MEKKITGYTT
NMFFVSANPW
MLNELQQ
MNAHTAFL

'0': {'1': -9, '2': -9, '3': -4}, sum = -22
'1': {'0': -9, '2': -9, '3': -4}, sum = -22
'2': {'0': -9, '1': -9, '3': -4}, sum = -22
'3': {'0': -4, '1': -4, '2': -4}, sum = -12

Centre = seqs[3]: {'0': -4, '1': -4,'2': -4}
Orders: ['0', '1', '2']

global_align(seqs[0], centre, match, mismatch, gap_open)

('MEKKITGYTT', 'M-NAHT-AFL', -4)
Centre = M-NAHT-AFL

global_align(seqs[1], centre, match, mismatch, gap_open)

('NM-FFVS-ANPW', '-M-NAHT-A-FL', -8)
Centre = -M-NAHT-A-FL

global_align(seqs[2], centre, match, mismatch, gap_open)
('-MLN--E-L-QQ', ' -M-NAHT-A-FL', -12)
Centre = -M-NAHT-A-FL

initial score: -45
initial alignment

-MEKKITGY-TT
NM-FFVS-ANPW
-MLN--E-L-QQ
-M-NAHT-A-FL

Blocks = 2:11

-MEKKITGYTT
NM-FFVSANPW
-MLN--EL-QQ
-M-NAHTA-FL

Blocks= 2:10
No improvment

S3: M-NAHT-AFL
S0: MEKKITGYTT

S3: -M-NAHT-A-FL
S0: -MEKKITGY-TT
S1: NM-FFVS-ANPW

S3: -M-NAHT-A-FL
S0: -MEKKITGY-TT
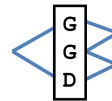S1: NM-FFVS-ANPW
S2: -MLN--E-L-QQ

Example of SP Score with Gap

Example of SP Score with Gap

	F	Y	G	D
F	5	-2	-2	-1
Y		7	1	-5
G			4	-3
D				5

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$$m = \begin{matrix} F \\ F \\ F \end{matrix} \quad \begin{matrix} - \\ - \\ Y \end{matrix} \quad \begin{matrix} G \\ G \\ D \end{matrix}$$

Gap penalty = -8
$s(-,-) = 0$

$$\begin{matrix} G \\ G \\ D \end{matrix}$$

$$\begin{aligned} S(m) &= S(m_1) + S(m_2) + S(m_3) \\ &= 3s(F,F) + 2s(-,Y) + s(-,-) + s(G,G) + 2s(G,D) \\ &= 15 - 16 + 0 + 4 - 6 = -3 \end{aligned}$$
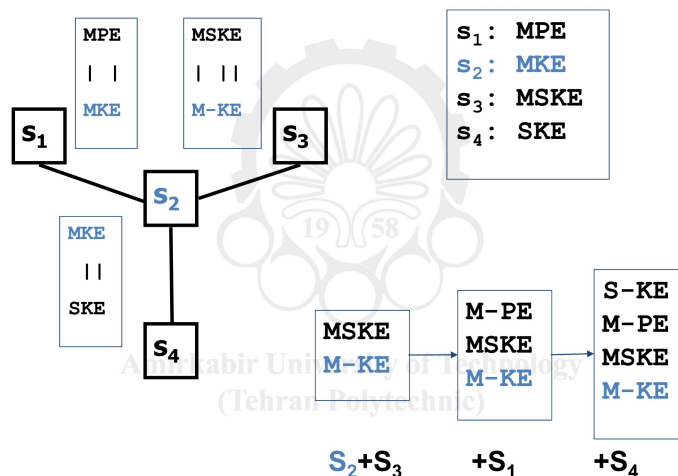
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Star Alignment

- Fast heuristic to compute MSA
- Good approximation of *optimal* MSA, if scoring scheme satisfies triangle inequality

Algorithm:

1. *Compute pairwise similarities*
2. *Select center s_c that maximizes $\Sigma_{i \neq c} S(s_c, s_i)$*
3. *Add sequences in decreasing order of similarity* to *center* s_c
   - Rule: "once a gap, always a gap"

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Step 3 - Add sequences in decreasing order


```
MPE          MSKE
| |          | ||
MKE          M-KE
S₁           S₃
```

```
S₁:  MPE
S₂:  MKE
S₃:  MSKE
S₄:  SKE
```

```
S₂
MKE
||
SKE
S₄
```

```
MSKE       M-PE       S-KE
M-KE       MSKE       M-PE
           M-KE       MSKE
                      M-KE

S₂+S₃      +S₁        +S₄
```

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Star-Alignment Example (Cont.)

S_1	A	T	T	G	C	C	A	T	T		
S_2	A	T	G	G	C	C	A	T	T		

S_1	A	T	T	G	C	C	A	T	T	-	-
S_3	A	T	C	-	C	A	A	T	T	T	T

S_1	A	T	T	G	C	C	A	T	T
S_4	A	T	C	T	T	C	-	T	T

S_1	A	T	T	G	C	C	A	T	T
S_5	A	C	T	G	A	C	C	-	-

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Star-Alignment Example (Cont.)

Let's use the alignment of S_1 and S_2.

S_1	A	T	T	G	C	C	A	T	T
S_2	A	T	G	G	C	C	A	T	T

S_1 and S_2 are aligned

Now, let's add S_3, using its alignment to S_1.

S_1	A	T	T	G	C	C	A	T	T	-	-
S_2	A	T	G	G	C	C	A	T	T	-	-
S_3	A	T	C	-	C	A	A	T	T	T	T

S_1, S_2, and S_3 are aligned

Then, let's add S_4, using its alignment to S_1.

S_1	A	T	T	G	C	C	A	T	T	-	-
S_2	A	T	G	G	C	C	A	T	T	-	-
S_3	A	T	C	-	C	A	A	T	T	T	T
S_4	A	T	C	T	T	C	-	T	T	-	-

S_1, S_2, S_3, and S_4 are aligned

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Star-Alignment Example (Cont.)

Finally, let's add S_5, using its alignment to S_1.

S_1	A	T	T	G	C	C	A	T	T	-	-
S_2	A	T	G	G	C	C	A	T	T	-	-
S_3	A	T	C	-	C	A	A	T	T	T	T
S_4	A	T	C	T	T	C	-	T	T	-	-
S_5	A	C	T	G	A	C	C	-	-	-	-

S_1, S_2, S_3, S_4 and S_5 are aligned

For consistency, once a gap is added, it is never removed.

(Tehran Polytechnic)

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