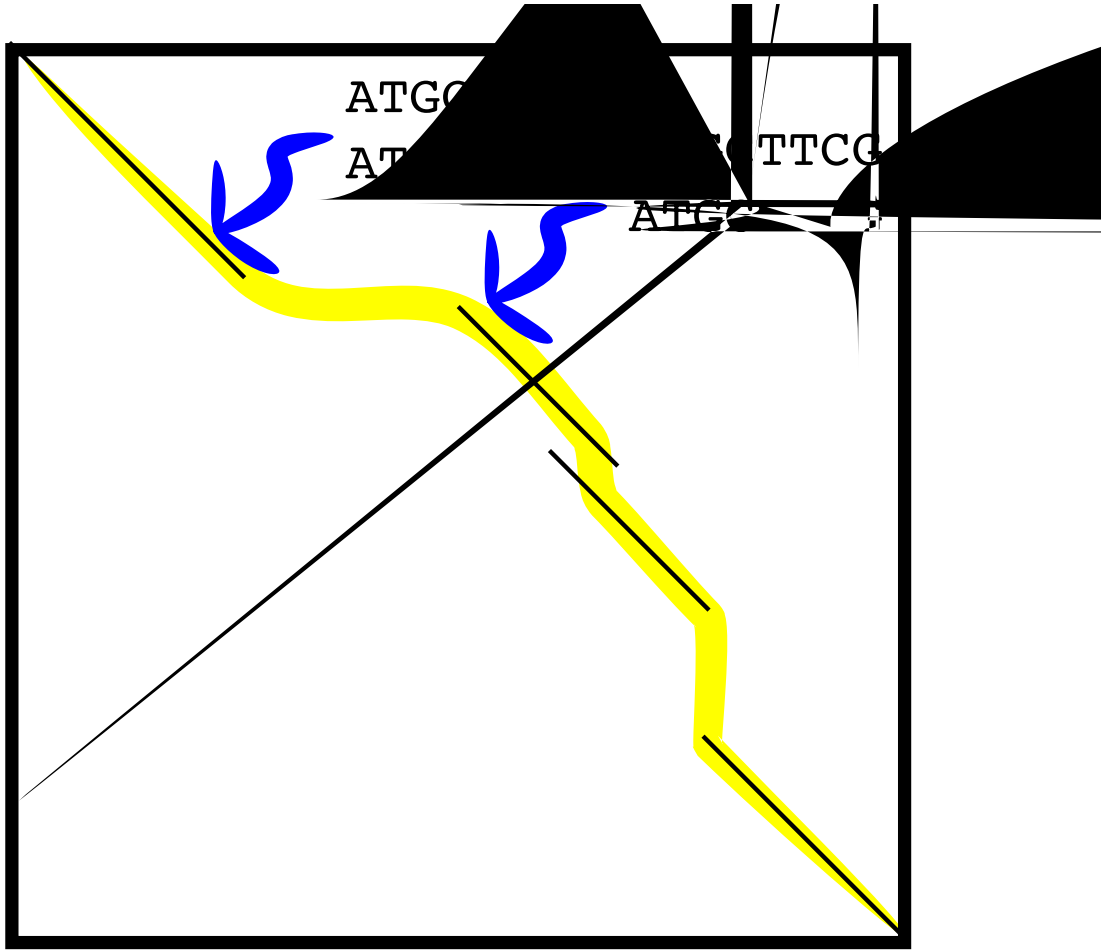

Alignment speeds

- DOTTER: $O(n^2)$
- Exhaustive search: $\frac{2^{2n}}{\sqrt{n}}$
- Dynamic programming: $O(n^2)$ to $O(n^3)$

Homework

- Play with some of your favorite sequences in CLUSTALX
- Experiment with varying the scoring matrices and gap parameters
- Which sequences are easier or harder to align?