Pairwise Alignment

Algorithmic Bioinformatics and Numerics

Knut Reinert (based partially on Sven Rahmans script)

WS 24/25

Overview

Previous Lectures

- Distance and similarity measures between two sequences
- Error-tolerant pattern search (edit distance) in a text:
- Alignments as visualization of edit process (global, semiglobal)

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Today

- From costs (distances) to scores (similarities) and general scoring schemes
- More general introduction of alignments
- Four variants of alignments:
  1. global
  2. semiglobal (pattern search)
  3. free end gaps (overlap detection)
  4. local (regions of similarity)
  5. affine gap costs

Scoring Schemes for Pairwise Sequence Comparison

Need for fine-grained similarity

- Comparison of biosequences (esp. protein sequences) needs a fine-grained notion of similarity instead of only “equal” vs. “not equal” amino acids.
- **Example:** Leucine (L) and Isoleucine (I) are physically and chemically similar. Tryptophan (W) has very different properties than most other amino acids.

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Change of paradigm: Zero-centered similarity

- Evaluate similarity (positive and negative) instead of distances (non-negative)
- Value of 0 means “neutral”, positive means “similar”, negative means “dissimilar”.

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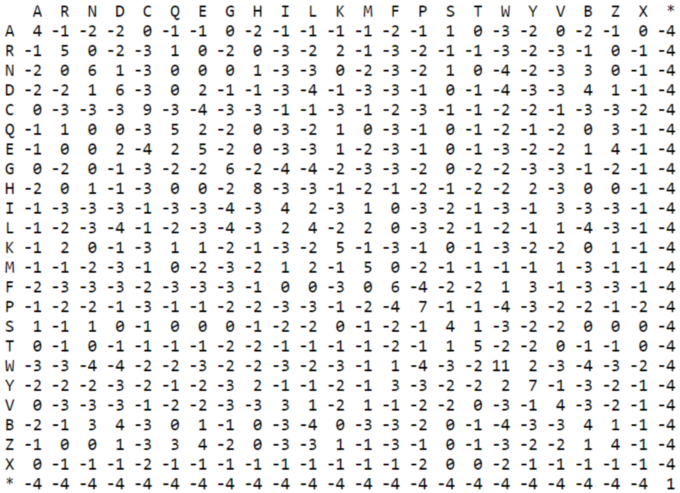
- Evaluate similarity (positive and negative) instead of distances (non-negative)
- Value of 0 means "neutral", positive means "similar", negative means "dissimilar".
- **Therefore:** Use a general **score matrix** $s = s(a, b)$ for any $a, b \in \Sigma$, and (negative) similarity values (**gap scores**) for insertions and deletions.

Example: BLOSUM62 Scoring Matrix for Amino Acids



	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V	B	Z	X	*
A	4	-1	-2	-2	0	-1	-1	0	-2	-1	-1	-1	-1	-2	-1	1	0	-3	-2	0	-2	-1	0	-4
R	-1	5	0	-2	-3	1	0	-2	0	-3	-2	2	-1	-3	-2	-1	-1	-3	-2	-3	-1	0	-1	-4
N	-2	0	6	1	-3	0	0	0	1	-3	-3	0	-2	-3	-2	1	0	-4	-2	-3	3	0	-1	-4
D	-2	-2	1	6	-3	0	2	-1	-1	-3	-4	-1	-3	-3	-1	0	-1	-4	-3	-3	4	1	-1	-4
C	0	-3	-3	-3	9	-3	-4	-3	-3	-1	-1	-3	-1	-2	-3	-1	-1	-2	-2	-1	-3	-3	-2	-4
Q	-1	1	0	0	-3	5	2	-2	0	-3	-2	1	0	-3	-1	0	-1	-2	-1	-2	0	3	-1	-4
E	-1	0	0	2	-4	2	5	-2	0	-3	-3	1	-2	-3	-1	0	-1	-3	-2	-2	1	4	-1	-4
G	0	-2	0	-1	-3	-2	-2	6	-2	-4	-4	-2	-3	-3	-2	0	-2	-2	-3	-3	-1	-2	-1	-4
H	-2	0	1	-1	-3	0	0	-2	8	-3	-3	-1	-2	-1	-2	-1	-2	-2	2	-3	0	0	-1	-4
I	-1	-3	-3	-3	-1	-3	-3	-4	-3	4	2	-3	1	0	-3	-2	-1	-3	-1	3	-3	-3	-1	-4
L	-1	-2	-3	-4	-1	-2	-3	-4	-3	2	4	-2	2	0	-3	-2	-1	-2	-1	1	-4	-3	-1	-4
K	-1	2	0	-1	-3	1	1	-2	-1	-3	-2	5	-1	-3	-1	0	-1	-3	-2	-2	0	1	-1	-4
M	-1	-1	-2	-3	-1	0	-2	-3	-2	1	2	-1	5	0	-2	-1	-1	-1	-1	1	-3	-1	-1	-4
F	-2	-3	-3	-3	-2	-3	-3	-3	-1	0	0	-3	0	6	-4	-2	-2	1	3	-1	-3	-3	-1	-4
P	-1	-2	-2	-1	-3	-1	-1	-2	-2	-3	-3	-1	-2	-4	7	-1	-1	-4	-3	-2	-2	-1	-2	-4
S	1	-1	1	0	-1	0	0	0	-1	-2	-2	0	-1	-2	-1	4	1	-3	-2	-2	0	0	0	-4
T	0	-1	0	-1	-1	-1	-1	-2	-2	-1	-1	-1	-1	-2	-1	1	5	-2	-2	0	-1	-1	0	-4
W	-3	-3	-4	-4	-2	-2	-3	-2	-2	-3	-2	-3	-1	1	-4	-3	-2	11	2	-3	-4	-3	-2	-4
Y	-2	-2	-2	-3	-2	-1	-2	-3	2	-1	-1	-2	-1	3	-3	-2	-2	2	7	-1	-3	-2	-1	-4
V	0	-3	-3	-3	-1	-2	-2	-3	-3	3	1	-2	1	-1	-2	-2	0	-3	-1	4	-3	-2	-1	-4
B	-2	-1	3	4	-3	0	1	-1	0	-3	-4	0	-3	-3	-2	0	-1	-4	-3	-3	4	1	-1	-4
Z	-1	0	0	1	-3	3	4	-2	0	-3	-3	1	-1	-3	-1	0	-1	-3	-2	-2	1	4	-1	-4
X	0	-1	-1	-1	-2	-1	-1	-1	-1	-1	-1	-1	-1	-1	-2	0	0	-2	-1	-1	-1	-1	-1	-4
*	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	1

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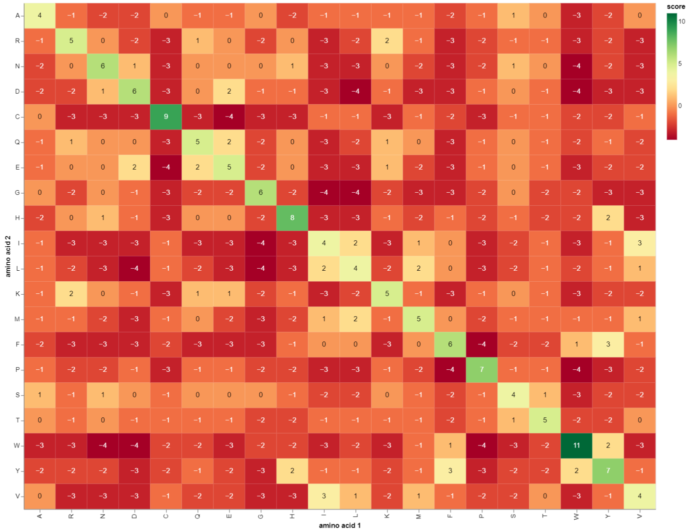

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V
A	4	−1	−2	−2	0	−1	−1	0	−2	−1	−1	−1	−1	−2	−1	1	0	−3	−2	0
R	−1	5	0	−2	−3	1	0	−2	0	−3	−2	2	−1	−3	−2	−1	−1	−3	−2	−3
N	−2	0	6	1	−3	0	0	0	1	−3	−3	0	−2	−3	−2	1	0	−4	−2	−3
D	−2	−2	1	6	−3	0	2	−1	−1	−3	−4	−1	−3	−3	−1	0	−1	−4	−3	−3
C	0	−3	−3	−3	9	−3	−4	−3	−3	−1	−1	−3	−1	−2	−3	−1	−1	−2	−2	−1
Q	−1	1	0	0	−3	5	2	−2	0	−3	−2	1	0	−3	−1	0	−1	−2	−1	−2
E	−1	0	0	2	−4	2	5	−2	0	−3	−3	1	−2	−3	−1	0	−1	−3	−2	−2
G	0	−2	0	−1	−3	−2	−2	6	−2	−4	−4	−2	−3	−3	−2	0	−2	−2	−3	−3
H	−2	0	1	−1	−3	0	0	−2	8	−3	−3	−1	−2	−1	−2	−1	−2	−2	2	−3
I	−1	−3	−3	−3	−1	−3	−3	−4	−3	4	2	−3	1	0	−3	−2	−1	−3	−1	3
L	−1	−2	−3	−4	−1	−2	−3	−4	−3	2	4	−2	2	0	−3	−2	−1	−2	−1	1
K	−1	2	0	−1	−3	1	1	−2	−1	−3	−2	5	−1	−3	−1	0	−1	−3	−2	−2
M	−1	−1	−2	−3	−1	0	−2	−3	−2	1	2	−1	5	0	−2	−1	−1	−1	−1	1
F	−2	−3	−3	−3	−2	−3	−3	−3	−1	0	0	−3	0	6	−4	−2	−2	1	3	−1
P	−1	−2	−2	−1	−3	−1	−1	−2	−2	−3	−3	−1	−2	−4	7	−1	−1	−4	−3	−2
S	1	−1	1	0	−1	0	0	0	−1	−2	−2	0	−1	−2	−1	4	1	−3	−2	−2
T	0	−1	0	−1	−1	−1	−1	−2	−2	−1	−1	−1	−1	−2	−1	1	5	−2	−2	0
W	−3	−3	−4	−4	−2	−2	−3	−2	−2	−3	−2	−3	−1	1	−4	−3	−2	11	2	−3
Y	−2	−2	−2	−3	−2	−1	−2	−3	2	−1	−1	−2	−1	3	−3	−2	−2	2	7	−1
V	0	−3	−3	−3	−1	−2	−2	−3	−3	3	1	−2	1	−1	−2	−2	0	−3	−1	4

Reminder: Alignments

Definition: Alignment, Projections π_1, π_2

An **alignment** is a string A over the **alignment alphabet** $(\Sigma \cup \{-\})^2 \setminus \{(-,-)\}$ (pairs of characters, or one character paired with a gap).
The **first (second) projection** π_1 (π_2) reads the first (second) elements without gaps, so π_1 is the string homomorphism with $\pi_1((a,b)) := a$ and $\pi_1((-,b)) := \epsilon$, etc.

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A **global alignment** between $s, t \in \Sigma^*$ is an alignment with $\pi_1(A) = s$, $\pi_2(A) = t$.

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A **global alignment** between $s, t \in \Sigma^*$ is an alignment with $\pi_1(A) = s$, $\pi_2(A) = t$.

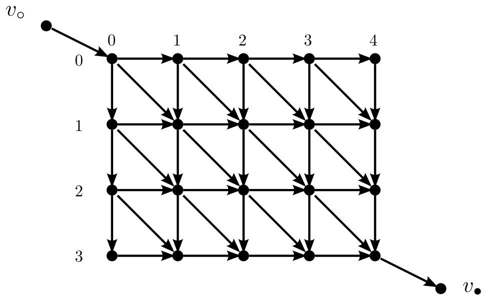
Definition: Semiglobal alignment

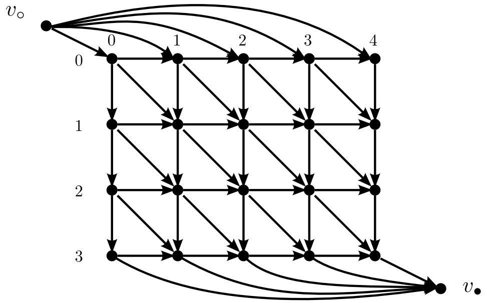
A **semiglobal alignment** between $P, T \in \Sigma^*$ is an alignment with $\pi_1(A) = P$, $\pi_2(A) = T'$, where T' is any substring of T.

Universal Alignment Algorithm

Given

- sequences s, t
- a scoring scheme
- an alignment graph topology (e.g., for global or semiglobal alignment)





Universal Alignment Algorithm

- **Given**: sequences s, t, scoring scheme, graph topology
- **Sought:**
  1. Maximum score among all paths $v_\circ \to v_\bullet$ (**optimal alignment score**)
  2. A path that maximizes the scores (**optimal alignment**)
- Let $S(v)$ be the maximal score of all paths $v_\circ \to v$, and $S(v_\circ) := 0$.
- Let $T(v)$ be the predecessor of v, from which the maximum $S(v)$ is obtained.
- For $v \neq v_\circ$:

$$S(v) = \max_{w\colon w \to v \in E} \{S(w) + \mathrm{score}(w \to v)\},$$

$$T(v) = \operatorname*{arg\,max}_{w\colon w \to v \in E} \{S(w) + \mathrm{score}(w \to v)\}.$$

- Compute nodes in topological order (graph is acyclic!)
- The optimal score is obtained as $S(v_\bullet)$.
- The optimal path (alignment) is obtained by traceback from $v_\bullet$:
  $v_\bullet \to T(v_\bullet) \to T(T(v_\bullet)) \to \cdots \to T^k(v_\bullet) \to \cdots \to v_\circ$.

Traceback

Traceback, also Backtracing

- Reconstruction of the optimal path by tracing back the predecessor nodes that lead to the optimal score value in each node
- Do not confuse with Backtracking!

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  Read the edge labels along the optimal path.

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Time and memory requirements

- **Running time:** $O(m+n)$ for an $m \times n$ matrix (maximum length of a path)
- **Memory:** $O(mn)$ because the full matrix T must be stored (improvement soon)

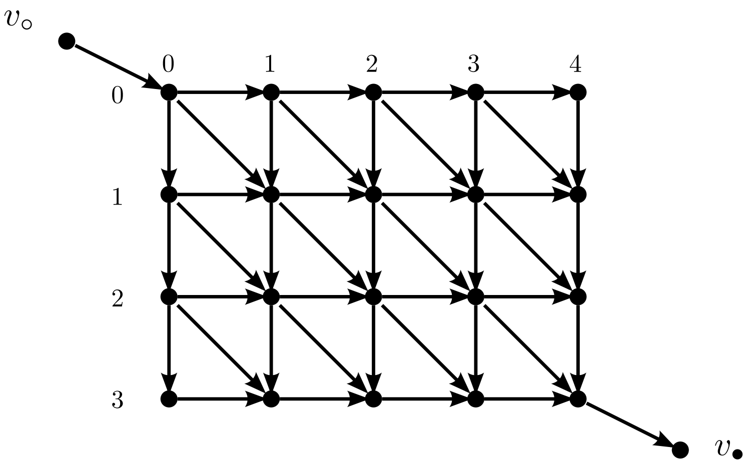
Variants of Alignments

Four Variants

1. Global alignment (similarity of full sequences)
2. Semiglobal alignment (pattern search)
3. Free end gaps alignment (good/optimal overlap)
4. local alignment (region[s] of high/optimal similarity)

We discuss the associated **graph topology** for each variant.
All variants can be handled uniformly with the **universal alignment algorithm**.

Global Alignment



Global Alignment

Definition: global alignment graph

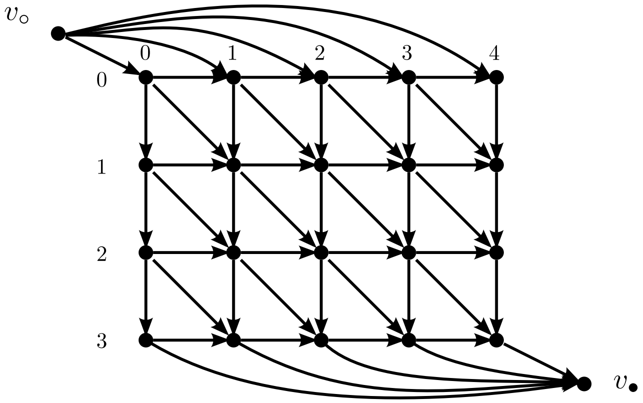
- Nodes $V := \{(i,j) : 0 \leq i \leq m, 0 \leq j \leq n\} \cup \{v_\circ, v_\bullet\}$
- Edges:

	Edge	label	**score**
horizontal	$(i,j) \to (i,j+1)$	$\left[\begin{smallmatrix} - \\ t_j \end{smallmatrix}\right]$	< 0 (*)
vertical	$(i,j) \to (i+1,j)$	$\left[\begin{smallmatrix} s_i \\ - \end{smallmatrix}\right]$	< 0 (*)
diagonal	$(i,j) \to (i+1,j+1)$	$\left[\begin{smallmatrix} s_i \\ t_j \end{smallmatrix}\right]$	any (*)
Initialization	$v_\circ \to (0,0)$	ϵ	0
Finalization	$(m,n) \to v_\bullet$	ϵ	0

(*): Meaningful scoring schemes have negative scores for gaps and most substitutions, and positive scores for identities.

Semiglobal Alignment (Pattern Search)

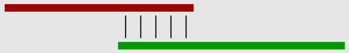
Additional initialization edges $v_\circ \to (0, j)$ and finalization edges $(m, j) \to v_\bullet$:



“Free End Gaps” Alignment (Overlap Detection)

Question

(How) Do two sequences overlap?



Gaps (overhangs) at either border of either sequence shall not be penalized.

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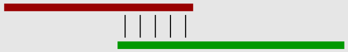
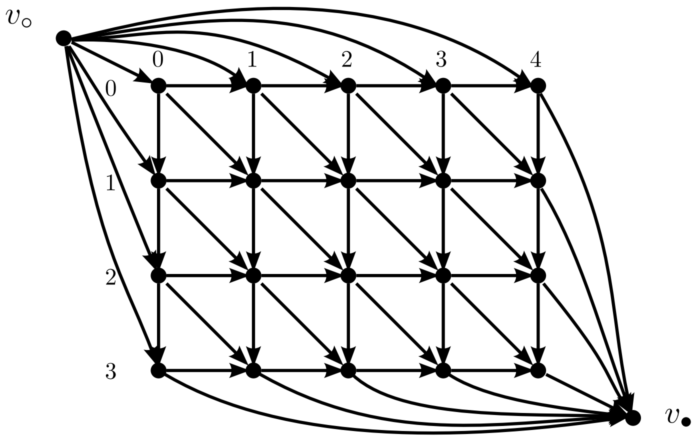


Gaps (overhangs) at either border of either sequence shall not be penalized.

Graph construction

Additional initialization edges $v_\circ \to (i,0)$ and $v_\circ \to (0,j)$,
and finalization edges $(i,n) \to v_\bullet$ and $(m,j) \to v_\bullet$.
(All such edges have empty labels and contribute score 0.)

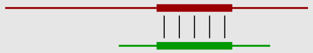
“Free End Gaps” Alignment (Overlap Detection)



Local Alignment

Question

- (Where) Are there regions (substrings) of high similarity between two sequences?
- Where are the most similar substrings (maximal score) ?



- **Formally:** Find alignment with maximal score among all substrings s' of s and t' of t.

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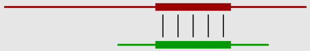

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Graph construction

- Initialization edges $v_\circ \rightarrow (i,j)$ for all $0 \leq i \leq m$, $0 \leq j \leq n$,
- Finalization edges $(i,j) \rightarrow v_\bullet$ for all $0 \leq i \leq m$, $0 \leq j \leq n$.
- Visualization is not helpful (far too many edges)

Alignment Variants and Distances vs. Scores

Meaningful combinations

Variant	**Distances**	**Scores**
Global alignment (similarity of full sequences)	✓	✓
Semiglobal alignment (pattern search)	✓	✓
Free end gap alignment (good/optimal overlap)		✓
Local alignment (region[s] of high/optimal similarity)		✓

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Why?

Optimal distance is always zero ($d \geq 0$).
Free end gap and local alignments allow trivial "empty" alignments, which always have distance zero. No incentive for non-trivial alignments.

Specializations of the Universal Alignment Algorithm

For each alignment variant (graph topology):

- What is the interpretation of the score $S(v)$ for any $v = (i, j)$?
  ("Score of an optimal alignment of ...")
- How does the universal algorithm specialize to matrix form ?
  - First row and column ?
  - $S[i, j] = \max\{\dots\}$?
  - Collection of interesting results or optimal result ?
- How do running time and memory requirements change vs. global alignment?
  (They typically do not change.)

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Algorithm Names

- Global alignment: Needleman-Wunsch algorithm (NW)
- Local alignment: Smith-Waterman algorithm (SW)

Needleman-Wunsch Algorithm (Score-Based, Global, Full Matrix)

```
def needleman_wunsch(s, t, score):
    m, n, gapscore = len(s), len(t), score(None)
    S = np.zeros((m+1, n+1), dtype=np.int32)  # scores
    T = np.zeros((m+1, n+1), dtype=np.uint8)  # traceback
    S[0,:] = np.arange(n+1, dtype=S.dtype) * gapscore
    S[:,0] = np.arange(m+1, dtype=S.dtype) * gapscore
    T[0,0] = HOME; T[0,1:] = HORIZONTAL; T[1:,0] = VERTICAL
    for i, si in zip(count(1), s):  # (row, character in s)
        for j, tj in zip(count(1), t):  # (col, character in t)
            d = S[i-1, j-1] + score(si, tj)
            h = S[i, j-1] + gapscore
            v = S[i-1, j] + gapscore
            S[i,j] = opt = max(d, h, v)
            T[i,j] = (d==opt)*DIAGONAL + (h==opt)*HORIZONTAL \
                   + (v==opt)*VERTICAL
    return S[m,n], traceback(m, n, T, s, t)
```

Smith-Waterman Algorithm (Score-Based, Local, Full Matrix)

```
def smith_waterman(s, t, score):
    m, n, gapscore = len(s), len(t), score(None)
    S = np.zeros((m+1, n+1), dtype=np.int32)  # scores
    T = np.zeros((m+1, n+1), dtype=np.uint8)  # traceback
    T[0,:] = HOME;  T[:,0] = HOME  # alignments end at border
    best = (-1, -1, -1)  # best (S, i, j)
    for i, si in zip(count(1), s):  # (row, character in s)
        for j, tj in zip(count(1), t):  # (col, character in t)
            d = S[i-1, j-1] + score(si, tj)
            h = S[i, j-1] + gapscore
            v = S[i-1, j] + gapscore
            S[i,j] = opt = max(0, d, h, v)  # note additional 0
            T[i,j] = (d==opt)*DIAGONAL + (h==opt)*HORIZONTAL \
                   + (v==opt)*VERTICAL  # can be HOME otherwise
            if S[i,j] > best[0]:  best = (S[i,j], i, j)
    result, i, j = best
    return result, traceback(i, j, T, s, t)
```

Implementation of Traceback

```
HOME, DIAGONAL, HORIZONTAL, VERTICAL = 0, 1, 2, 4
def traceback(i, j, T, s, t, *, GAP='-'):
    # We reconstruct the alignment by traceback (T) from i, j
    As, At = [], []  # rows of alignment: As (for s), At (for t)
    while T[i,j] != HOME:
        trace = T[i,j]
        if (trace & DIAGONAL):
            i -= 1;  As.append(s[i])
            j -= 1;  At.append(t[j])
        elif (trace & HORIZONTAL):
            As.append(GAP)
            j -= 1; At.append(t[j])
        elif (trace & VERTICAL):
            i -= 1; As.append(s[i])
            At.append(GAP)
    # create the final alignment (pair of strings)
    return ("".join(As[::-1]), "".join(At[::-1]))
```

Gap costs

Finer distinction

So far we simply assumed a constant negative gapscore, which is used in practice especially for nucleic acids. Often, however, it is better to

1. distinguish the type of a mismatch, and
2. take the length of consecutive gaps into account.

Linear and affine gap cost

Gaps in an alignment are undesirable and thus penalized. In its simplest form, the cost associated with a gap of length $g \geq 1$ is given by a **linear** score,

$$\gamma(g) = -g \cdot d\,.$$

An **affine** score, however,

$$\gamma(g) = -d - (g-1)e$$

often produces better results.

Here d is the **gap open** penalty and e is the **gap extension** penalty.

Gap costs

Usually one sets $e < d$, i.e., there is a large penalty for opening a gap, but a smaller penalty for extending it. Then affine gap costs favor alignments with fewer but larger gaps.

Example

```
    GSAQVKGHGKKVADALTNAVAHVDDMPNALSALSDLHAHKL
    GSAQVKGHGKK--------VA--D----A-SALSDLHAHKL
```

Using affine gap penalties:

```
    GSAQVKGHGKKVADALTNAVAHVDDMPNALSALSDLHAHKL
    GSAQVKGHGKKVADA---------------SALSDLHAHKL
```

The case $d < e$ is sometimes used when comparing output of DNA sequencing machines. There it happens frequently that single bases are left out near the end of a read.

Gap costs

Affine gap costs

The standard alternative to using the above recursion is to use an **affine gap score**

$$\gamma(g) = -d - (g-1)e,$$

with d the **gap-open score** and e the **gap-extension** score. We will discuss how to modify the Needleman-Wunsch algorithm for global alignment so as to incorporate affine gap costs. The resulting algortithm is due to Osamu Gotoh (1982).

In the justification of the Needleman-Wunsch algorithm we made a case distinction based on the **last** column of an optimal alignment of the prefixes of both sequences. For affine gap costs, we will need to consider the **second last** column as well.
As a consequence, instead of using just one matrix $S(i,j)$ to represent the best score attainable up to x_i and y_j, we will now use three matrices M, I_x and I_y, and distinguish the state of the second last column.

Gap costs

Affine gap costs

Reminder (from Needleman-Wunsch): there are three ways how the last column of an alignment of $(x_1, x_2, \ldots, x_i)$ and $(y_1, y_2, \ldots, y_j)$ can look like:

x_i aligns to y_j:

I	G	A	x_i
L	G	V	y_j

x_i aligns to a gap:

A	I	G	A	x_i
G	V	C	y_j	-

y_j aligns to a gap:

G	A	x_i	-	-
S	L	G	V	y_j

We introduce three matrices:

1. $M(i,j)$ is the best score up to (i,j), given that x_i is aligned to y_j,
2. $I_x(i,j)$ is the best score up to (i,j), given that x_i is aligned to a gap, and
3. $I_y(i,j)$ is the best score up to (i,j), given that y_j is aligned to a gap.

Gap costs

Affine gap costs

Now we will distinguish the state of the second last column as well:

	x_i aligns to y_j:	x_i aligns to a gap:	y_j aligns to a gap:
M	$\begin{array}{cccc} \texttt{I} & \texttt{G} & \texttt{A} & x_i \\ \texttt{L} & \texttt{G} & \texttt{V} & y_j \end{array}$	$\begin{array}{ccccc} \texttt{A} & \texttt{I} & \texttt{G} & \texttt{A} & x_i \\ \texttt{G} & \texttt{V} & \texttt{C} & y_j & - \end{array}$	$\begin{array}{ccccc} \texttt{G} & \texttt{A} & \texttt{G} & x_i & - \\ \texttt{S} & \texttt{L} & \texttt{G} & \texttt{V} & y_j \end{array}$
I_x	$\begin{array}{cccc} \texttt{I} & \texttt{G} & \texttt{A} & x_i \\ \texttt{L} & \texttt{G} & - & y_j \end{array}$	$\begin{array}{ccccc} \texttt{A} & \texttt{I} & \texttt{G} & \texttt{A} & x_i \\ \texttt{G} & \texttt{V} & y_j & - & - \end{array}$	$\begin{array}{ccccc} \texttt{G} & \texttt{A} & \texttt{G} & x_i & - \\ \texttt{S} & \texttt{L} & \texttt{G} & - & y_j \end{array}$
I_y	$\begin{array}{cccc} \texttt{I} & \texttt{G} & - & x_i \\ \texttt{L} & \texttt{G} & \texttt{V} & y_j \end{array}$	$\begin{array}{ccccc} \texttt{A} & \texttt{I} & \texttt{G} & - & x_i \\ \texttt{G} & \texttt{V} & \texttt{C} & y_j & - \end{array}$	$\begin{array}{ccccc} \texttt{G} & x_i & - & - & - \\ \texttt{S} & \texttt{L} & \texttt{G} & \texttt{V} & y_j \end{array}$

Gap costs

Recursion

The cases in the gray boxes are undesirable because a gap in one sequence is immediately followed by a gap in the other. We will explicitly exclude them from consideration. (The optimal alignment does not use them anyway, if $-d - e$ is less than the lowest mismatch score. However the scoring scheme does not always have this property, so we are really enforcing a new requirement.)

Gap costs

Recursion affine gap costs

From the remaining seven cases we obtain the following recursions:

Recursion:

$$M(i,j) = \max \begin{cases} M(i-1,j-1) + s(x_i,y_j), \\ I_x(i-1,j-1) + s(x_i,y_j), \\ I_y(i-1,j-1) + s(x_i,y_j); \end{cases}$$

$$I_x(i,j) = \max \begin{cases} M(i-1,j) - d, \\ I_x(i-1,j) - e; \end{cases}$$

$$I_y(i,j) = \max \begin{cases} M(i,j-1) - d, \\ I_y(i,j-1) - e. \end{cases}$$

Gap costs

The formulas for initialization at the upper and left margin ($i = 0$ respectively $j = 0$) are derived from the recursion. However, there are some “impossible cases”, represented by $I_x(0, j)$ and $I_y(i, 0)$. We assign a value of $-\infty$ to these matrix entries, such that they will not have an influence on the maximum computations.

Initialization affine gap costs

$$\begin{array}{lll} M(0,0) = 0, & I_x(0,0) = I_y(0,0) = -\infty & \\ I_x(i,0) = -d - (i-1)e, & M(i,0) = I_y(i,0) = -\infty, & \text{for } i = 1, \dots, n \\ I_y(0,j) = -d - (j-1)e, & M(0,j) = I_x(0,j) = -\infty, & \text{for } j = 1, \dots, m. \end{array}$$

The traceback uses the same ideas as the Needleman-Wunsch algorithm. There are just a few more cases to consider. . . ~ ;-)

Gap costs

Example

Given two sequences $x = \texttt{ttagat}$ and $y = \texttt{ttgt}$. We use 1, -1, 2 and 1 for the match-, mismatch-, gap-open and gap-extension scores, respectively:

Summary

Pairwise sequence alignment (four variants)

- Motivation of scoring schemes vs. cost functions
- Definition of pairwise alignments in general
- Definition of four pairwise sequence alignment variants
- Alignment graphs and four topology variants
- Universal alignment algorithm on graphs
- Universal traceback
- Specialization: Needleman-Wunsch (global)
- Specialization: Smith-Waterman (local)
- Specialization: Gotoh (affine gap costs)
- Other specialzations: Homework

Possible Exam Questions

- Define alignment (in general).
- Define global (semiglobal, etc.) alignment of two strings s, t.
- Explain five variants of alignments and their use cases.
- What is the difference between score and cost function and why is it important?
- Why can't we use costs for free end gap and local alignment?
- How can sequence alignment be formulated as a graph problem?
- Show the alignment graph topology for each variant.
- Explain the universal alignment algorithm on the alignment graph.
- Give the DP formulation for computing an alignment score (any variant).
- Compute an optimal alignment (any variant) for two given strings.
- Explain traceback.