Pairwise Alignment

Anything can align to anything…

BIOL 435/535: Bioinformatics

January 25, 2021

With enough gaps, any sequence can be aligned to any other sequence

```
Seq1 — ABCNJROCLCRPM
Seq2 — AJCJNRCKCRBP
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With enough gaps, any sequence can be aligned to any other sequence

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Seq1 — ABCNJROCLCR-PM
Seq2 — AJCJNR-CKCRBP-
```
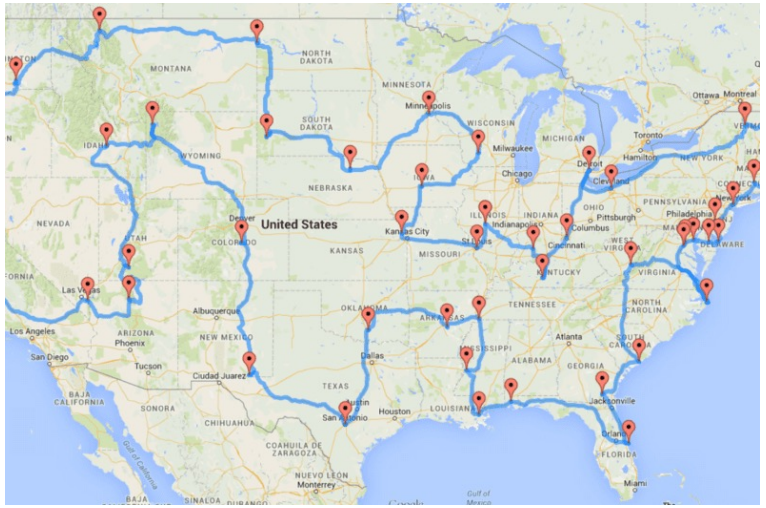

Seems reasonable…

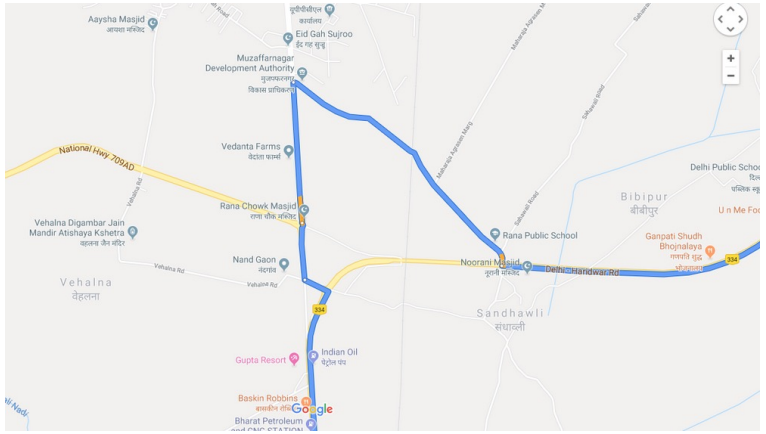
but not systematic/repeatable

How best to align two sequences

- **Global alignment** –
  - Best overall alignment from end-to-end



- **Local alignment** –
  - Short regions of the sequences that have homology



Needleman & Wunsch Global Pairwise Alignment

- Construct scoring matrix starting at origin
- Trace path through scoring matrix by selecting local maximum (start at bottom right corner, end at origin)

Needleman & Wunsch Global Pairwise Alignment Matrix construction

Rules:

Start at origin at 0

Match (diagonal) = +1

Mismatch (diagonal) = 0

Gap (right or down) = -1

Each cell gets highest possible score from three adjacent cells

		A	B	C	N	J	R	O	C	L	C	R	P	M
	0													
A														
J														
C														
J														
N														
R														
C														
K														
C														
R														
B														
P														

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		A	B	C	N	J	R	O	C	L	C	R	P	M
	0 →	-1 →	-2 →	-3 →	-4 →	-5 →	-6 →	-7 →	-8 →	-9 →	-10 →	-11 →	-12 →	-13
A	-1 ↓													
J	-2 ↓													
C	-3 ↓													
J	-4 ↓													
N	-5 ↓													
R	-6 ↓													
C	-7 ↓													
K	-8 ↓													
C	-9 ↓													
R	-10 ↓													
B	-11 ↓													
P	-12 ↓													

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		A	B	C	N	J	R	O	C	L	C	R	P	M
	0 →	-1 →	-2 →	-3 →	-4 →	-5 →	-6 →	-7 →	-8 →	-9 →	-10 →	-11 →	-12 →	-13
A	-1	1 -2 -2 1												
J	-2													
C	-3													
J	-4													
N	-5													
R	-6													
C	-7													
K	-8													
C	-9													
R	-10													
B	-11													
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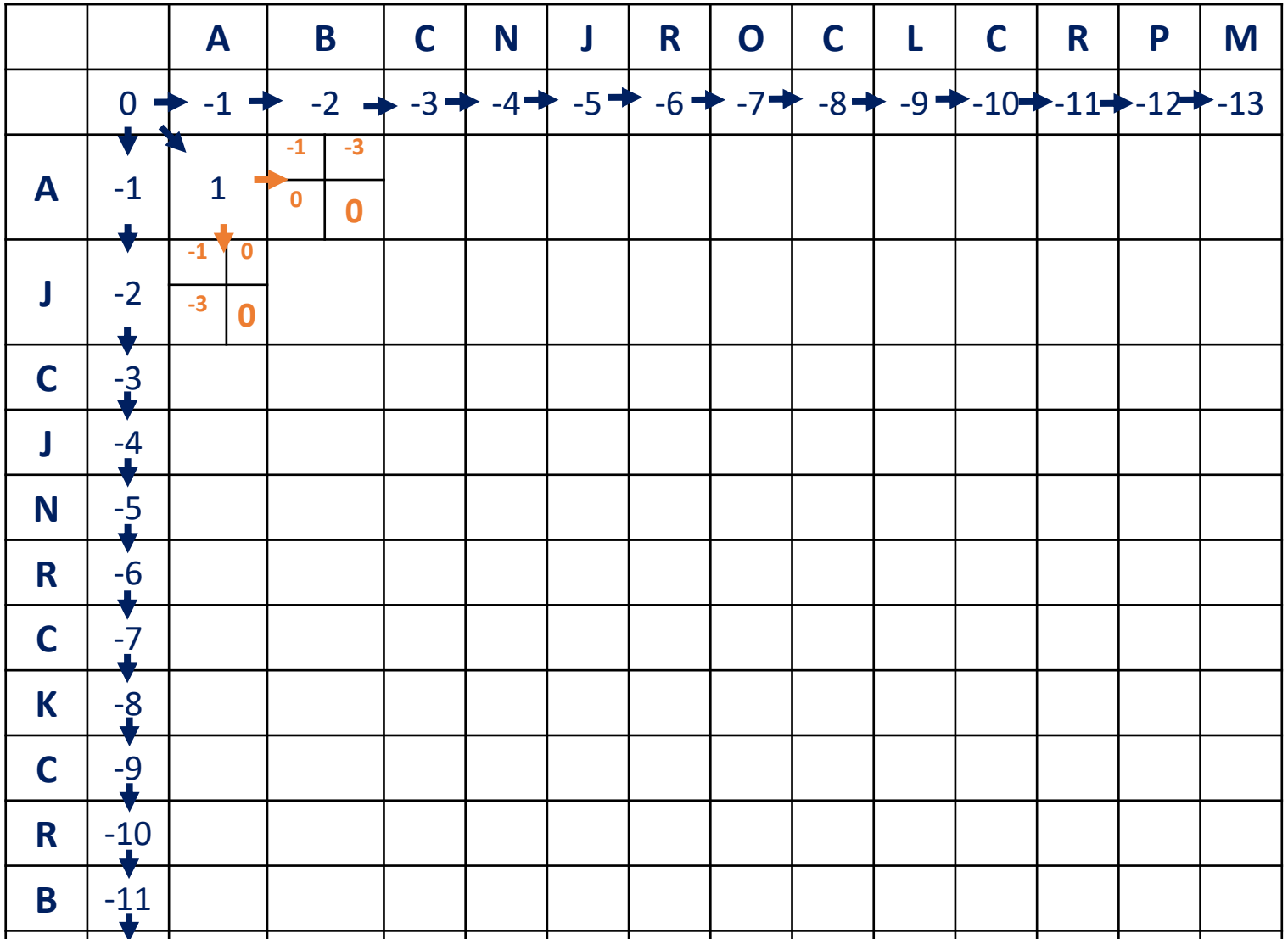

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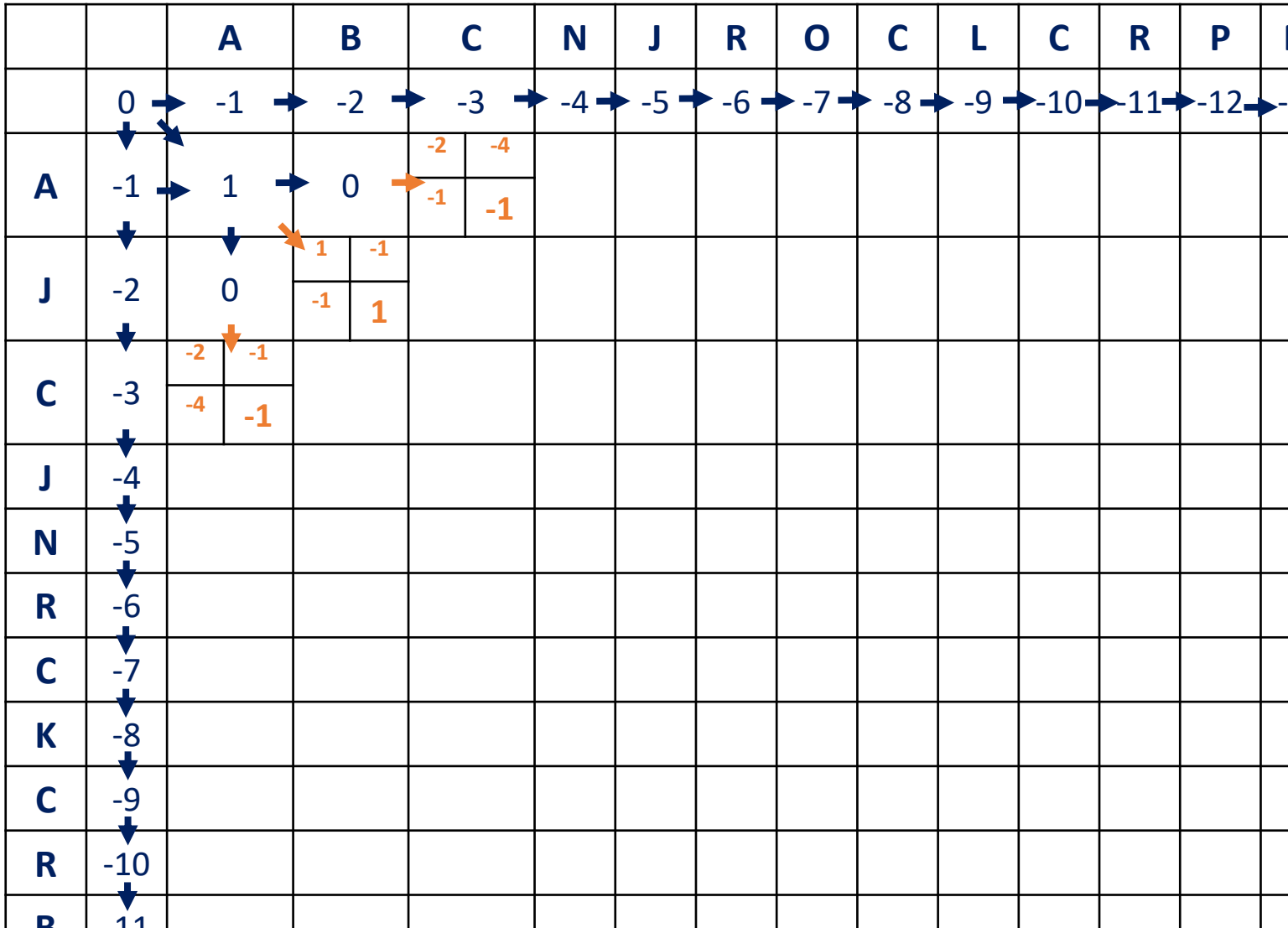

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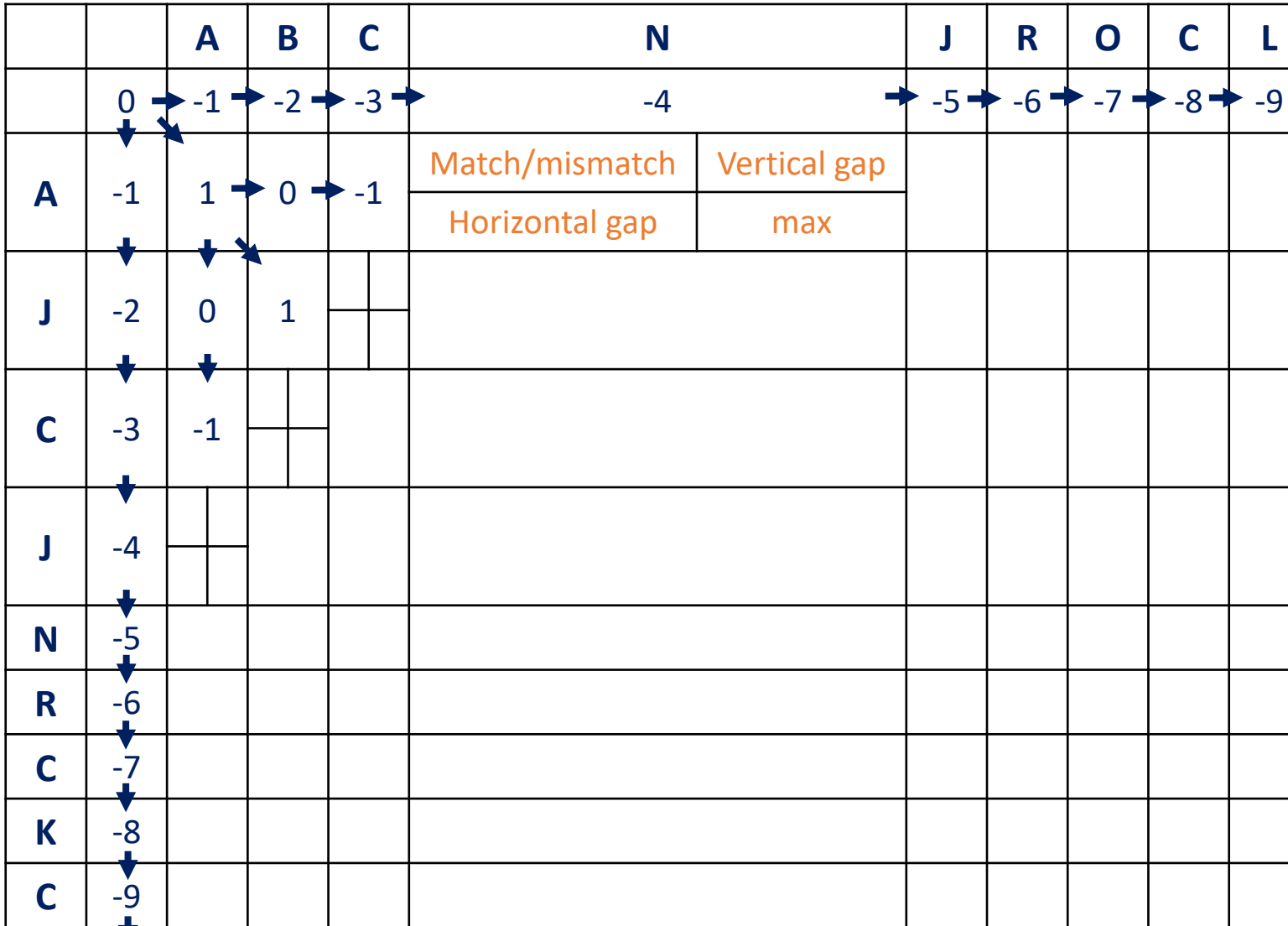

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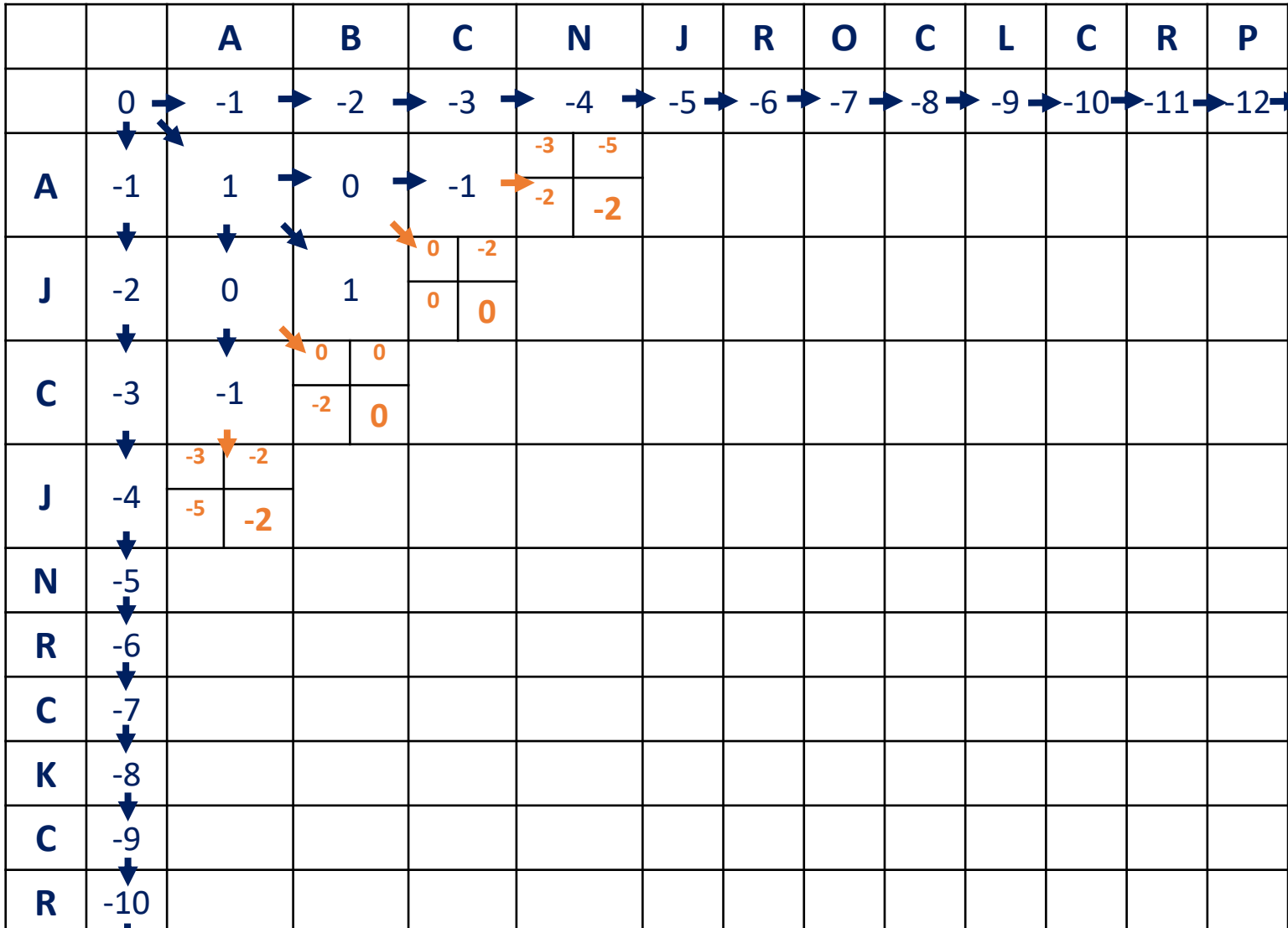

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		A	B	C	N	J	R	O	C	L	C	R	P	M
	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13
A	-1	1	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11
J	-2	0	1	0	-1	-1	-2	-3	-4	-5	-6	-7	-8	-9
C	-3	-1	0	2	1	0	-1	-2	-2	-3	-4	-5	-6	-7
J	-4	-2	-1	1	2	2	1	0	-1	-2	-3	-4	-5	-6
N	-5	-3	-2	0	2	2	2	1	0	-1	-2	-3	-4	-5
R	-6	-4	-3	-1	1	2	3	2	1	0	-1	-1	-2	-3
C	-7	-5	-4	-2	0	1	2	3	3	2	1	0	-1	-2
K	-8	-6	-5	-3	-1	0	1	2	3	3	2	1	0	-1
C	-9	-7	-6	-4	-2	-1	0	1	3	3	4	3	2	1
R	-10	-8	-7	-5	-3	-2	0	0	2	3	3	5	3	2
B	-11	-9	-7	-6	-4	-3	-1	0	1	2	3	4	4	3
P	-12	-10	-8	-7	-5	-4	-2	-1	0	1	2	3	5	4

Needleman & Wunsch Global Pairwise Alignment Traceback

Rules:

Start at bottom right corner, proceed through highest scoring path at each cell, (follow the arrows)

		A	B	C	N	J	R	O	C	L	C	R	P	M
	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13
A	-1	1	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11
J	-2	0	1	0	-1	-1	-2	-3	-4	-5	-6	-7	-8	-9
C	-3	-1	0	2	1	0	-1	-2	-2	-3	-4	-5	-6	-7
J	-4	-2	-1	1	2	2	1	0	-1	-2	-3	-4	-5	-6
N	-5	-3	-2	0	2	2	2	1	0	-1	-2	-3	-4	-5
R	-6	-4	-3	-1	1	2	3	2	1	0	-1	-1	-2	-3
C	-7	-5	-4	-2	0	1	2	3	3	2	1	0	-1	-2
K	-8	-6	-5	-3	-1	0	1	2	3	3	2	1	0	-1
C	-9	-7	-6	-4	-2	-1	0	1	3	3	4	3	2	1
R	-10	-8	-7	-5	-3	-2	0	0	2	3	3	5	3	2
B	-11	-9	-7	-6	-4	-3	-1	0	1	2	3	4	4	3
P	-12	-10	-8	-7	-5	-4	-2	-1	0	1	2	3	5	

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		A	B	C	N	J	R	O	C	L	C	R	P	M
	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13
A	-1	1	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11
J	-2	0	1	0	-1	-1	-2	-3	-4	-5	-6	-7	-8	-9
C	-3	-1	0	2	1	0	-1	-2	-2	-3	-4	-5	-6	-7
J	-4	-2	-1	1	2	2	1	0	-1	-2	-3	-4	-5	-6
N	-5	-3	-2	0	2	2	2	1	0	-1	-2	-3	-4	-5
R	-6	-4	-3	-1	1	2	3	2	1	0	-1	-1	-2	-3
C	-7	-5	-4	-2	0	1	2	3	3	2	1	0	-1	-2
K	-8	-6	-5	-3	-1	0	1	2	3	3	2	1	0	-1
C	-9	-7	-6	-4	-2	-1	0	1	3	3	4	3	2	1
R	-10	-8	-7	-5	-3	-2	0	0	2	3	3	5	3	2
B	-11	-9	-7	-6	-4	-3	-1	0	1	2	3	4	4	3
P	-12	-10	-8	-7	-5	-4	-2	-1	0	1	2	3	5	

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		A	B	C	N	J	R	O	C	L	C	R	P	M
	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13
A	-1	1	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11
J	-2	0	1	0	-1	-1	-2	-3	-4	-5	-6	-7	-8	-9
C	-3	-1	0	2	1	0	-1	-2	-2	-3	-4	-5	-6	-7
J	-4	-2	-1	1	2	2	1	0	-1	-2	-3	-4	-5	-6
N	-5	-3	-2	0	2	2	2	1	0	-1	-2	-3	-4	-5
R	-6	-4	-3	-1	1	2	3	2	1	0	-1	-1	-2	-3
C	-7	-5	-4	-2	0	1	2	3	3	2	1	0	-1	-2
K	-8	-6	-5	-3	-1	0	1	2	3	3	2	1	0	-1
C	-9	-7	-6	-4	-2	-1	0	1	3	3	4	3	2	1
R	-10	-8	-7	-5	-3	-2	0	0	2	3	3	5	3	2
B	-11	-9	-7	-6	-4	-3	-1	0	1	2	3	4	4	3
P	-12	-10	-8	-7	-5	-4	-2	-1	0	1	2	3	5	

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Rules:

Start at bottom right corner, proceed through highest scoring path at each cell, (follow the arrows)

		A	B	C	N	J	R	O	C	L	C	R	P	M
	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11	-12	-13
A	-1	1	0	-1	-2	-3	-4	-5	-6	-7	-8	-9	-10	-11
J	-2	0	1	0	-1	-1	-2	-3	-4	-5	-6	-7	-8	-9
C	-3	-1	0	2	1	0	-1	-2	-2	-3	-4	-5	-6	-7
J	-4	-2	-1	1	2	2	1	0	-1	-2	-3	-4	-5	-6
N	-5	-3	-2	0	2	2	2	1	0	-1	-2	-3	-4	-5
R	-6	-4	-3	-1	1	2	3	2	1	0	-1	-1	-2	-3
C	-7	-5	-4	-2	0	1	2	3	3	2	1	0	-1	-2
K	-8	-6	-5	-3	-1	0	1	2	3	3	2	1	0	-1
C	-9	-7	-6	-4	-2	-1	0	1	3	3	4	3	2	1
R	-10	-8	-7	-5	-3	-2	0	0	2	3	3	5	3	2
B	-11	-9	-7	-6	-4	-3	-1	0	1	2	3	4	4	3
P	-12	-10	-8	-7	-5	-4	-2	-1	0	1	2	3	5	

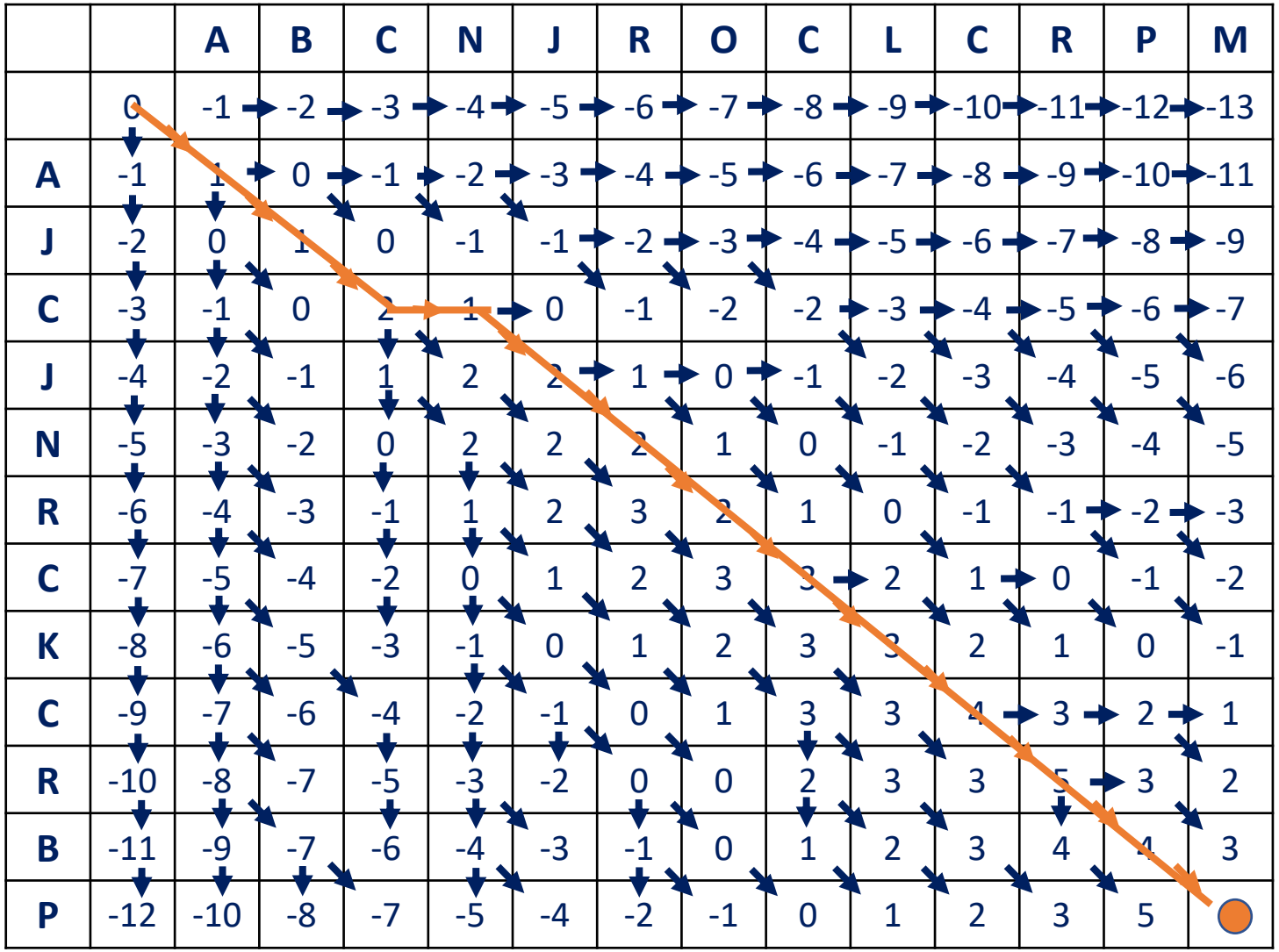
Needleman & Wunsch Global Pairwise Alignment Traceback

Rules:

Start at bottom right corner, proceed through highest scoring path at each cell, (tie goes to the diagonal)

ABCNJROCLCRPM

AJC–JNRCKCRBP



Smith & Waterman Local Pairwise Alignment

- Construct scoring matrix (no negative numbers, lowest cell score possible is 0)
- Trace path through scoring matrix by selecting local maximum (start at global high score, trace toward origin until hitting a 0)

Smith & Waterman Local Pairwise Alignment Traceback

Rules:

Start at highest score, proceed through highest scoring path at each cell, (through the source from each cell), until you hit a 0

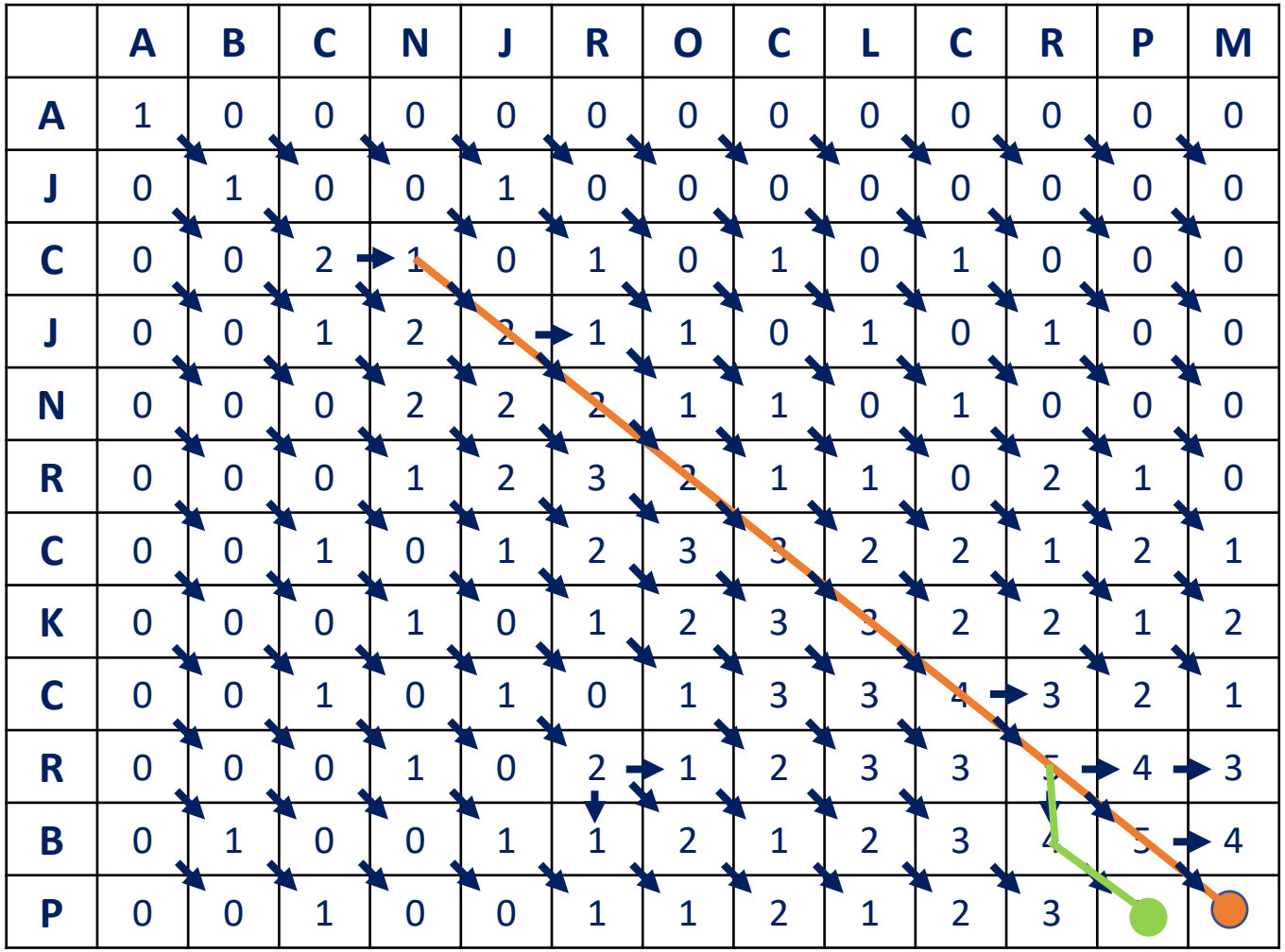
NJROCLCRPM

CJNRCKCRBP

or

NJROCLCR–P

CJNRCKCRBP



	A	B	C	N	J	R	O	C	L	C	R	P	M
A	1	0	0	0	0	0	0	0	0	0	0	0	0
J	0	1	0	0	1	0	0	0	0	0	0	0	0
C	0	0	2	1	0	1	0	1	0	1	0	0	0
J	0	0	1	2	2	1	1	0	1	0	1	0	0
N	0	0	0	2	2	2	1	1	0	1	0	0	0
R	0	0	0	1	2	3	2	1	1	0	2	1	0
C	0	0	1	0	1	2	3	2	2	1	1	2	1
K	0	0	0	1	0	1	2	3	3	2	2	1	2
C	0	0	1	0	1	0	1	3	3	4	3	2	1
R	0	0	0	1	0	2	1	2	3	3	4	4	3
B	0	1	0	0	1	1	2	1	2	3	4	5	4
P	0	0	1	0	0	1	1	2	1	2	3		

Practice Run!

Go to GitHub page, download activity ppt

Next up: Multiple Sequence Alignment

Download MEGA

Homework #2 will be posted this afternoon

Please read: Needleman & Wunsch 1970, Smith & Waterman 1981