**BIOINFORMATYKA**

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wykład 5

# Dopasowanie par sekwencji (2)

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# Plan wykładu

1. Macierze substytucji
2. Znaczenie kary za otwarcie przerwy - model afiniczny
3. Algorytm o liniowej złożoności pamięciowej
4. Dopasowanie lokalne - algorytm Smitha-Watermana

# Macierze substytucji

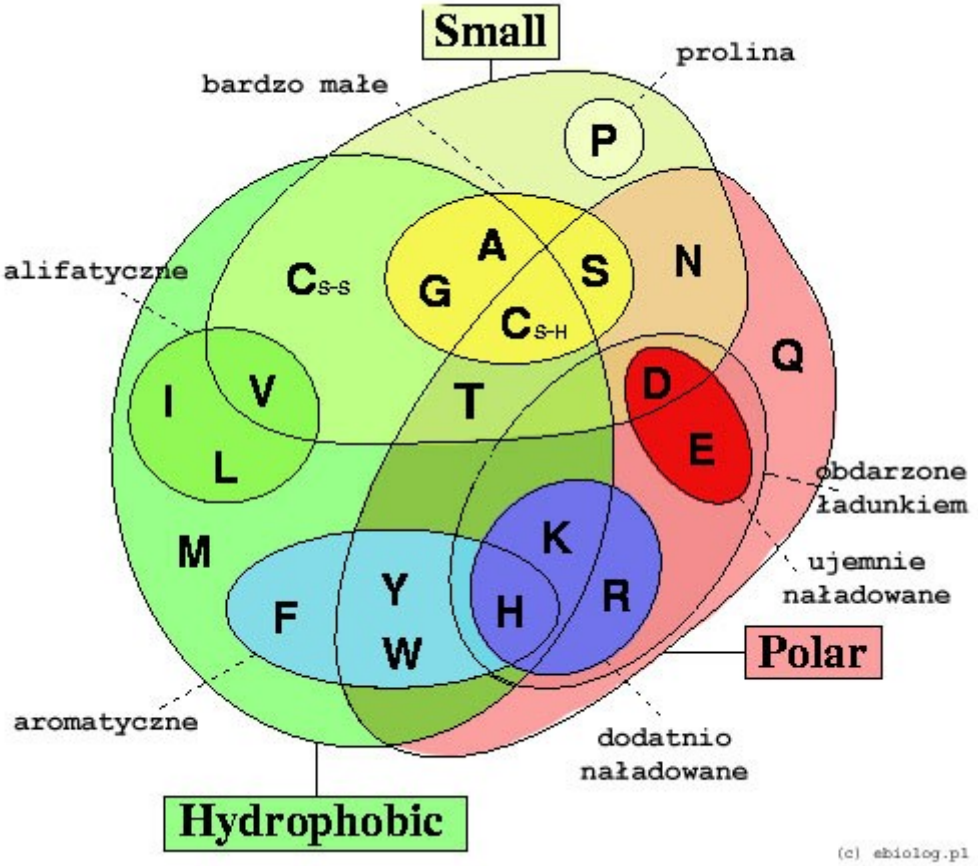
# Cel konstrukcji macierzy substytucji

Uwzględnienie w dopasowaniach rzeczywistych częstości substytucji pomiędzy różniącymi się aminokwasami.

Każdy aminokwas ma inne właściwości.

Niektóre pod pewnymi względami są do siebie podobne.

Substytucje między aminokwasami podobnymi są bardziej prawdopodobne.



# Macierze PAM

PAM = *Point Accepted Mutation*

Macierze oparte na modelu ewolucyjnym akceptowanych (możliwych do zaistnienia) mutacji punktowych.

1 jednostka PAM – stopień zróżnicowania ewolucyjnego, w którym zmienił się 1% aminokwasów.

Dla zdefiniowania wartości PAM, wprowadzono pojęcia:
- Częstość tła – częstość zmian „przypadkowych”
- Częstość docelowa – częstość substytucji; obrazuje zmiany pojawiające się w białkach spokrewnionych

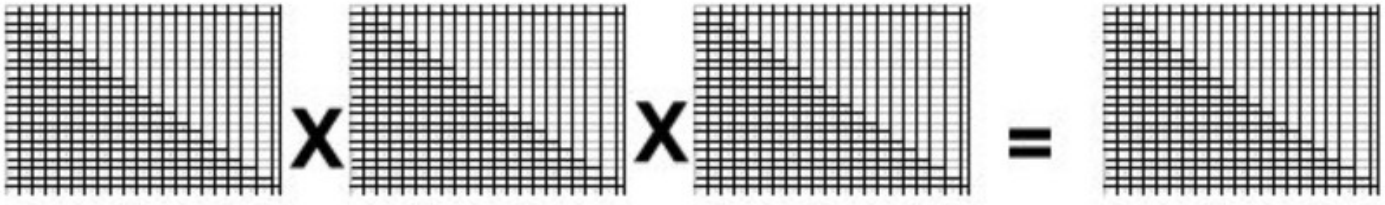
# Macierze PAM (2)

Wartości w macierzy są proporcjonalne do logarytmu ilorazu:

*częstość docelowa / częstość tła*

Podstawowa macierz (1PAM) zbudowana została na podstawie analizy par blisko spokrewnionych.

Macierz można ekstrapolować do większych odległości ewolucyjnych PAM.




Multiply Matrices N times to make PAM "X"; then take the Log

„Duże" PAM (np. PAM 250) stosuje się do porównywania sekwencji o dużym stopniu dywergencji ewolucyjnej.

„Małe" PAM do badania sekwencji podobnych.

# Oryginalne macierze Dayhoff

W 1978 roku Dayhoff, Schwartz i Orcutt przeanalizowali 1572 możliwe mutacje pomiędzy 71 grupami blisko spokrewnionych sekwencji (>85% identyczności).

Zobacz też: https://www.inf.ethz.ch/personal/gonnet/DarwinManual/node151.html

| | | Ala | Arg | Asn | Asp | Cys | Gln | Glu | Gly | His | Ile | Leu | Lys | Met | Phe | Pro | Ser | Thr | Trp | Tyr | Val |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | A | R | N | D | C | Q | E | G | H | I | L | K | M | F | P | S | T | W | Y | V |
| Ala | A | 9867 | 2 | 9 | 10 | 3 | 8 | 17 | 21 | 2 | 6 | 4 | 2 | 6 | 2 | 22 | 35 | 32 | 0 | 2 | 18 |
| Arg | R | 1 | 9913 | 1 | 0 | 1 | 10 | 0 | 0 | 10 | 3 | 1 | 19 | 4 | 1 | 4 | 6 | 1 | 8 | 0 | 1 |
| Asn | N | 4 | 1 | 9822 | 36 | 0 | 4 | 6 | 6 | 21 | 3 | 1 | 13 | 0 | 1 | 2 | 20 | 9 | 1 | 4 | 1 |
| Asp | D | 6 | 0 | 42 | 9859 | 0 | 6 | 53 | 6 | 4 | 1 | 0 | 3 | 0 | 0 | 1 | 5 | 3 | 0 | 0 | 1 |
| Cys | C | 1 | 1 | 0 | 0 | 9973 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 5 | 1 | 0 | 3 | 2 |
| Gln | Q | 3 | 9 | 4 | 5 | 0 | 9876 | 27 | 1 | 23 | 1 | 3 | 6 | 4 | 0 | 6 | 2 | 2 | 0 | 0 | 1 |
| Glu | E | 10 | 0 | 7 | 56 | 0 | 35 | 9865 | 4 | 2 | 3 | 1 | 4 | 1 | 0 | 3 | 4 | 2 | 0 | 1 | 2 |
| Gly | G | 21 | 1 | 12 | 11 | 1 | 3 | 7 | 9935 | 1 | 0 | 1 | 2 | 1 | 1 | 3 | 21 | 3 | 0 | 0 | 5 |
| His | H | 1 | 8 | 18 | 3 | 1 | 20 | 1 | 0 | 9912 | 0 | 1 | 1 | 0 | 2 | 3 | 1 | 1 | 1 | 4 | 1 |
| Ile | I | 2 | 2 | 3 | 1 | 2 | 1 | 2 | 0 | 0 | 9872 | 9 | 2 | 12 | 7 | 0 | 1 | 7 | 0 | 1 | 33 |
| Leu | L | 3 | 1 | 3 | 0 | 0 | 6 | 1 | 1 | 4 | 22 | 9947 | 2 | 45 | 13 | 3 | 1 | 3 | 4 | 2 | 15 |
| Lys | K | 2 | 37 | 25 | 6 | 0 | 12 | 7 | 2 | 2 | 4 | 1 | 9926 | 20 | 0 | 3 | 8 | 11 | 0 | 1 | 1 |
| Met | M | 1 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 8 | 4 | 9874 | 1 | 0 | 1 | 2 | 0 | 0 | 4 |
| Phe | F | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 2 | 8 | 6 | 0 | 4 | 9946 | 0 | 2 | 1 | 3 | 28 | 0 |
| Pro | P | 13 | 5 | 2 | 1 | 1 | 8 | 3 | 2 | 5 | 1 | 2 | 2 | 1 | 1 | 9926 | 12 | 4 | 0 | 0 | 2 |
| Ser | S | 28 | 11 | 34 | 7 | 11 | 4 | 6 | 16 | 2 | 2 | 1 | 7 | 4 | 3 | 17 | 9840 | 38 | 5 | 2 | 2 |
| Thr | T | 22 | 2 | 13 | 4 | 1 | 3 | 2 | 2 | 1 | 11 | 2 | 8 | 6 | 1 | 5 | 32 | 9871 | 0 | 2 | 9 |
| Trp | W | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 9976 | 1 | 0 |
| Tyr | Y | 1 | 0 | 3 | 0 | 3 | 0 | 1 | 0 | 4 | 1 | 1 | 0 | 0 | 21 | 0 | 1 | 1 | 2 | 9945 | 1 |
| Val | V | 13 | 2 | 1 | 1 | 3 | 2 | 2 | 3 | 3 | 57 | 11 | 1 | 17 | 1 | 3 | 2 | 10 | 0 | 2 | 9901 |

Macierz prawdopodobieństwa mutacji będąca podstawą konstrukcji PAM1.

# PAM 30

```
Diagonal: Min:   6.0  Max:  13.0  Mean:  8.20  Sigma: 1.81
Rest:     Min: -17.0  Max:   2.0  Mean: -6.47  Sigma: 4.14
Matrix:   Min: -17.0  Max:  13.0  Mean: -5.08  Sigma: 5.87

  A   R   N   D   C   Q   E   G   H   I   L   K   M   F   P   S   T   W   Y   V   B   Z   X ..
  6  -7  -4  -3  -6  -4  -2  -2  -7  -5  -6  -7  -5  -8  -2   0  -1 -13  -8  -2  -3  -3  -3   A
      8  -6 -10  -8  -2  -9  -9  -2  -5  -8   0  -4  -9  -4  -3  -6  -2 -10  -8  -7  -4  -6   R
          8   2 -11  -3  -2  -3   0  -5  -7  -1  -9  -9  -6   0  -2  -8  -4  -8   6  -3  -3   N
              8 -14  -2   2  -3  -4  -7 -12  -4 -11 -15  -8  -4  -5 -15 -11  -8   6   1  -5   D
                 10 -14 -14  -9  -7  -6 -15 -14 -13 -13  -8  -3  -8 -15  -4  -6 -12 -14  -9   C
                      8   1  -7   1  -8  -5  -3  -4 -13  -3  -5  -5 -13 -12  -7  -3   6  -5   Q
                          8  -4  -5  -5  -9  -4  -7 -14  -5  -4  -6 -17  -8  -6   1   6  -5   E
                             6  -9 -11 -10  -7  -8  -9  -6  -2  -6 -15 -14  -5  -3  -5  -5   G
                                 9  -9  -6  -6 -10  -6  -4  -6  -7  -7  -3  -6  -1  -1  -5   H
                                    8  -1  -6  -1  -2  -8  -7  -2 -14  -6   2  -6  -6  -5   I
                                       7  -8   1  -3  -7  -8  -7  -6  -7  -2  -9  -7  -6   L
                                          7  -2 -14  -6  -4  -3 -12  -9  -9  -2  -4  -5   K
                                             11  -4  -8  -5  -4 -13 -11  -1 -10  -5  -5   M
                                                  9 -10  -6  -9  -4   2  -8 -10 -13  -8   F
                                                     8  -2  -4 -14 -13  -6  -7  -4  -5   P
                                                        6   0  -5  -7  -6  -1  -5  -3   S
                                                           7 -13  -6  -3  -3  -6  -4   T
                                                              13  -5 -15 -10 -14 -11   W
                                                                  10  -7  -6  -9  -7   Y
                                                                      7  -8  -6  -5   V
                                                                         6   0  -5   B
                                                                             6  -5   Z
                                                                                -5   X
```

# PAM 180

```
Diagonal: Min:   3.0  Max:  18.0  Mean:  7.30  Sigma: 3.72
Rest:     Min: -10.0  Max:   7.0  Mean: -2.38  Sigma: 3.06
Matrix:   Min: -10.0  Max:  18.0  Mean: -1.46  Sigma: 4.22
```

| A | R | N | D | C | Q | E | G | H | I | L | K | M | F | P | S | T | W | Y | V | B | Z | X | .. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 | -3 | 0 | 0 | -3 | -1 | 0 | 1 | -2 | -1 | -3 | -2 | -2 | -5 | 1 | 1 | 2 | -8 | -5 | 0 | 0 | 0 | -1 | A |
| | 8 | -1 | -3 | -5 | 1 | -2 | -4 | 2 | -3 | -4 | 4 | -1 | -6 | -1 | -1 | -2 | 2 | -6 | -4 | -2 | 0 | -2 | R |
| | | 4 | 3 | -5 | 0 | 2 | 0 | 2 | -3 | -4 | 1 | -3 | -5 | -1 | 1 | 0 | -5 | -2 | -3 | 3 | 1 | -1 | N |
| | | | 5 | -7 | 2 | 4 | 0 | 0 | -3 | -6 | 0 | -4 | -8 | -2 | 0 | -1 | -9 | -6 | -3 | 4 | 3 | -1 | D |
| | | | | 13 | -7 | -7 | -5 | -4 | -3 | -8 | -7 | -7 | -6 | -4 | 0 | -3 | -10 | 0 | -3 | -6 | -7 | -4 | C |
| | | | | | 6 | 3 | -2 | 4 | -3 | -2 | 0 | -1 | -6 | 0 | -1 | -2 | -6 | -6 | -3 | 1 | 5 | -1 | Q |
| | | | | | | 5 | 0 | 0 | -3 | -5 | -1 | -3 | -7 | -1 | -1 | -1 | -9 | -6 | -3 | 3 | 5 | -1 | E |
| | | | | | | | 6 | -3 | -4 | -6 | -3 | -4 | -6 | -1 | 1 | -1 | -9 | -7 | -2 | 0 | -1 | -2 | G |
| | | | | | | | | 8 | -4 | -3 | -1 | -3 | -3 | -1 | -2 | -2 | -4 | 0 | -3 | 1 | 2 | -1 | H |
| | | | | | | | | | 6 | 2 | -3 | 2 | 1 | -3 | -2 | 0 | -7 | -2 | 5 | -3 | -3 | -1 | I |
| | | | | | | | | | | 7 | -4 | 4 | 1 | -4 | -4 | -3 | -3 | -2 | 2 | -5 | -3 | -2 | L |
| | | | | | | | | | | | 6 | 1 | -7 | -2 | -1 | 0 | -5 | -6 | -4 | 0 | 0 | -1 | K |
| | | | | | | | | | | | | 9 | 0 | -3 | -2 | -1 | -6 | -4 | 2 | -3 | -2 | -1 | M |
| | | | | | | | | | | | | | 10 | -6 | -4 | -4 | 0 | 7 | -2 | -6 | -7 | -3 | F |
| | | | | | | | | | | | | | | 8 | 1 | 0 | -7 | -7 | -2 | -2 | -1 | -1 | P |
| | | | | | | | | | | | | | | | 3 | 2 | -3 | -4 | -2 | 1 | -1 | 0 | S |
| | | | | | | | | | | | | | | | | 4 | -7 | -4 | 0 | 0 | -1 | -1 | T |
| | | | | | | | | | | | | | | | | | 18 | -1 | -8 | -7 | -8 | -6 | W |
| | | | | | | | | | | | | | | | | | | 11 | -4 | -4 | -6 | -3 | Y |
| | | | | | | | | | | | | | | | | | | | 6 | -3 | -3 | -1 | V |
| | | | | | | | | | | | | | | | | | | | | 4 | 3 | -1 | B |
| | | | | | | | | | | | | | | | | | | | | | 5 | -1 | Z |
| | | | | | | | | | | | | | | | | | | | | | | -1 | X |

# PAM 250

```
Diagonal: Min:   2.0  Max:  17.0  Mean:  5.90  Sigma: 3.78
Rest:     Min:  -8.0  Max:   7.0  Mean: -1.51  Sigma: 2.40
Matrix:   Min:  -8.0  Max:  17.0  Mean: -0.80  Sigma: 3.35

  A   R   N   D   C   Q   E   G   H   I   L   K   M   F   P   S   T   W   Y   V   B   Z   X  ..
  2  -2   0   0  -2   0   0   1  -1  -1  -2  -1  -1  -3   1   1   1  -6  -3   0   0   0   0   A
      6   0  -1  -4   1  -1  -3   2  -2  -3   3   0  -4   0   0  -1   2  -4  -2  -1   0  -1   R
          2   2  -4   1   1   0   2  -2  -3   1  -2  -3   0   1   0  -4  -2  -2   2   1   0   N
              4  -5   2   3   1   1  -2  -4   0  -3  -6  -1   0   0  -7  -4  -2   3   3  -1   D
                 12  -5  -5  -3  -3  -2  -6  -5  -5  -4  -3   0  -2  -8   0  -2  -4  -5  -3   C
                      4   2  -1   3  -2  -2   1  -1  -5   0  -1  -1  -5  -4  -2   1   3  -1   Q
                          4   0   1  -2  -3   0  -2  -5  -1   0   0  -7  -4  -2   3   3  -1   E
                              5  -2  -3  -4  -2  -3  -5   0   1   0  -7  -5  -1   0   0  -1   G
                                  6  -2  -2   0  -2  -2   0  -1  -1  -3   0  -2   1   2  -1   H
                                      5   2  -2   2   1  -2  -1   0  -5  -1   4  -2  -2  -1   I
                                          6  -3   4   2  -3  -3  -2  -2  -1   2  -3  -3  -1   L
                                              5   0  -5  -1   0   0  -3  -4  -2   1   0  -1   K
                                                  6   0  -2  -2  -1  -4  -2   2  -2  -2  -1   M
                                                      9  -5  -3  -3   0   7  -1  -4  -5  -2   F
                                                         6   1   0  -6  -5  -1  -1   0  -1   P
                                                             2   1  -2  -3  -1   0   0   0   S
                                                                 3  -5  -3   0   0  -1   0   T
                                                                    17   0  -6  -5  -6  -4   W
                                                                        10  -2  -3  -4  -2   Y
                                                                            4  -2  -2  -1   V
                                                                               3   2  -1   B
                                                                                   3  -1   Z
                                                                                      -1   X
```

# PAM 300

```
Diagonal: Min:   1.0  Max:  22.0  Mean:  6.60  Sigma: 5.17
Rest:     Min:  -9.0  Max:   9.0  Mean: -1.57  Sigma: 2.77
Matrix:   Min:  -9.0  Max:  22.0  Mean: -0.80  Sigma: 3.88

  A   R   N   D   C   Q   E   G   H   I   L   K   M   F   P   S   T   W   Y   V   B   Z   X  ..
  2  -1   0   0  -2   0   0   2  -1   0  -2  -1  -1  -4   1   1   1  -6  -4   0   0   0   0   A
      7   0  -1  -4   2  -1  -2   2  -2  -3   4   0  -5   0   0  -1   3  -5  -3   0   0  -1   R
          2   2  -4   1   2   1   2  -2  -3   1  -2  -4   0   1   0  -5  -2  -2   2   1   0   N
              4  -6   2   4   1   1  -2  -4   0  -3  -6  -1   0   0  -7  -5  -2   3   3  -1   D
                 15  -6  -6  -4  -4  -3  -7  -6  -6  -5  -3   0  -2  -9   1  -2  -5  -6  -3   C
                      4   3  -1   3  -2  -2   1  -1  -5   0   0  -1  -5  -4  -2   2   3   0   Q
                          4   0   1  -2  -4   0  -2  -6   0   0   0  -8  -5  -2   3   3  -1   E
                              5  -2  -3  -4  -2  -3  -5   0   1   0  -8  -6  -1   1   0  -1   G
                                  7  -2  -2   0  -2  -2   0  -1  -1  -3   0  -2   1   2   0   H
                                     5   3  -2   3   1  -2  -1   0  -6  -1   4  -2  -2  -1   I
                                         7  -3   4   3  -3  -3  -2  -2   0   2  -4  -3  -1   L
                                             5   0  -6  -1   0   0  -4  -5  -2   1   1  -1   K
                                                 6   1  -2  -2  -1  -5  -2   2  -2  -2  -1   M
                                                    11  -5  -4  -3   1   9  -1  -5  -5  -2   F
                                                         6   1   1  -6  -5  -1   0   0  -1   P
                                                             1   1  -3  -3  -1   1   0   0   S
                                                                 2  -6  -3   0   0   0   0   T
                                                                    22   0  -7  -6  -6  -4   W
                                                                        12  -3  -4  -5  -2   Y
                                                                             5  -2  -2   0   V
                                                                                 3   2   0   B
                                                                                     3  -1   Z
                                                                                        -1   X
```

# Macierze BLOSUM

Powstały w oparciu o bazę BLOCKS – dopasowanie sekwencji daleko spokrewnionych
(oszacowanie częstotliwości docelowych, bez modelu ewolucyjnego)

Rodzina macierzy:
różnice indeksu związane są z maksymalnym stopniem identyczności sekwencji wziętych do obliczeń.

Przykłady:
BLOSUM90 – do analizy sekwencji blisko spokrewnionych
BLOSUM62 – najczęściej używana
BLOSUM30 – do analizy odległych ewolucyjnie sekwencji

# Rodziny macierzy PAM i BLOSUM

| BLOSUM 45<br>PAM 250 | BLOSUM 62<br>PAM 160 | BLOSUM 90<br>PAM 100 |
|---|---|---|
| ← | | → |
| bardziej zróżnicowane | | mniej zróżnicowane |

Zastosowanie:
BLOSUM – lokalne przyrównania sekwencji
PAM – konstrukcja drzew filogenetycznych

PAM 250 matrix

```
X=0
C 12
S  0  2
T -2  1  3
P -3  1  0  6
A -2  1  1  1  2
G -3  1  0 -1  1  5
N -4  1  0 -1  0  0  2
D -5  0  0 -1  0  1  2  4
E -5  0  0 -1  0  0  1  3  4
Q -5 -1 -1  0  0 -1  1  2  2  4
H -3 -1 -1  0 -1 -2  2  1  1  3  6
R -4  0 -1  0 -2 -3  0 -1 -1  1  2  6
K -5  0  0 -1 -1 -2  1  0  0  1  0  3  5
M -5 -2 -1 -2 -1 -3 -2 -3 -2 -1 -2  0  0  6
I -2 -1  0 -2 -1 -3 -2 -2 -2 -2 -2 -2 -2  2 5
L -6 -3 -2 -3 -2 -4 -3 -4 -3 -2 -2 -3 -3  4 2  6
V -2 -1  0 -1  0 -1 -2 -2 -2 -2 -2 -2 -2  2 4  2  4
F -4 -3 -3 -5 -4 -5 -4 -6 -5 -5 -2 -4 -5  0 1  2 -1  9
W  0 -3 -3 -5 -3 -5 -2 -4 -4 -4  0 -4 -4 -2 -1 -1 -2  7 10
Y -8 -2 -5 -6 -6 -7 -4 -7 -7 -5 -3  2 -3 -4 -5 -2 -6  0  0 17
   C  S  T  P  A  G  N  D  E  Q  H  R  K  M  I  L  V  F  W  Y
```

(c) David Gilbert, 2003 [Sequence Comparison]

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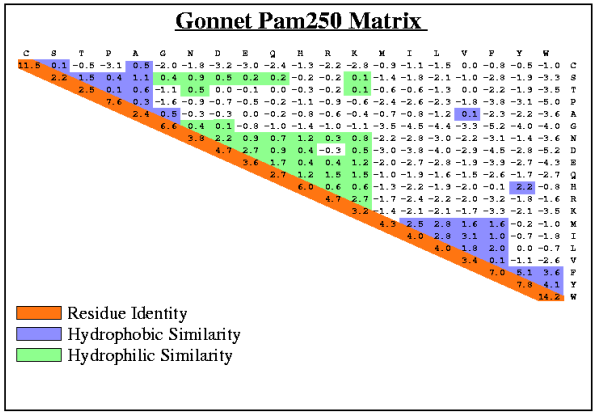


# BLOSUM 45

```
Diagonal: Min:   4.0  Max:  15.0  Mean:  7.05  Sigma: 2.79
Rest:     Min:  -5.0  Max:   3.0  Mean: -1.34  Sigma: 1.60
Matrix:   Min:  -5.0  Max:  15.0  Mean: -0.54  Sigma: 3.02

  A   R   N   D   C   Q   E   G   H   I   L   K   M   F   P   S   T   W   Y   V   B   Z   X  ..
  5  -2  -1  -2  -1  -1  -1   0  -2  -1  -1  -1  -1  -2  -1   1   0  -2  -2   0  -1  -1   0   A
      7   0  -1  -3   1   0  -2   0  -3  -2   3  -1  -2  -2  -1  -1  -2  -1  -2  -1   0  -1   R
          6   2  -2   0   0   0   1  -2  -3   0  -2  -2  -2   1   0  -4  -2  -3   4   0  -1   N
              7  -3   0   2  -1   0  -4  -3   0  -3  -4  -1   0  -1  -4  -2  -3   5   1  -1   D
                 12  -3  -3  -3  -3  -3  -2  -3  -2  -2  -4  -1  -1  -5  -3  -1  -2  -3  -2   C
                      6   2  -2   1  -2  -2   1   0  -4  -1   0  -1  -2  -1  -3   0   4  -1   Q
                          6  -2   0  -3  -2   1  -2  -3   0   0  -1  -3  -2  -3   1   4  -1   E
                              7  -2  -4  -3  -2  -2  -3  -2   0  -2  -2  -3  -3  -1  -2  -1   G
                                 10  -3  -2  -1   0  -2  -2  -1  -2  -3   2  -3   0   0  -1   H
                                      5   2  -3   2   0  -2  -2  -1  -2   0   3  -3  -3  -1   I
                                          5  -3   2   1  -3  -3  -1  -2   0   1  -3  -2  -1   L
                                             5  -1  -3  -1  -1  -1  -2  -1  -2   0   1  -1   K
                                                 6   0  -2  -2  -1  -2   0   1  -2  -1  -1   M
                                                     8  -3  -2  -1   1   3   0  -3  -3  -1   F
                                                        9  -1  -1  -3  -3  -3  -2  -1  -1   P
                                                           4   2  -4  -2  -1   0   0   0   S
                                                               5  -3  -1   0   0  -1   0   T
                                                                  15   3  -3  -4  -2  -2   W
                                                                       8  -1  -2  -2  -1   Y
                                                                          5  -3  -3  -1   V
                                                                             4   2  -1   B
                                                                                 4  -1   Z
                                                                                    -1   X
```

# BLOSUM 62

```
Diagonal: Min:   4.0  Max:  11.0  Mean:  5.80  Sigma: 1.90
Rest:     Min:  -4.0  Max:   3.0  Mean: -1.43  Sigma: 1.51
Matrix:   Min:  -4.0  Max:  11.0  Mean: -0.74  Sigma: 2.63

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

# BLOSUM 90

```
Diagonal: Min:   5.0  Max:  11.0  Mean:  6.70  Sigma: 1.60
Rest:     Min:  -6.0  Max:   3.0  Mean: -2.32  Sigma: 1.84
Matrix:   Min:  -6.0  Max:  11.0  Mean: -1.46  Sigma: 3.22

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

# BLOSUM 62 - wizualizacja

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

# Macierze substytucji - biopython

```
from Bio.SubsMat import MatrixInfo
```

```
available_matrices = ['benner6', 'benner22', 'benner74', 'blos...
benner6 = {('A', 'A'): 2.5, ('A', 'C'): -1.7, ('A', 'P'): 1.1,...
benner22 = {('A', 'A'): 2.5, ('A', 'C'): -1.2, ('A', 'P'): 0.8...
benner74 = {('A', 'A'): 2.4, ('A', 'C'): 0.3, ('A', 'P'): 0.4,...
blosum100 = {('A', 'A'): 5, ('B', 'A'): -3, ('B', 'B'): 4, ('B...
blosum30 = {('A', 'A'): 4, ('B', 'A'): 0, ('B', 'B'): 5, ('B',...
blosum35 = {('A', 'A'): 5, ('B', 'A'): -1, ('B', 'B'): 5, ('B'...
blosum40 = {('A', 'A'): 5, ('B', 'A'): -1, ('B', 'B'): 5, ('B'...
blosum45 = {('A', 'A'): 5, ('B', 'A'): -1, ('B', 'B'): 4, ('B'...
blosum50 = {('A', 'A'): 5, ('B', 'A'): -2, ('B', 'B'): 5, ('B'...
blosum55 = {('A', 'A'): 5, ('B', 'A'): -2, ('B', 'B'): 5, ('B'...
blosum60 = {('A', 'A'): 4, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum62 = {('A', 'A'): 4, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum65 = {('A', 'A'): 4, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum70 = {('A', 'A'): 4, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum75 = {('A', 'A'): 4, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum80 = {('A', 'A'): 5, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum85 = {('A', 'A'): 5, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum90 = {('A', 'A'): 5, ('B', 'A'): -2, ('B', 'B'): 4, ('B'...
blosum95 = {('A', 'A'): 5, ('B', 'A'): -3, ('B', 'B'): 4, ('B'...
feng = {('A', 'A'): 6, ('A', 'C'): 2, ('A', 'P'): 5, ('A', 'S'...
```

# Macierze substytucji - praktyka

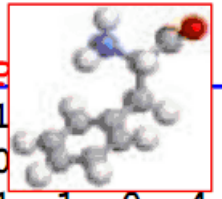
Najczęściej używane macierze:

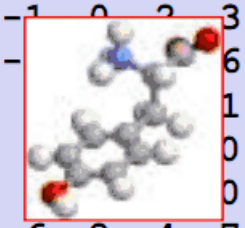
- **BLOSUM62** (standard dla programu BLAST)
- **PAM250**

# Interpretacja: częste podstawienia (1)

Dayhoff PAM 250 Matrix

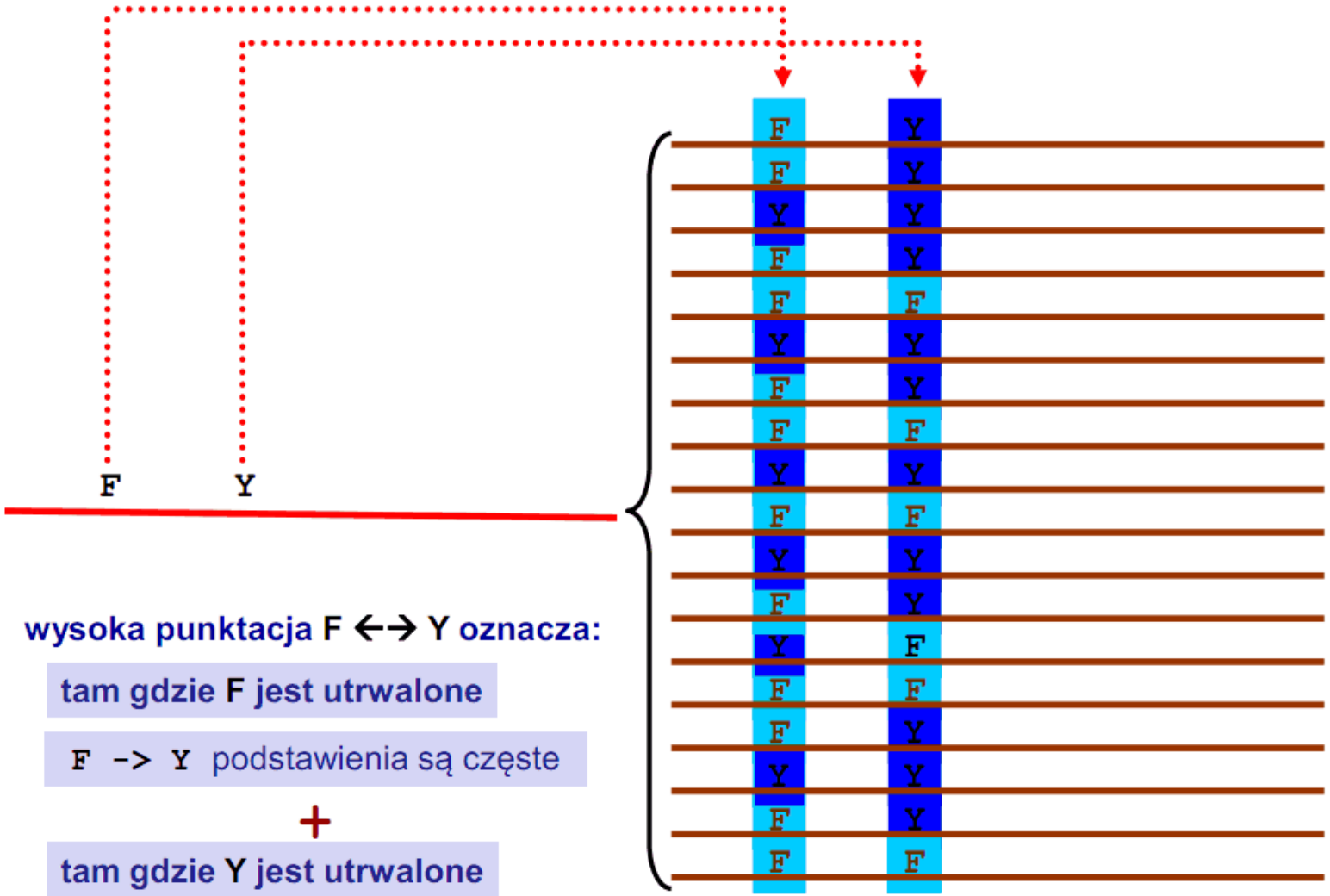
| | A | R | N | D | C | Q | E | G | H | I | L | K | M | F | P | S | T | W | Y | V | B | Z | X |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 2 | -2 | 0 | 0 | -2 | 0 | 0 | 1 | -1 | -1 | -2 | -1 | -1 | -4 | 1 | 1 | 1 | -6 | -3 | 0 | 0 | 0 | 0 |
| R | -2 | 6 | 0 | -1 | -4 | 1 | -1 | -3 | 2 | -2 | -3 | 3 | 0 | -4 | 0 | 0 | -1 | 2 | -4 | -2 | -1 | 0 | 0 |
| N | 0 | 0 | 2 | 2 | -4 | 1 | 1 | 0 | 2 | -2 | -3 | 1 | -2 | -4 | -1 | 1 | 0 | -4 | -2 | -2 | 2 | 1 | 0 |
| D | 0 | -1 | 2 | 4 | -5 | 2 | 3 | 1 | 1 | -2 | -4 | 0 | -3 | -6 | -1 | 0 | 0 | -7 | -4 | -2 | 3 | 3 | 0 |
| C | -2 | -4 | -4 | -5 | 12 | -5 | -5 | -3 | -3 | -2 | -6 | -5 | -5 | -4 | -3 | 0 | -2 | -8 | 0 | -2 | -4 | -5 | 0 |
| Q | 0 | 1 | 1 | 2 | -5 | 4 | 2 | -1 | 3 | -2 | -2 | 1 | -1 | -5 | 0 | -1 | -1 | -5 | -4 | -2 | 1 | 3 | 0 |
| E | 0 | -1 | 1 | 3 | -5 | 2 | 4 | 0 | 1 | -2 | -3 | 0 | -2 | -5 | -1 | 0 | 0 | -7 | -4 | -2 | 2 | 3 | 0 |
| G | 1 | -3 | 0 | 1 | -3 | -1 | 0 | 5 | -2 | -3 | -4 | -2 | -3 | -5 | -1 | 1 | 0 | -7 | -5 | -1 | 0 | -1 | 0 |
| H | -1 | 2 | 2 | 1 | -3 | 3 | 1 | -2 | 6 | -2 | -2 | 0 | -2 | -2 | 0 | -1 | -1 | -3 | 0 | -2 | 1 | 2 | 0 |
| I | -1 | -2 | -2 | -2 | -2 | -2 | -2 | -3 | -2 | 5 | 2 | -2 | 2 | 1 | -2 | -1 | 0 | -5 | -1 | 4 | -2 | -2 | 0 |
| L | -2 | -3 | -3 | -4 | -6 | -2 | -3 | -4 | -2 | -2 | 6 | -3 | 4 | 2 | -3 | -3 | -2 | -2 | -1 | 2 | -3 | -3 | 0 |
| K | -1 | 3 | 1 | 0 | -5 | 1 | 0 | -2 | 0 | -2 | 4 | 5 | 0 | -5 | -1 | 0 | 0 | -3 | -4 | -2 | 1 | 0 | 0 |
| M | -1 | 0 | 2 | 3 | -5 | -1 | -2 | -3 | -2 | 2 | 2 | 0 | 6 | 0 | -2 | -2 | -1 | -4 | 2 | 2 | -2 | -2 | 0 |
| F | -4 | -4 | -4 | -6 | -4 | -5 | -5 | -5 | -2 | 1 | 2 | -5 | 0 | 9 | -5 | -3 | -3 | 0 | 7 | -1 | -5 | -5 | 0 |
| P | 1 | 0 | -1 | -1 | -3 | 0 | -1 | -1 | 0 | -2 | -3 | -1 | -2 | -5 | 6 | 1 | 0 | -6 | -5 | -1 | -1 | 0 | 0 |
| S | 1 | 0 | 1 | 0 | 0 | -1 | 1 | 1 | -1 | -1 | -3 | 0 | -2 | -3 | 1 | 2 | 1 | -2 | -3 | -1 | 0 | 0 | 0 |
| T | 1 | -1 | 0 | 0 | -2 | -2 | 0 | 0 | -1 | 0 | -2 | 0 | -1 | -3 | 0 | 1 | 3 | -5 | -3 | 0 | 0 | -1 | 0 |
| W | -6 | 2 | -4 | -7 | -8 | -5 | -7 | -7 | -3 | -5 | -2 | -3 | -4 | 0 | -6 | -2 | -5 | 17 | 0 | -6 | -5 | -6 | 0 |
| Y | -3 | -4 | -2 | -4 | 0 | -4 | -4 | -5 | 0 | -1 | -1 | -4 | -2 | 7 | -5 | -3 | -3 | 0 | 10 | -2 | -3 | -4 | 0 |
| V | 0 | -2 | -2 | -2 | -2 | -2 | -2 | -1 | -2 | 4 | 2 | -2 | 2 | -1 | -1 | -1 | 0 | -6 | -2 | 4 | -2 | -2 | 0 |
| B | 0 | -1 | 2 | 3 | -4 | 1 | 2 | 0 | 1 | -2 | -3 | 1 | -2 | -5 | -1 | 0 | 0 | -5 | -3 | -2 | 2 | 2 | 0 |
| Z | 0 | 0 | 1 | 3 | -5 | 3 | 3 | -1 | 2 | -2 | -3 | 0 | -2 | -5 | 0 | 0 | -1 | -6 | -4 | -2 | 2 | 3 | 0 |
| X | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |





Macierz PAM 250, podstawienie fenyloanalina (F) – tyrozyna (Y)

# Interpretacja: częste podstawienia (2)




**wysoka punktacja F ←→ Y oznacza:**

**tam gdzie F jest utrwalone**

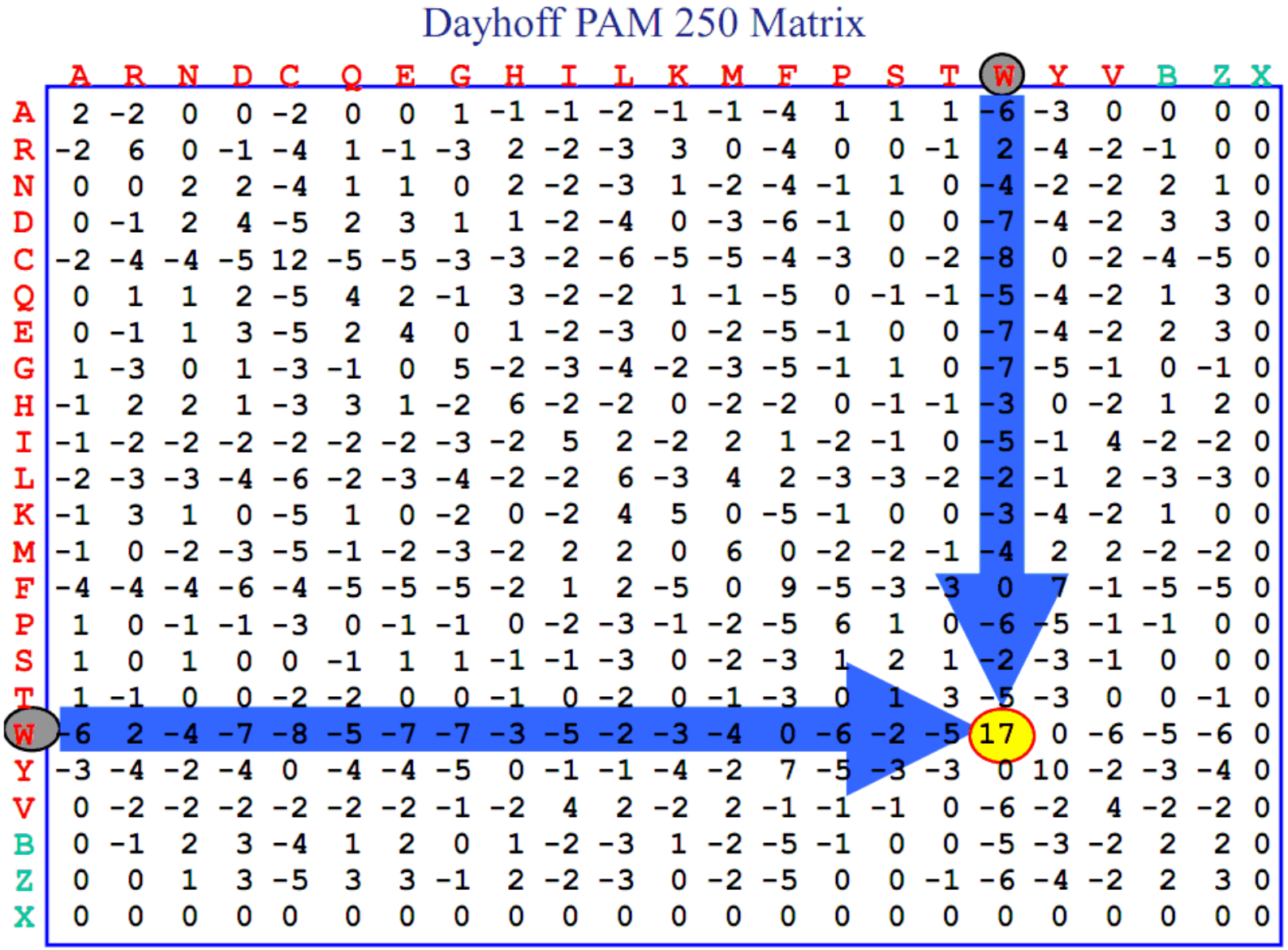
`F -> Y` podstawienia są częste

+

**tam gdzie Y jest utrwalone**

`Y -> F` podstawienia są częste

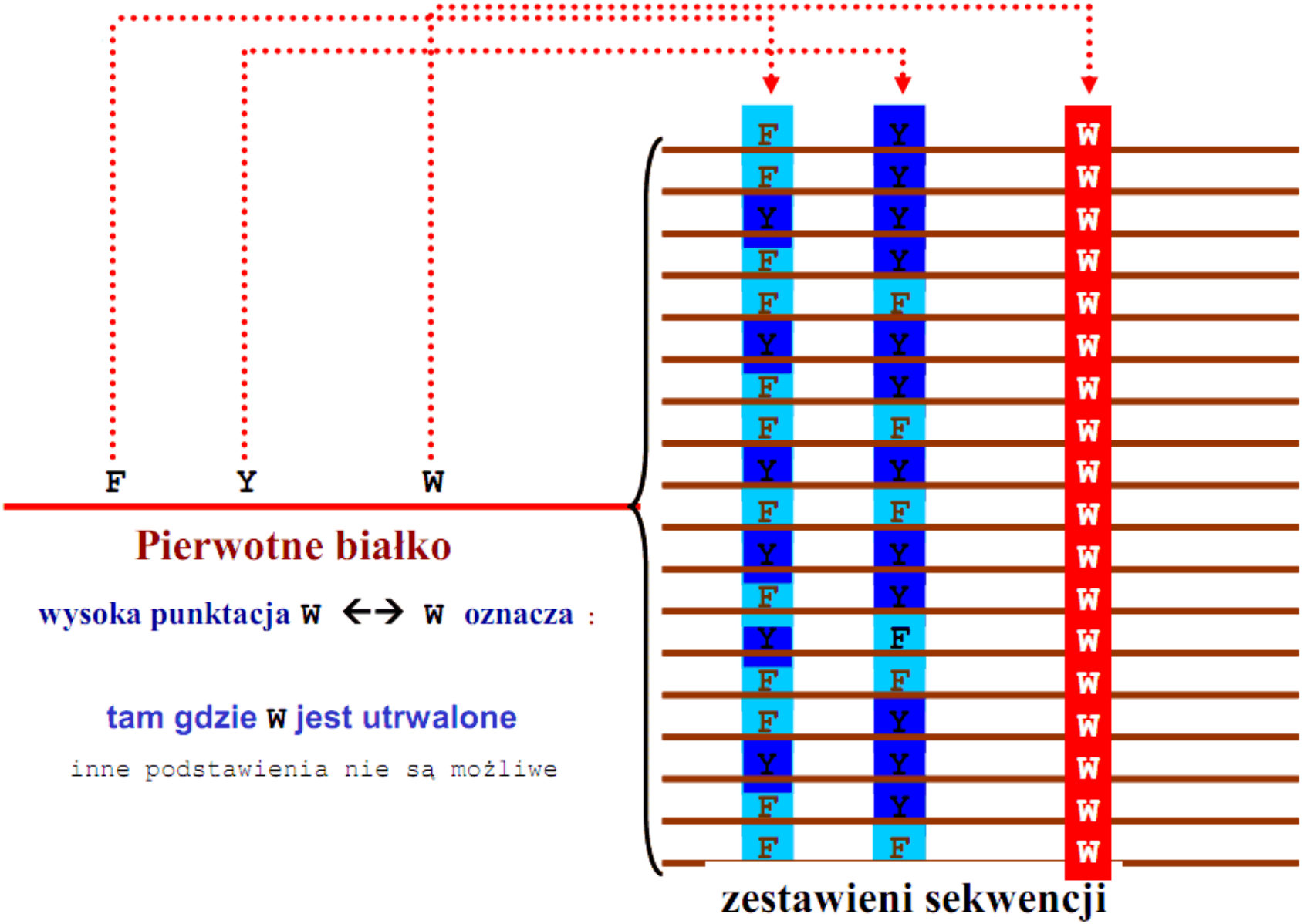
# Interpretacja: utrwalona pozycja (1)




| | A | R | N | D | C | Q | E | G | H | I | L | K | M | F | P | S | T | W | Y | V | B | Z | X |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A | 2 | -2 | 0 | 0 | -2 | 0 | 0 | 1 | -1 | -1 | -2 | -1 | -1 | -4 | 1 | 1 | 1 | -6 | -3 | 0 | 0 | 0 | 0 |
| R | -2 | 6 | 0 | -1 | -4 | 1 | -1 | -3 | 2 | -2 | -3 | 3 | 0 | -4 | 0 | 0 | -1 | 2 | -4 | -2 | -1 | 0 | 0 |
| N | 0 | 0 | 2 | 2 | -4 | 1 | 1 | 0 | 2 | -2 | -3 | 1 | -2 | -4 | -1 | 1 | 0 | -4 | -2 | -2 | 2 | 1 | 0 |
| D | 0 | -1 | 2 | 4 | -5 | 2 | 3 | 1 | 1 | -2 | -4 | 0 | -3 | -6 | -1 | 0 | 0 | -7 | -4 | -2 | 3 | 3 | 0 |
| C | -2 | -4 | -4 | -5 | 12 | -5 | -5 | -3 | -3 | -2 | -6 | -5 | -5 | -4 | -3 | 0 | -2 | -8 | 0 | -2 | -4 | -5 | 0 |
| Q | 0 | 1 | 1 | 2 | -5 | 4 | 2 | -1 | 3 | -2 | -2 | 1 | -1 | -5 | 0 | -1 | -1 | -5 | -4 | -2 | 1 | 3 | 0 |
| E | 0 | -1 | 1 | 3 | -5 | 2 | 4 | 0 | 1 | -2 | -3 | 0 | -2 | -5 | -1 | 0 | 0 | -7 | -4 | -2 | 2 | 3 | 0 |
| G | 1 | -3 | 0 | 1 | -3 | -1 | 0 | 5 | -2 | -3 | -4 | -2 | -3 | -5 | -1 | 1 | 0 | -7 | -5 | -1 | 0 | -1 | 0 |
| H | -1 | 2 | 2 | 1 | -3 | 3 | 1 | -2 | 6 | -2 | -2 | 0 | -2 | -2 | 0 | -1 | -1 | -3 | 0 | -2 | 1 | 2 | 0 |
| I | -1 | -2 | -2 | -2 | -2 | -2 | -2 | -3 | -2 | 5 | 2 | -2 | 2 | 1 | -2 | -1 | 0 | -5 | -1 | 4 | -2 | -2 | 0 |
| L | -2 | -3 | -3 | -4 | -6 | -2 | -3 | -4 | -2 | -2 | 6 | -3 | 4 | 2 | -3 | -3 | -2 | -2 | -1 | 2 | -3 | -3 | 0 |
| K | -1 | 3 | 1 | 0 | -5 | 1 | 0 | -2 | 0 | -2 | 4 | 5 | 0 | -5 | -1 | 0 | 0 | -3 | -4 | -2 | 1 | 0 | 0 |
| M | -1 | 0 | -2 | -3 | -5 | -1 | -2 | -3 | -2 | 2 | 2 | 0 | 6 | 0 | -2 | -2 | -1 | -4 | 2 | 2 | -2 | -2 | 0 |
| F | -4 | -4 | -4 | -6 | -4 | -5 | -5 | -5 | -2 | 1 | 2 | -5 | 0 | 9 | -5 | -3 | -3 | 0 | 7 | -1 | -5 | -5 | 0 |
| P | 1 | 0 | -1 | -1 | -3 | 0 | -1 | -1 | 0 | -2 | -3 | -1 | -2 | -5 | 6 | 1 | 0 | -6 | -5 | -1 | -1 | 0 | 0 |
| S | 1 | 0 | 1 | 0 | 0 | -1 | 1 | 1 | -1 | -1 | -3 | 0 | -2 | -3 | 1 | 2 | 1 | -2 | -3 | -1 | 0 | 0 | 0 |
| T | 1 | -1 | 0 | 0 | -2 | -2 | 0 | 0 | -1 | 0 | -2 | 0 | -1 | -3 | 0 | 1 | 3 | -5 | -3 | 0 | 0 | -1 | 0 |
| W | -6 | 2 | -4 | -7 | -8 | -5 | -7 | -7 | -3 | -5 | -2 | -3 | -4 | 0 | -6 | -2 | -5 | 17 | 0 | -6 | -5 | -6 | 0 |
| Y | -3 | -4 | -2 | -4 | 0 | -4 | -4 | -5 | 0 | -1 | -1 | -4 | -2 | 7 | -5 | -3 | -3 | 0 | 10 | -2 | -3 | -4 | 0 |
| V | 0 | -2 | -2 | -2 | -2 | -2 | -2 | -1 | -2 | 4 | 2 | -2 | 2 | -1 | -1 | -1 | 0 | -6 | -2 | 4 | -2 | -2 | 0 |
| B | 0 | -1 | 2 | 3 | -4 | 1 | 2 | 0 | 1 | -2 | -3 | 1 | -2 | -5 | -1 | 0 | 0 | -5 | -3 | -2 | 2 | 2 | 0 |
| Z | 0 | 0 | 1 | 3 | -5 | 3 | 3 | -1 | 2 | -2 | -3 | 0 | -2 | -5 | 0 | 0 | -1 | -6 | -4 | -2 | 2 | 3 | 0 |
| X | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

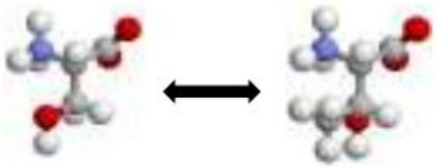
Macierz PAM 250, tryptofan (W)

# Interpretacja: utrwalona pozycja (2)



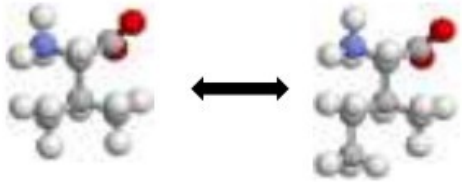
# Przykłady innych częstych podstawień

Małe, polarne



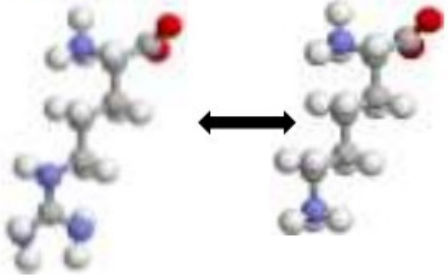
S, Ser T, Thr

Małe, hydrofobowe



V,Val I,Ile

Duże, nałądowane



R, Arg K, Lys

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C Cys | 12 | | | | | | | | | | | | | | | | | | |
| S Ser | 0 | 2 | | | | | | | | | | | | | | | | | |
| T Thr | -2 | 1 | 3 | | | | | | | | | | | | | | | | |
| P Pro | -3 | 1 | 0 | 6 | | | | | | | | | | | | | | | |
| A Ala | -2 | 1 | 1 | 1 | 2 | | | | | | | | | | | | | | |
| G Gly | -3 | 1 | 0 | -1 | 1 | 5 | | | | | | | | | | | | | |
| N Asn | -4 | 1 | 0 | -1 | 0 | 0 | 2 | | | | | | | | | | | | |
| D Asp | -5 | 0 | 0 | -1 | 0 | 1 | 2 | 4 | | | | | | | | | | | |
| E Glu | -5 | 0 | 0 | -1 | 0 | 0 | 1 | 3 | 4 | | | | | | | | | | |
| Q Gln | -5 | -1 | -1 | 0 | 0 | -1 | 1 | 2 | 2 | 4 | | | | | | | | | |
| H His | -3 | -1 | -1 | 0 | -1 | -2 | 2 | 1 | 1 | 3 | 6 | | | | | | | | |
| R Arg | -4 | 0 | -1 | 0 | -2 | -3 | 0 | -1 | -1 | 1 | 2 | 6 | | | | | | | |
| K Lys | -5 | 0 | 0 | -1 | -1 | -2 | 1 | 0 | 0 | 1 | 0 | 3 | 5 | | | | | | |
| M Met | -5 | -2 | -1 | -2 | -1 | -3 | -2 | -3 | -2 | -1 | -2 | 0 | 0 | 6 | | | | | |
| I Ile | -2 | -1 | 0 | -2 | -1 | -3 | -2 | -2 | -2 | -2 | -2 | -2 | -2 | 2 | 5 | | | | |
| L Leu | -6 | -3 | -2 | -3 | -2 | -4 | -3 | -4 | -3 | -2 | -2 | -3 | -3 | 4 | 2 | 6 | | | |
| V Val | -2 | -1 | 0 | -1 | 0 | -1 | -2 | -2 | -2 | -2 | -2 | -2 | -2 | 2 | 4 | 2 | 4 | | |
| F Phe | -4 | -3 | -3 | -5 | -5 | -5 | -4 | -6 | -5 | -5 | -2 | -4 | -5 | 0 | 1 | 2 | -1 | 9 | |
| Y Tyr | 0 | -3 | -3 | -5 | -3 | -5 | -2 | -4 | -4 | -4 | 0 | -4 | -4 | -2 | -1 | -1 | -2 | 7 | 10 |
| W Trp | -8 | -2 | -5 | -6 | -6 | -7 | -4 | -7 | -7 | -5 | -3 | 2 | -3 | -4 | -5 | -2 | -6 | 0 | 0 | 17 |
| | C | S | T | P | A | G | N | D | E | Q | H | R | K | M | I | L | V | F | Y | W |

Źródło: http://www.cryst.bbk.ac.uk/pps97/assignments/projects/leluk/project.htm

# Algorytm Needlemana-Wunscha
# **model afiniczny**

# Kary za przerwy

Niech:
$k$ – długość przerwy;
$G_p$ – całkowita kara za przerwę

**Model liniowy:**
$G_p = k*G$ (każda przerwa traktowana jest tak samo)

**Model afiniczny:**
$G_p = G_o + k^* G_e$,*

$G_o$ *(gap opening)* – otwarcie przerwy;
$G_e$ *(gap extension)* – wydłużenie przerwy;

* można się też spotkać z notacją: $G_p = G_o + (k-1)*G_e$
wówczas $G_o > G_e$

# Kary za przerwy – przykład

```
S1 = ATCTA
S2 = ATTTTTA

1)    AT-C-TA
      ATTTTTA      4-1-2-2 = -1

2)    ATC--TA
      ATTTTTA      4-1-2-1 = 0

3)    AT-C--TA
      ATT-TTTA     4-2-2-2-1 = -3
```

**Punktacja**

| | |
|---|---|
| zgodność: | +1 |
| niezgodność: | -1 |
| przerwa: | -1 |
| +otwarcie przerwy: | -1 |

Wg alternatywnej notacji

| | |
|---|---|
| zgodność: | +1 |
| niezgodność: | -1 |
| otwarcie przerwy: | -2 |
| wydłużenie przerwy: | -1 |

Tworzymy trzy macierze: *H, E* i *F*:

$$H_{i,j} = \max\begin{cases} H_{i-1,j-1} + s(a_i, b_j) \\ E_{i,j} \\ F_{i,j} \end{cases}$$

$$E_{i,j} = \max\begin{cases} H_{i-1,j} + Go + Ge \\ E_{i-1,j} + Ge \end{cases}$$

$$F_{i,j} = \max\begin{cases} H_{i,j-1} + Go + Ge \\ F_{i,j-1} + Ge \end{cases}$$

# Model afiniczny – warunki brzegowe

$$H_{0,0} = 0$$
$$H_{i,0} = G_o + i*G_e$$
$$H_{0,j} = G_o + j*G_e$$

$$E_{0,0} = -\infty$$
$$E_{i,0} = G_o + i*G_e$$
$$E_{0,j} = -\infty$$

$$F_{0,0} = -\infty$$
$$F_{i,0} = -\infty$$
$$F_{0,j} = G_o + j*G_e$$

Zgodnie z kierunkiem, z którego mogliśmy przyjść:

Z $H_{i,j}$ idziemy do $H_{i-1,j-1}$, $E_{i,j}$ lub $F_{i,j}$

Z $E_{i,j}$ idziemy do $E_{i-1,j}$, lub $H_{i-1,j}$

Z $F_{i,j}$ idziemy do $F_{i,j-1}$, lub $H_{i,j-1}$

$$H_{i,j} = \max\begin{cases} H_{i-1,j-1} + s(a_i, b_j) \\ E_{i,j} \\ F_{i,j} \end{cases}$$

$$E_{i,j} = \max\begin{cases} H_{i-1,j} + Go + Ge \\ E_{i-1,j} + Ge \end{cases}$$

$$F_{i,j} = \max\begin{cases} H_{i,j-1} + Go + Ge \\ F_{i,j-1} + Ge \end{cases}$$

# Model afiniczny – przykład

Z $H_{i,j}$ idziemy do $H_{i-1,j-1}$, $E_{i,j}$ lub $F_{i,j}$
Z $E_{i,j}$ idziemy do $E_{i-1,j}$, lub $H_{i-1,j}$

Z $F_{i,j}$ idziemy do $F_{i,j-1}$, lub $H_{i,j-1}$

$H[][]$

| | | V | L | S | P | A |
|---|---|---|---|---|---|---|
| | 0 | −8 | −9 | −10 | −11 | −12 |
| V | −8 | ↖ 2 | −6 | −7 | −8 | −9 |
| S | −9 | −6 | ↖ 1 | −4 | ↖ −8 | −9 |
| A | −10 | −7 | −7 | 0 | −5 | ↖ −6 |

$E[][]$

| | | V | L | S | P | A |
|---|---|---|---|---|---|---|
| | −∞ | −∞ | −∞ | −∞ | −∞ | −∞ |
| V | −8 | −16 | −17 | −18 | −19 | −20 |
| S | −9 | −6 | −14 | −15 | −16 | −17 |
| A | −10 | −7 | −7 | −12 | −16 | −17 |

$F[][]$

| | | V | L | S | P | A |
|---|---|---|---|---|---|---|
| | −∞ | −8 | −9 | −10 | −11 | −12 |
| V | −∞ | −16 | ← −6 | ← −7 | −8 | −9 |
| S | −∞ | −17 | −14 | ← −7 | ← −8 | −9 |
| A | −∞ | −18 | −15 | −15 | −8 | −9 |

| | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| 0 | V | S | – | – | A |
| 1 | V | L | S | P | A |

| | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| 0 | V | – | – | S | A |
| 1 | V | L | S | P | A |

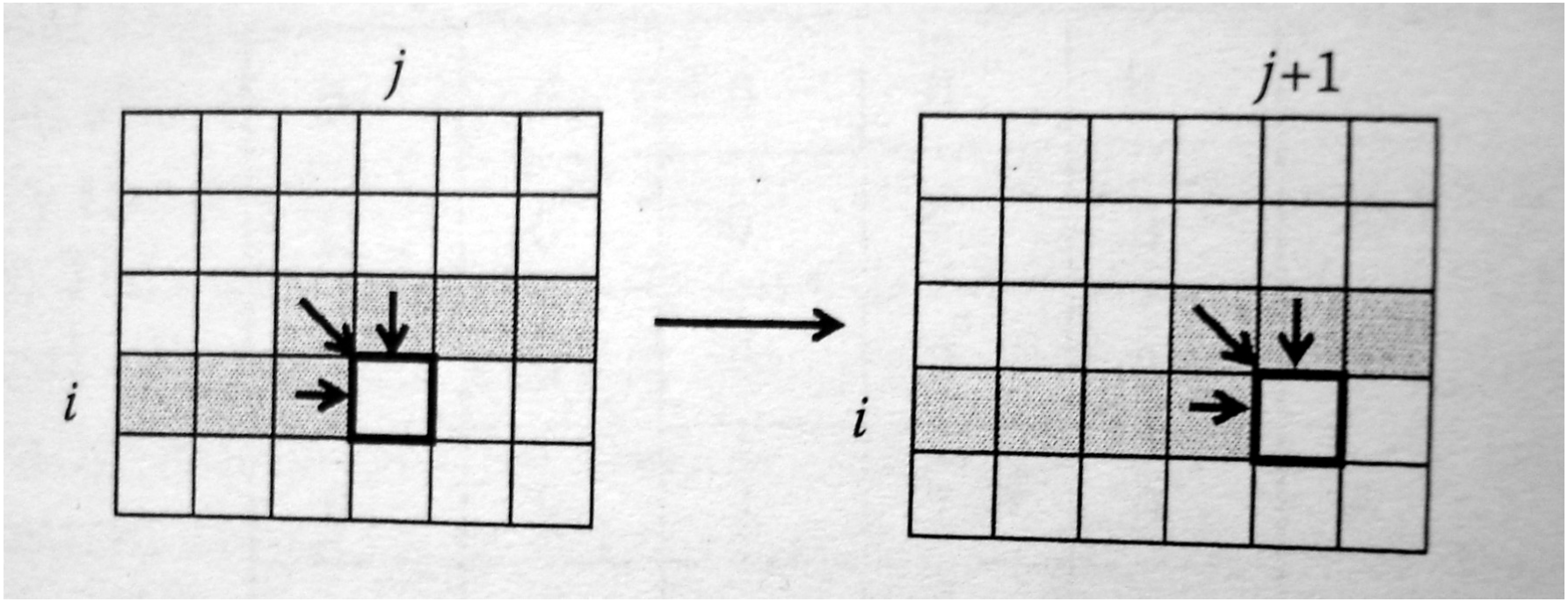
# Algorytm Needlemana-Wunscha
# **liniowa złożoność pamięciowa**

# Zastosowanie

Przydatny, gdy chcemy porównywać długie sekwencje.

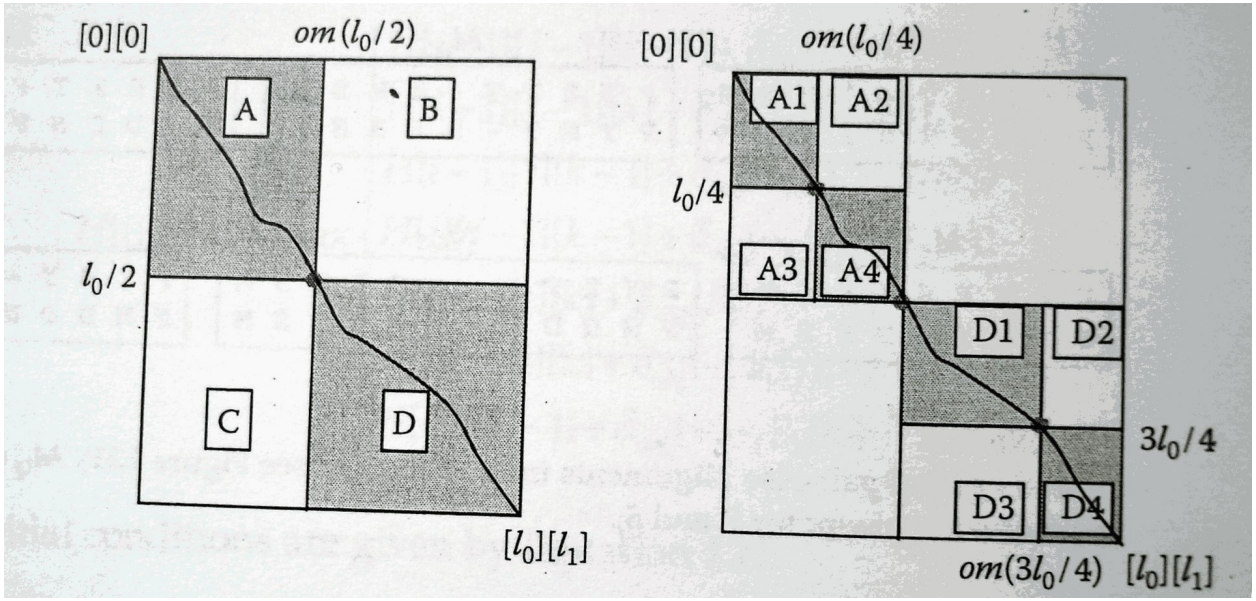
np. dla porównania dwóch sekwencji o długości 1000000 nukleotydów każda, potrzeba ok. Tb pamięci dla zapamiętania samej macierzy.

# Obliczanie punktacji




Pamiętamy tylko ostatni wiersz (n+2 komórki).

# Poszukiwanie dopasowania - metoda

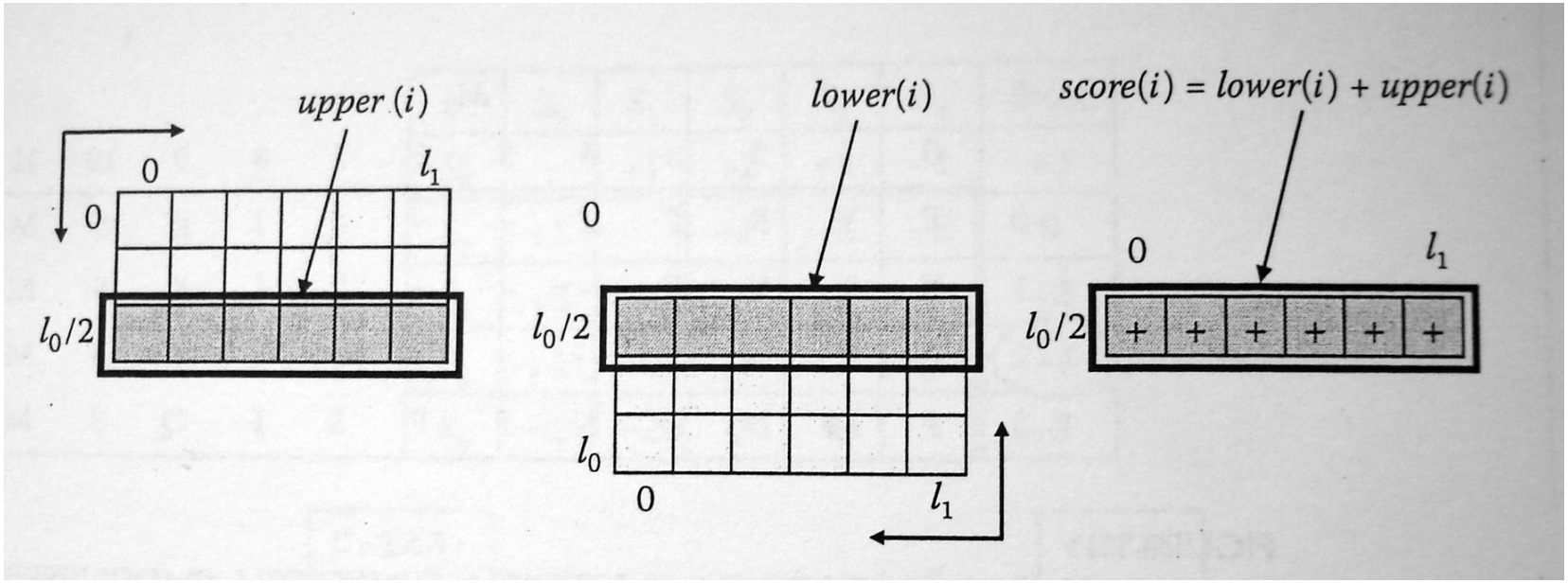



Metoda „dziel i zwyciężaj”. Stosujemy rekurencyjnie:

Idea pojedynczego etapu: W ustalonym wierszu na wysokości połowy rozważanej macierzy znajdujemy punkt o największej wartości dopasowania (szczegóły na następnym slajdzie); w tym miejscu dzielimy macierz na 4 prostokąty.

Rozważamy oddzielnie lewy górny i prawy dolny prostokąt, dla każdego z nich powtarzając powyższą procedurę.

# Poszukiwanie dopasowania – wybór punktu podziału

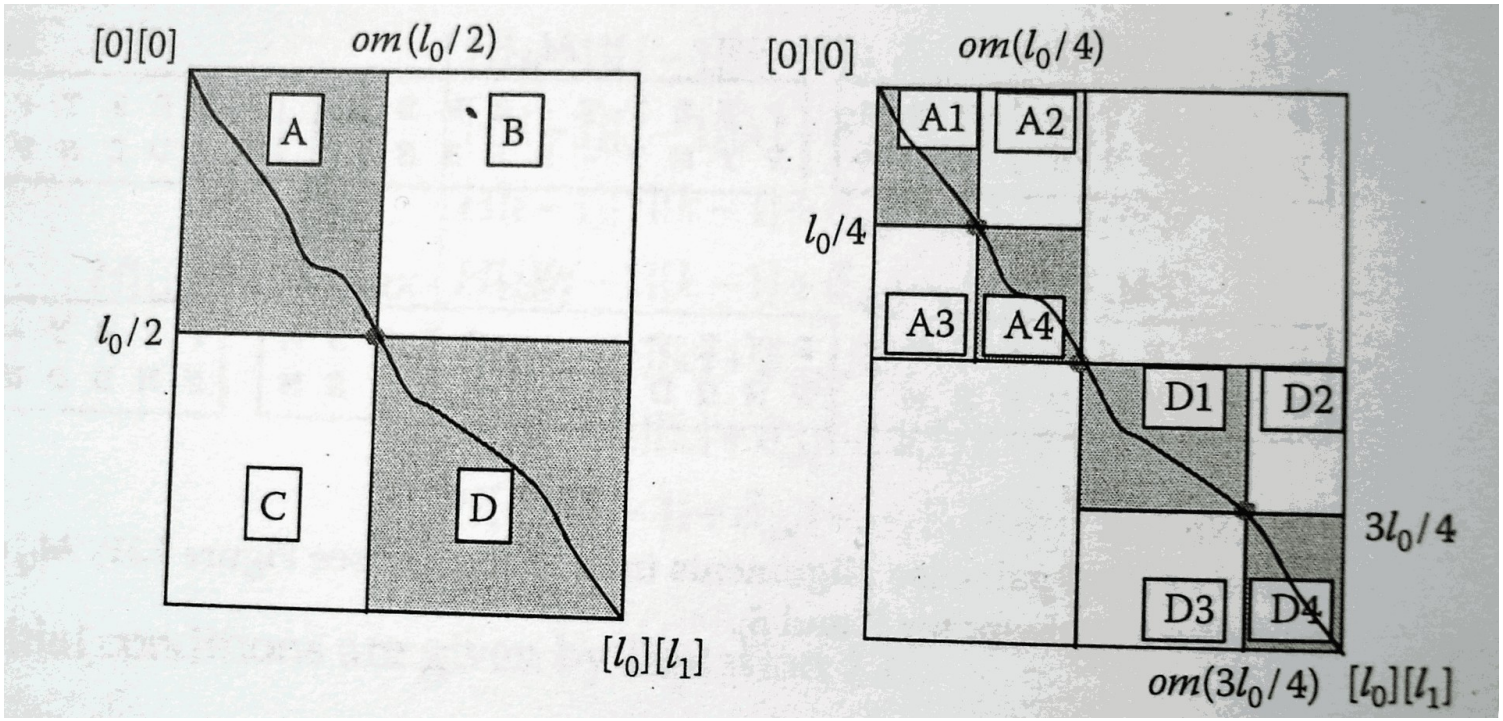



krok 1) przeprowadzamy dopasowanie dla górnej części, poczynając od punktu [0,0], kończąc na wierszu $l_0/2$.

krok 2) przeprowadzamy dopasowanie dla dolnej części od tyłu (czyli dopasowujemy odwrócone sekwencje), poczynając od punktu $[l_0, l_0]$, kończąc na wierszu $l_0/2$.

krok 3) znajdujemy punktację *upper* dla górnej części macierzy i *lower* dla dolnej (sekwencja odwrócona). Sumujemy, znajdujemy punkt o najwyższej punktacji.

# Poszukiwanie dopasowania - uściślenie




krok 1: cała macierz
krok 2: A
krok 3: A1
...
krok k: D
krok k+1: D1
...

Jak głęboko schodzimy z rekurencją?

Do momentu aż rozmiar podmacierzy pozwoli nam na uruchomienie algorytmu w tradycyjnej formie.

# Ograniczenie algorytmu Needlemana-Wunscha

Metody programowania dynamicznego mają zastosowanie dla porównywania par lub niewielkich zbiorów sekwencji.

W praktyce zwykle chcemy porównać naszą sekwencję ze wszystkimi sekwencjami zdeponowanymi w bazie – metoda staje się zbyt czasochłonna.

# Dopasowania lokalne

# Dopasowanie lokalne - idea

Stosujemy dla sekwencji istotnie różniących się długością
(np. poszukiwanie krótkich motywów w całym genie
lub poszukiwanie genu w całym genomie)

Istota dopasowania lokalnego:
poszukiwanie regionów o dużym stopniu podobieństwa
(np. analiza białek wielodomenowych, poszukiwanie motywów)

# Algorytm Smitha-Watermana

Algorytm jest bardzo podobny do algorytmu N-W. Podobnie jak w N-W wykorzystujemy ideę programowania dynamicznego.

Różnica polega na tym, że w wypełnianej macierzy nie dopuszczemy wartości ujemnych.

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

H – macierz punktacji;
s – wartość dopasowania symboli $a_i$ i $b_j$
g – kara za przerwę

# Algorytm S-W: przykład (1)

**Scoring Metric:**

Match: $s(a_i, b_j) = 1$

Mismatch: $s(a_i, b_j) = -1$

Gap: -2 penalty

Maximum of possible scores:

(a) 0 + s(A,A) = 0 + 1 = 1

(b) 0 - g = 0 - 2 = -2

(c) 0 - g = 0 - 2 = -2

(d) 0 (no pointer)

| | | A | A | T | G | T |
|---|---|---|---|---|---|---|
| | 0 | 0 | 0 | 0 | 0 | 0 |
| A | 0 | ? | | | | |
| T | 0 | | | | | |
| G | 0 | | | | | |
| A | 0 | | | | | |
| C | 0 | | | | | |

# Algorytm S-W: przykład (2)

**Scoring Metric:**

Match: $s(a_i, b_j) = 1$

Mismatch: $s(a_i, b_j) = -1$

Gap: -2 penalty

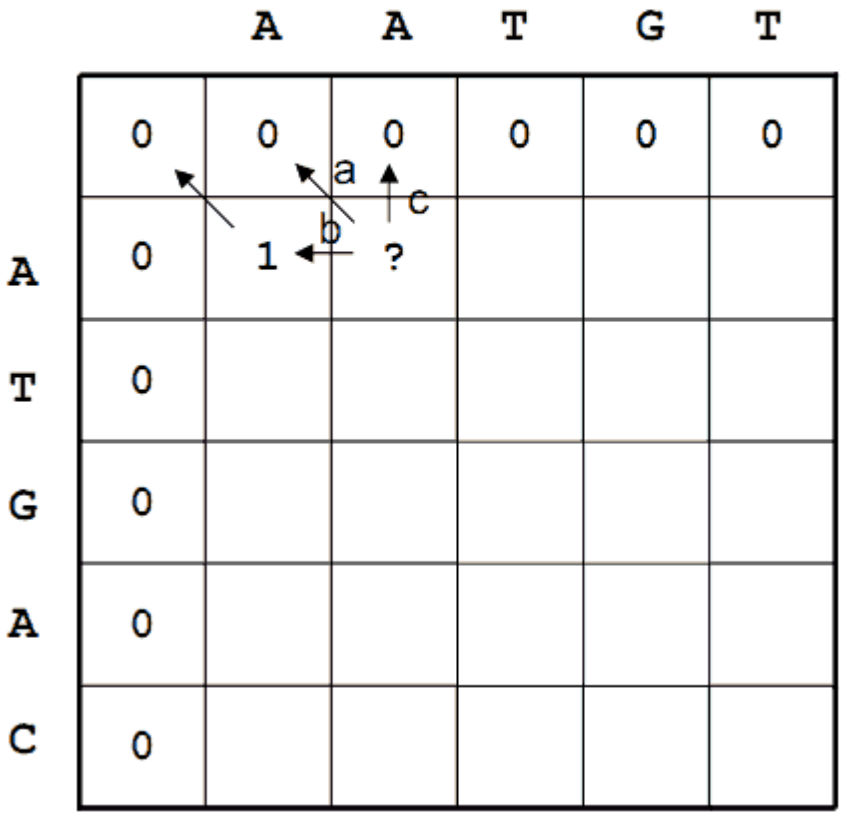
Maximum of possible scores:

(a) 0 + s(A,A) = 0 + 1 = 1

(b) 1 - g = 1 - 2 = -1

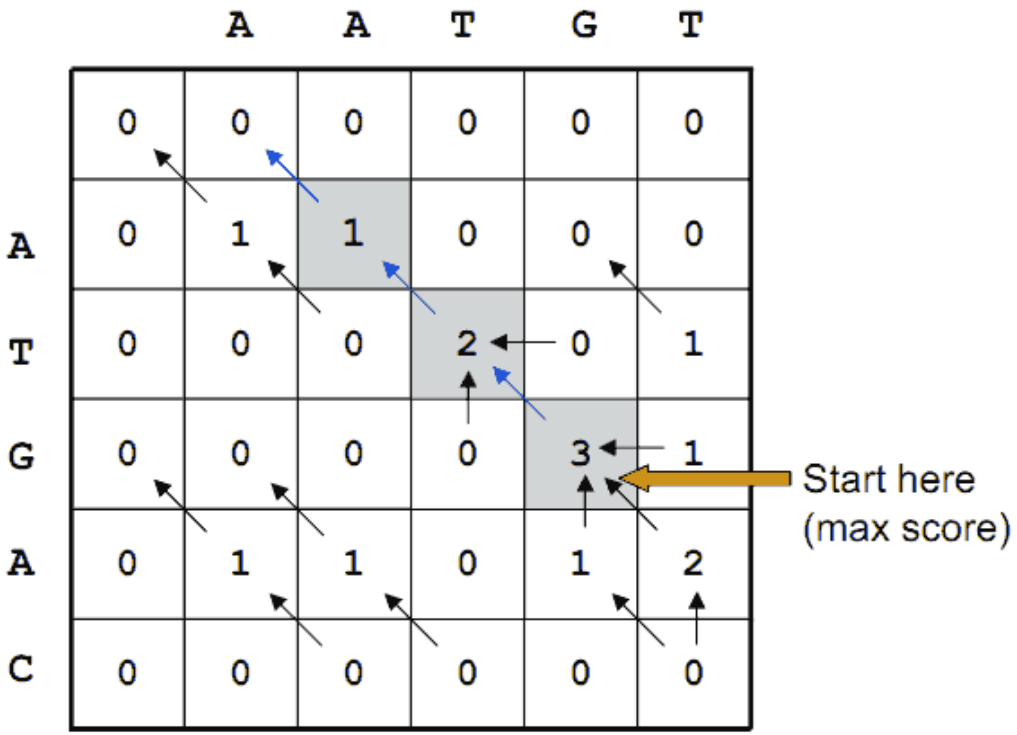
(c) 0 - g = 0 - 2 = -2

(d) 0 (no pointer)



# Algorytm S-W: rekonstrukcja ścieżki

1. Startujemy z komórki o najwyższej wartości.
2. Kontynuujemy dopóki nie osiągniemy wartości 0.




Local Alignment shown in blue:

AATGT
ATGAC

# Optymalne dopasowania

Podobnie jak w algorytmie N-W, może istnieć wiele optymalnych dopasowań.

Mogą one mieć różną długość.

| | | A | E | K | P | C | A | Y | E | N | N | E | F |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| E | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 |
| K | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| C | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| A | 0 | 1 | 0 | 0 | 0 | 1 | 3 | 2 | 1 | 0 | 0 | 0 | 0 |
| Y | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 4 | 3 | 2 | 1 | 0 | 0 |
| E | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 3 | 5 | 4 | 3 | 2 | 1 |
| N | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 4 | 6 | 5 | 4 | 3 |
| E | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 3 | 5 | 5 | 6 | 5 |
| P | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 4 | 4 | 5 | 4 |
| I | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 3 | 4 | 3 |
| L | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 3 | 2 |
| A | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 2 | 1 |

EKPCAYEN
EK-CAYEN

EKPCAYENNE
EK-CAYEN-E

EKPCAYENNE
EK-CAYE-NE

Tworzymy trzy macierze: *H, E i F* z warunkami brzegowymi:

$$H_{i,j} = \max\begin{cases} H_{i-1,j-1} + s(a_i, b_j) \\ E_{i,j} \\ F_{i,j} \\ 0 \end{cases}$$

$$H_{0,0} = 0$$
$$H_{i,0} = 0$$
$$H_{0,j} = 0$$

$$E_{i,j} = \max\begin{cases} H_{i-1,j} + Go + Ge \\ E_{i-1,j} + Ge \end{cases}$$

$$E_{0,0} = -\infty$$
$$E_{i,0} = Go + i*Ge$$
$$E_{0,j} = -\infty$$

$$F_{i,j} = \max\begin{cases} H_{i,j-1} + Go + Ge \\ F_{i,j-1} + Ge \end{cases}$$

$$F_{0,0} = -\infty$$
$$F_{i,0} = -\infty$$
$$F_{0,j} = Go + j*Ge$$