Smith-Waterman Algorithm and Hardware implementation

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Outline

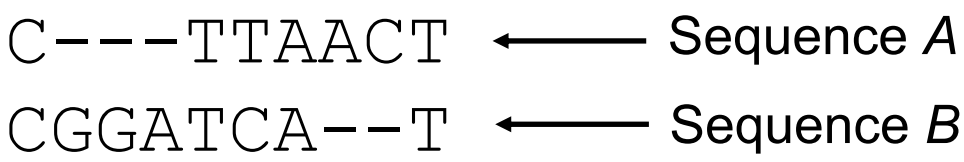
- Pairwise Alignment
  - Overview
  - Simple scoring scheme
  - Example
- Local Alignment
  - Smith-Waterman Algorithm
  - Example
  - Affine Gap
- Hardware Implementation

Pairwise Alignment

Sequence *A* : CTTAACT

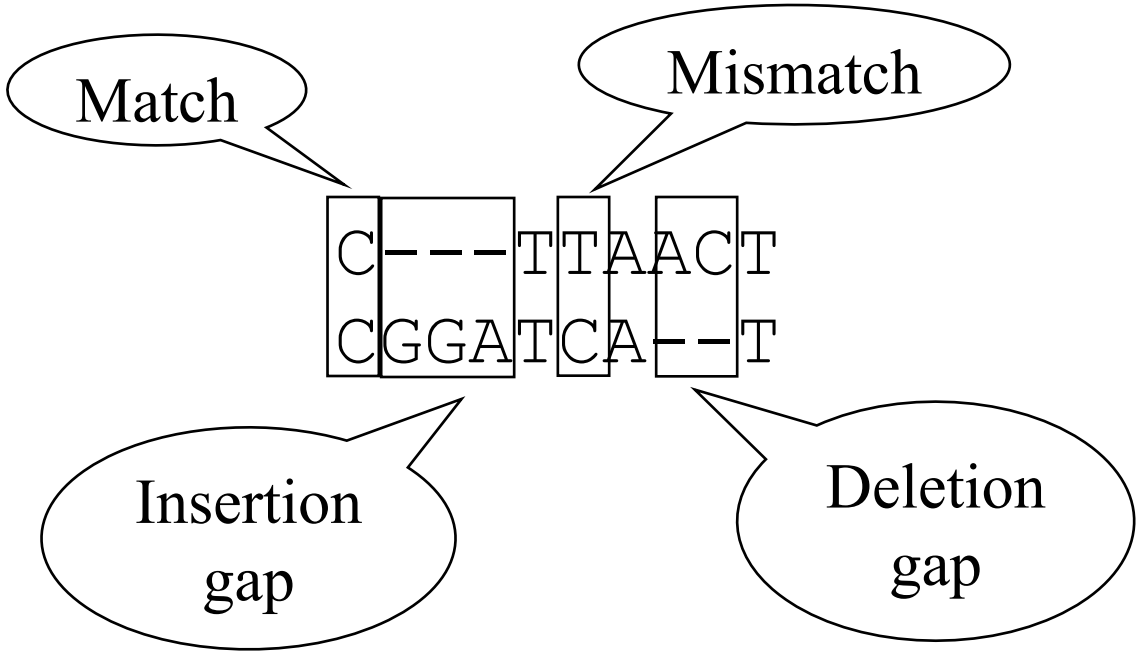
Sequence *B* : CGGATCAT

An alignment of *A* and *B* :

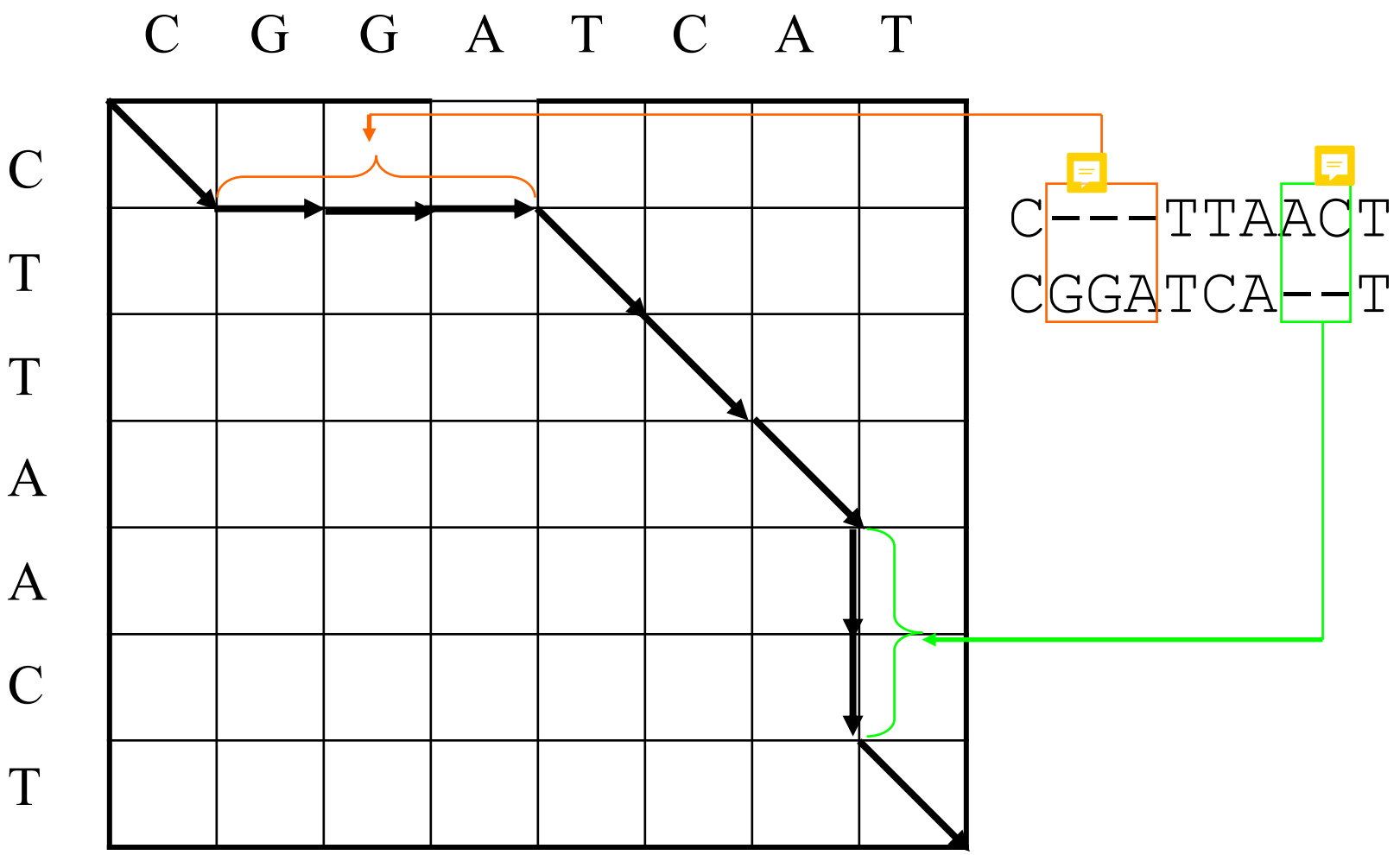


Pairwise Alignment

An alignment of *A* and *B* :



Alignment Graph



Scoring Scheme

- Match = +8
- Mismatch = -5
- Each Gap = -3

C	–	–	–	T	T	A	A	C	T	
C	G	G	A	T	C	A	–	–	T	
+8	-3	-3	-3	+8	-5	+8	-3	-3	+8	= +12

Scoring Scheme

- Let $A = a_1a_2\ldots a_m$ and $B = b_1b_2\ldots b_n$
- $S_{i,j}$: the score of an optimal alignment between $a_1a_2\ldots a_i$ and $b_1b_2\ldots b_j$

$$s_{i,j} = \max \begin{cases} s_{i-1,j} + w(a_i, -) \\ s_{i,j-1} + w(-, b_j) \\ s_{i-1,j-1} + w(a_i, b_j) \end{cases}$$

Gap Penalty

Match / Mismatch

Example

Match : 8

Mismatch : -5

Gap penalty : -3

C A A T – T G A

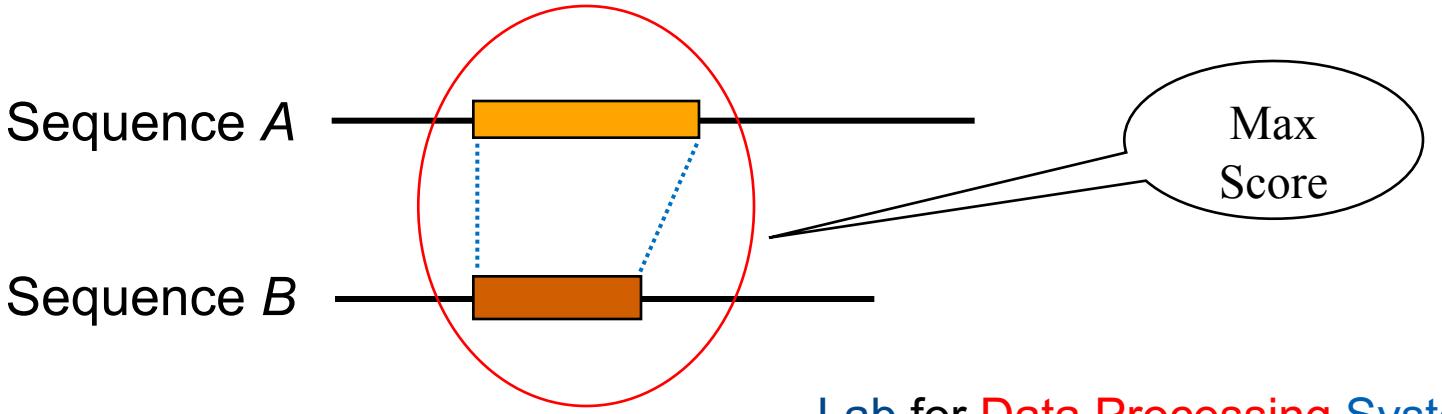
G A A T C T G C

		G	A	A	T	C	T	G	C
	0	-3	-6	-9	-12	-15	-18	-21	-24
C	-3	-5	-8	-11	-14	-4	-7	-10	-13
A	-6	-8	3	0	-3	-6	-9	-12	-15
A	-9	-11	0	11	8	5	2	-1	-4
T	-12	-14	-3	8	19	16	13	10	7
T	-15	-17	-6	5	16	14	24	21	18
G	-18	-7	-9	2	13	11	21	32	29
A	-21	-10	1	-1	10	8	18	29	27

Local Alignment

- Global Alignment

- Local Alignment



Smith-Waterman Algorithm

- Let $A = a_1a_2\ldots a_m$ and $B = b_1b_2\ldots b_n$
- $S_{i,j}$: the score of an optimal alignment between $a_1a_2\ldots a_i$ and $b_1b_2\ldots b_j$

$$s_{i,j} = \max \begin{cases} 0 \\ s_{i-1,j} + w(a_i, -) \\ s_{i,j-1} + w(-, b_j) \\ s_{i-1,j-1} + w(a_i, b_j) \end{cases}$$

Initial Condition

Match : 8

Mismatch : -5

Gap penalty : -3

		G	A	A	T	C	T	G	C
	0	0	0	0	0	0	0	0	0
C	0								
A	0								
A	0								
T	0								
T	0								
G	0								
A	0								

Example

Match : 8

Mismatch : -5

Gap penalty : -3

		G	A	A	T	C	T	G	C
	0	0	0	0	0	0	0	0	0
C	0	0	0	0	0	8	5	2	8
A	0	0	8	8	5	5	3	0	5
A	0	0	8	16	13	10	7	4	2
T	0	0	5	13	24	21	18	15	12
T	0	0	2	10	21	24-5=19 21-3=18 21-3=18			
G									
A									

Example

Match : 8

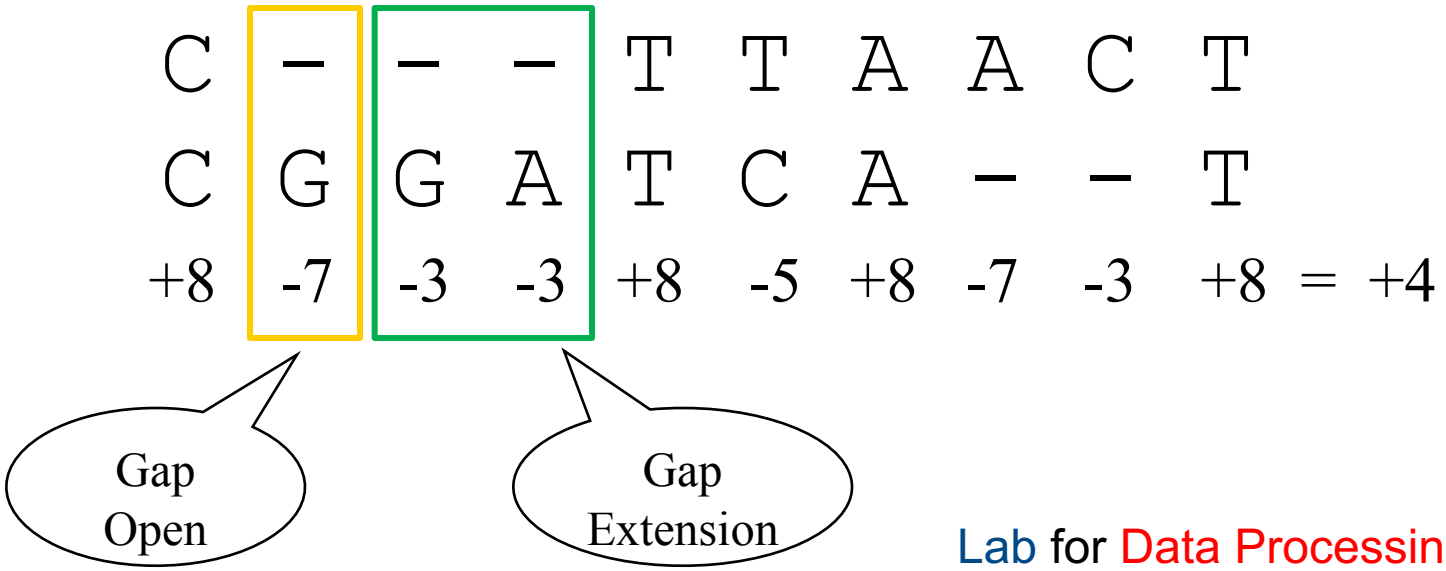
Mismatch : -5

Gap penalty : -3

		G	A	A	T	C	T	G	C
	0	0	0	0	0	0	0	0	0
C	0	0	0	0	0	8	5	2	8
A	0	0	8	8	5	5	3	0	5
A	0	0	8	16	13	10	7	4	2
T	0	0	5	13	24	21	18	15	12
T	0	0	2	10	21	19	29	26	23
G	0	8	5	7	18	16	26	37	34
A	0	5	16	13	15	13	23	34	32

Affine Gap

- Match : +8
- Mismatch : -5
- ***Gap Open*** : -7
- Gap extension : -3



Affine Gap Penalty

$$D(i,j) = \max\begin{cases} D(i-1,j) - gap\_ext \\ S(i-1,j) - gap\_open \end{cases}$$

$$I(i,j) = \max\begin{cases} I(i,j-1) - gap\_ext \\ S(i,j-1) - gap\_open \end{cases}$$

$$S(i,j) = \max\begin{cases} S(i-1,j-1) + w(a_i, b_j) \\ D(i,j) \\ I(i,j) \\ 0 \end{cases}$$

Hardware Implementation

Hardware Implementation

- Sequence : S & T
- Gap open penalty = α
- Gap extension penalty = β

Hardware Implementation

- Rewrite the equation :

$$E(i,j) = \max\begin{cases} E(i,j-1) - \beta \\ V(i,j-1) - \alpha \end{cases}$$

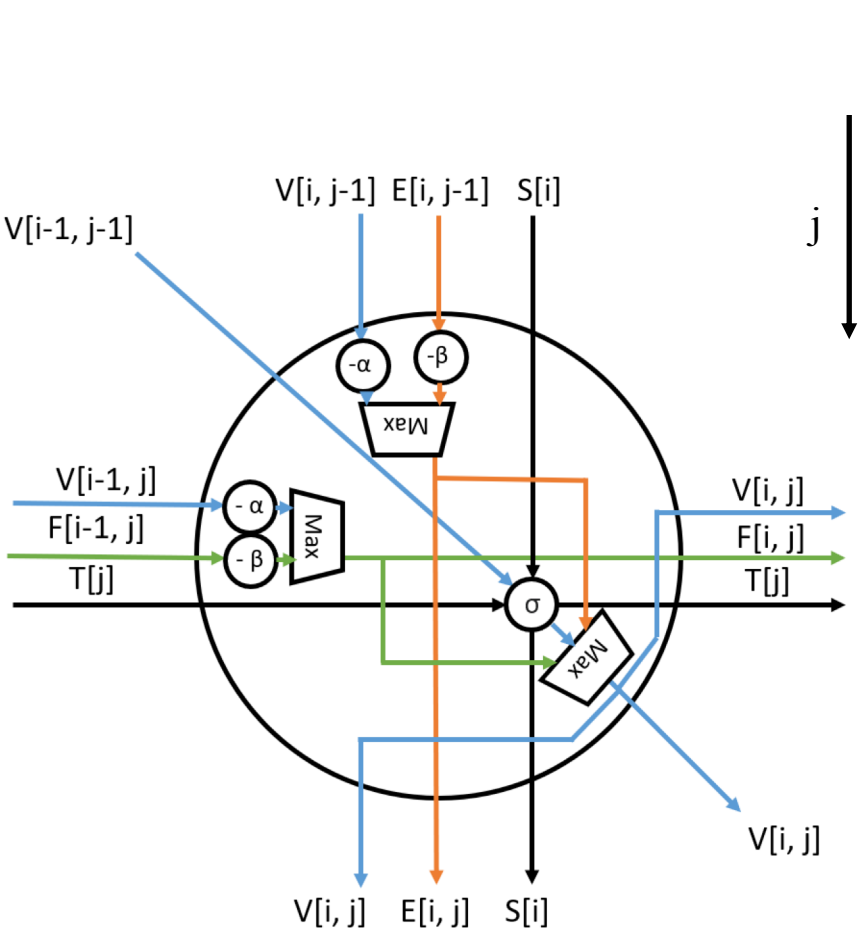
$$F(i,j) = \max\begin{cases} F(i-1,j) - \beta \\ V(i-1,j) - \alpha \end{cases}$$

$$V(i,j) = \max\begin{cases} V(i-1,j-1) + \sigma(S_i, T_j) \\ E(i,j) \\ F(i,j) \\ 0 \end{cases}$$

- Initial Condition
  - E[*,0] = -inf
  - F[0,*] = -inf
  - V[0,*] = 0
  - V[*,0] = 0

➢ *E[*,0], F[0,*] can be assigned as 0 as well*

PE design

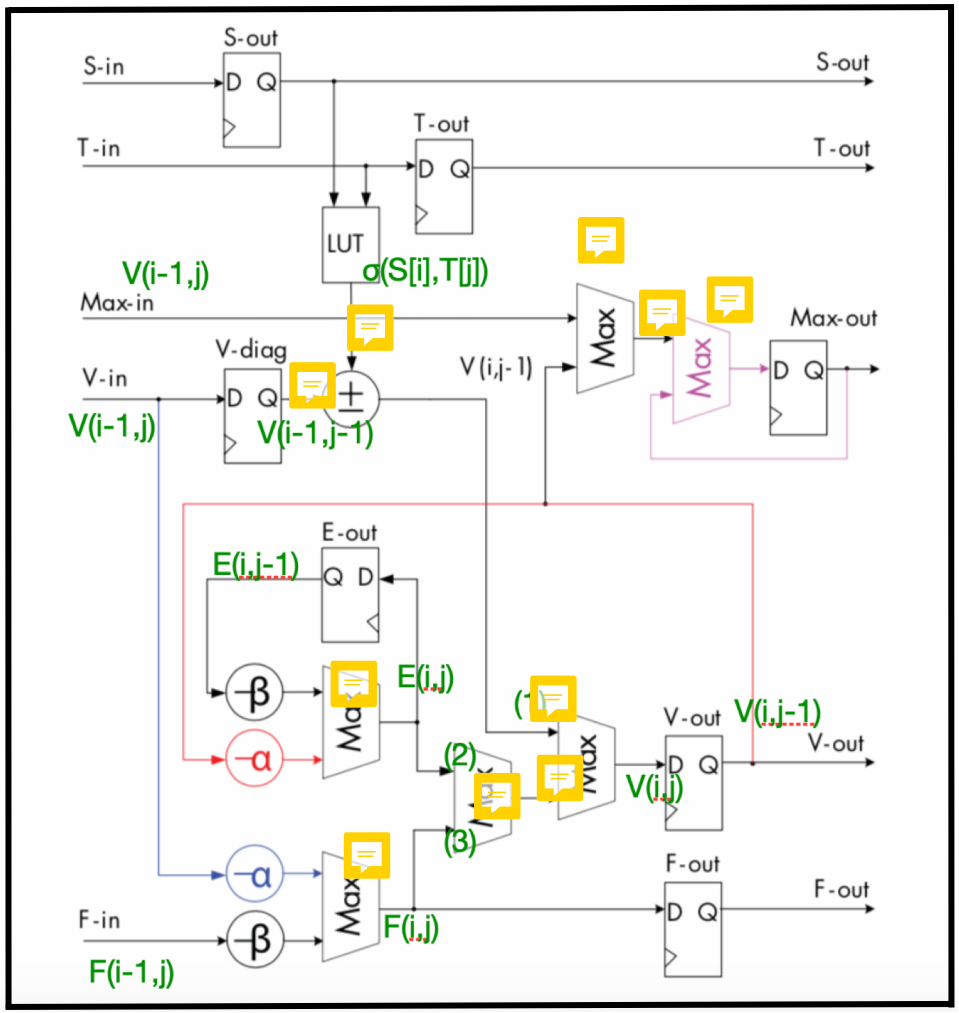


$$E(i,j) = \max\begin{cases} E(i,j-1) - \beta \\ V(i,j-1) - \alpha \end{cases}$$

$$F(i,j) = \max\begin{cases} F(i-1,j) - \beta \\ V(i-1,j) - \alpha \end{cases}$$

$$V(i,j) = \max\begin{cases} V(i-1,j-1) + \sigma(S_i, T_j) \\ E(i,j) \\ F(i,j) \\ 0 \end{cases}$$

PE design



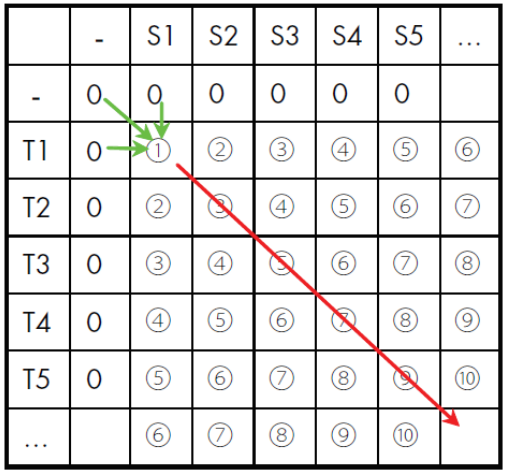
$$E(i,j)=\max\begin{cases}E(i,j-1)-\beta\\V(i,j-1)-\alpha\end{cases}$$

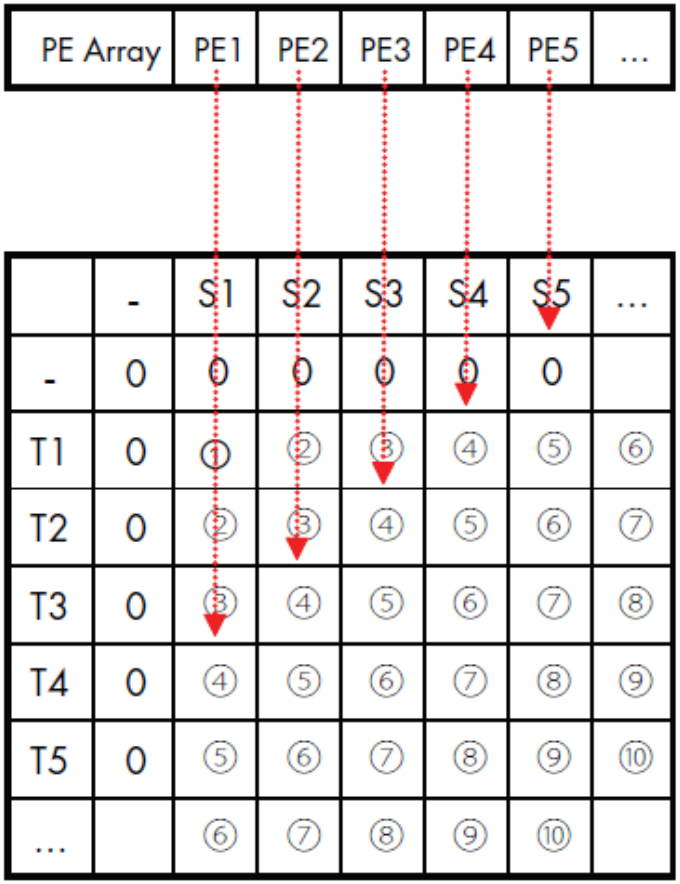
$$F(i,j)=\max\begin{cases}F(i-1,j)-\beta\\V(i-1,j)-\alpha\end{cases}$$

$$V(i,j)=\max\begin{cases}V(i-1,j-1)+\sigma(S_i,T_j)\\E(i,j)\\F(i,j)\\0\end{cases}$$

Parallelization

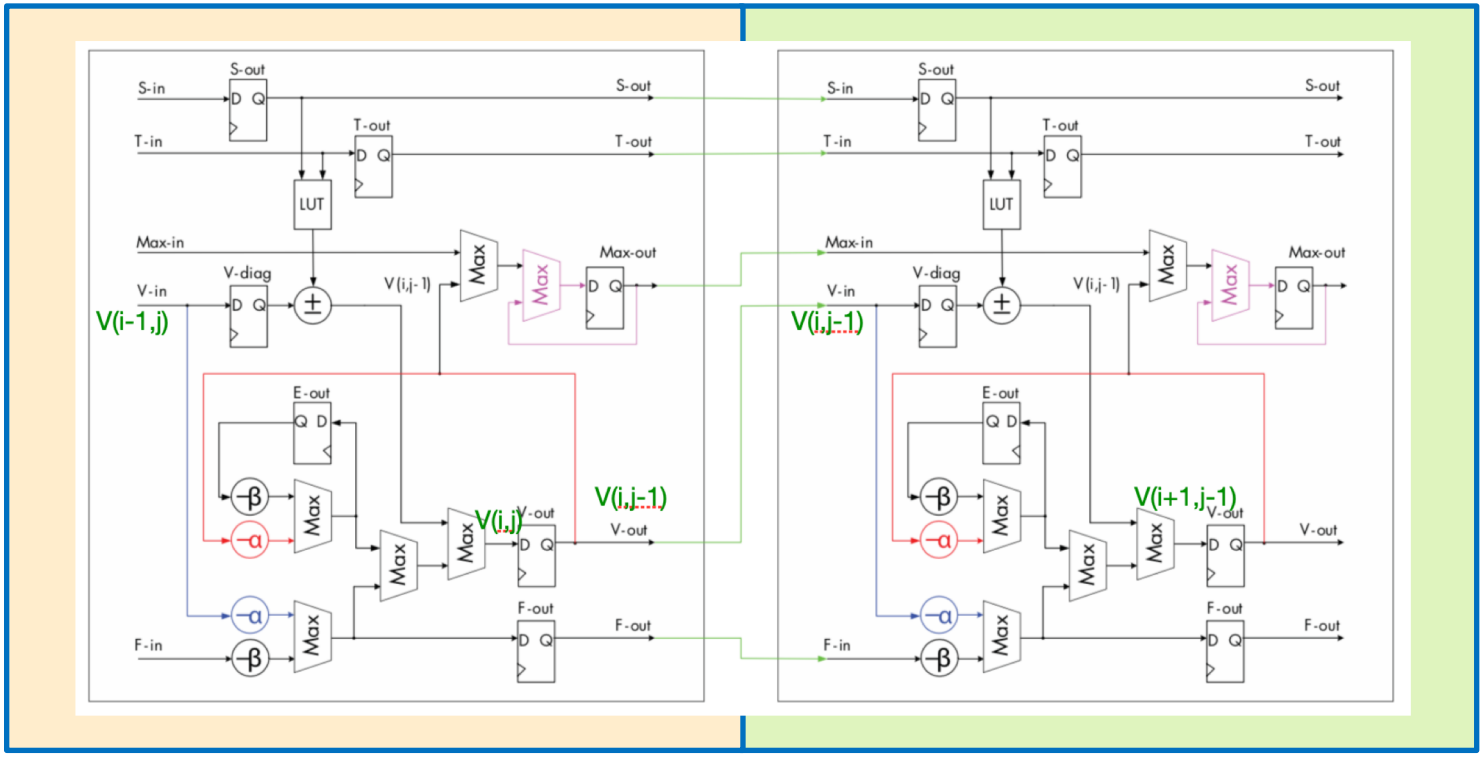
- Every node can be assigned value when it's upper, left, upper left nodes have value
- Which implies that it has a very good potential parallelity





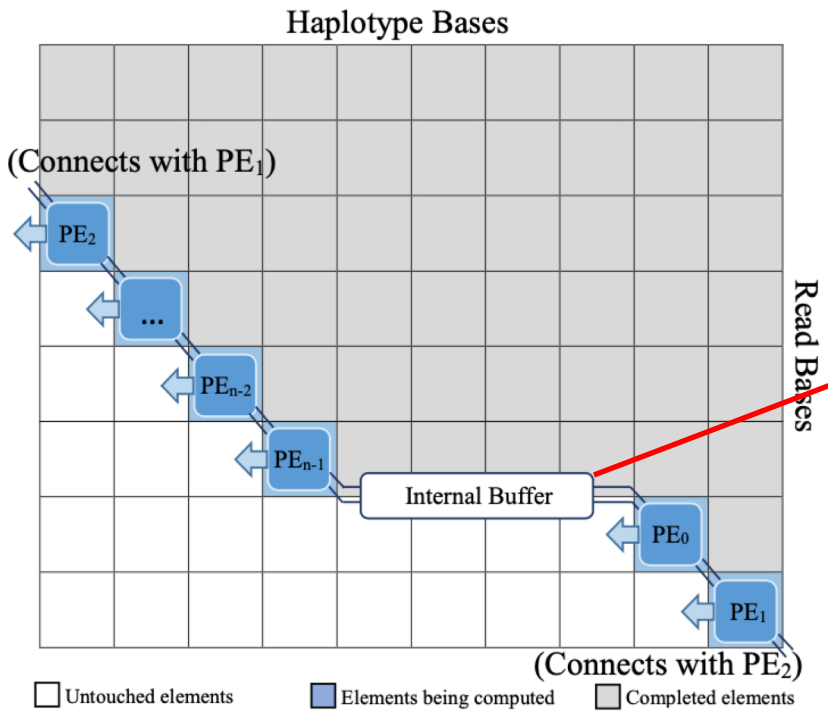
Architecture

- Example for combining PE :



Architecture

- When number of PEs < len(sequence)



Record boundary value

Spec

- Length of sequence S = 256
- Length of sequence T = 256

- Number of PEs = 128

- Scoring Scheme :
  - Match = +8
  - Mismatch = -5
  - Gap_open(α) = -7
  - Gap_ext(β) = -3

Spec

- Input : Sequence S & Sequence T
- Output : Max alignment score

Some Idea

- How many bits to store sequence ?
- Max bit number of the score matrix ?
- How to store the boundary ?

Example

- Length of sequence S = 10
  - ACCTTAGGCA
- Length of sequence T = 10
  - GCCGGTTGCT

Golden

E		G	C	C	G	G	T	T	G	C	T
		-∞	-∞	-∞	-∞	-∞	-∞	-∞	-∞	-∞	-∞
A	-	-7	-7	-7	-7	-7	-7	-7	-7	-7	-7
C	-	-7	-7	-7	-7	-7	-7	-7	-7	-7	-7
C	-	-7	1	1	-6	-7	-7	-7	-7	1	-6
T	-	-7	1	9	2	-1	-4	-7	-7	1	-4
T	-	-7	-2	6	4	-3	7	4	-3	-2	9
A	-	-7	-5	3	1	-1	5	15	8	5	6
G	-	-7	-7	0	-2	-4	2	12	10	3	3
G	-	1	-6	-3	4	2	-1	9	16	9	6
C	-	1	-4	-6	1	12	5	6	13	11	4
A	-	-2	9	4	-1	9	7	3	10	21	14

Golden

F		G	C	C	G	G	T	T	G	C	T
		-	-	-	-	-	-	-	-	-	-
A	-∞	-7	-7	-7	-7	-7	-7	-7	-7	-7	-7
C	-∞	-7	-7	1	1	-2	-5	-7	-7	-7	1
C	-∞	-7	-7	1	9	6	3	0	-3	-6	1
T	-∞	-7	-7	-6	2	4	1	7	4	1	-2
T	-∞	-7	-7	-7	-1	-3	-1	5	15	12	9
A	-∞	-7	-7	-7	-4	-6	-7	-2	8	10	7
G	-∞	-7	1	-2	-5	4	2	-1	5	16	13
G	-∞	-7	1	-2	-5	1	12	9	6	13	11
C	-∞	-7	-6	9	6	3	5	7	4	6	21
A	-∞	-7	-7	2	4	1	2	0	2	3	14

Golden

V		G	C	C	G	G	T	T	G	C	T
		0	0	0	0	0	0	0	0	0	0
A	0	0	0	0	0	0	0	0	0	0	0
C	0	0	8	8	1	0	0	0	0	8	1
C	0	0	8	16	9	6	3	0	0	8	3
T	0	0	1	9	11	4	14	11	4	1	16
T	0	0	0	6	4	6	12	22	15	12	9
A	0	0	0	3	1	0	5	15	17	10	7
G	0	8	1	0	11	9	2	12	23	16	13
G	0	8	3	0	8	19	12	9	20	18	11
C	0	1	16	11	6	12	14	7	13	28	21
A	0	0	9	11	6	9	7	9	10	21	23

Reference

- Kun-Mao Chao, Algorithms for Biological Sequence Analysis class note, the Department of Computer Science and Information Engineering, National Taiwan University (NTU), Taipei, Taiwan, 2020.

- Zhang, Peiheng, Guangming Tan, and Guang R. Gao. "Implementation of the Smith-Waterman algorithm on a reconfigurable supercomputing platform." *Proceedings of the 1st international workshop on High-performance reconfigurable computing technology and applications: held in conjunction with SC07*. 2007.