On DNA Sequences and graphs

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Contact info:

- Course website `regulomics.mimuw.edu.pl/wp/categories/wbo`
- e-mail `bartek@mimuw.edu.pl`
- meeting: Wed 8:30–10:00, room 5770, or by e-mail appointment

Grading scheme

- Homework - optional - max 10 points total
- Project assignments: 1 small project (10pts) 1 large project (20 pts) (50 percent penalty if late)
- Writen test (open questions) - 30 pts
- Passing grade: $>$ 35 pts
- Oral exam - only for students with a passing grade
- if you have enough points, you don't have to take the oral exam

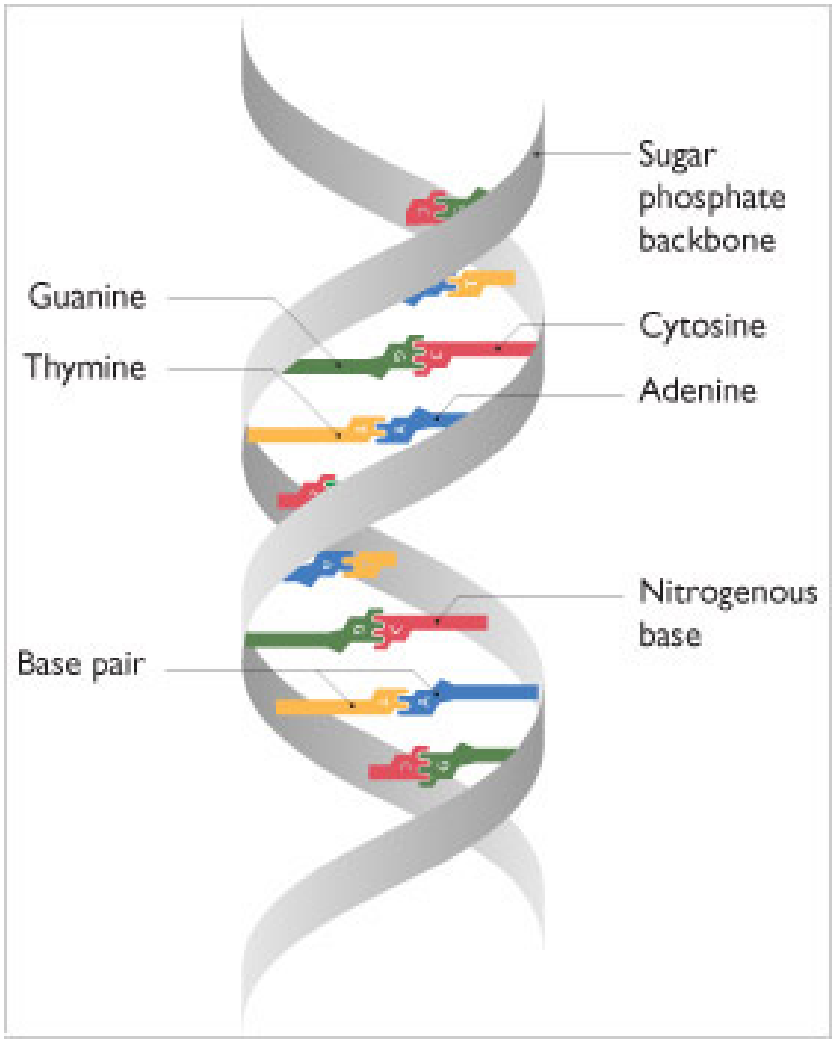
Topics

- Biological sequences (DNA, RNA and amino-acid chains)
- Sequence similarity and evolution
- Comparing biological sequences
- Phylogenetic trees - construction and applications
- Hidden Markov Models for biological sequences
- Non-coding sequences
- Next-generation sequencing and sequence assembly

Books

- Computational Molecular Biology (P. Pevzner)
- Biological Sequence Analysis (R. Durbin i in.)
- Sequence – Evolution – Function (Koonin i Galperin)

DNA and its role



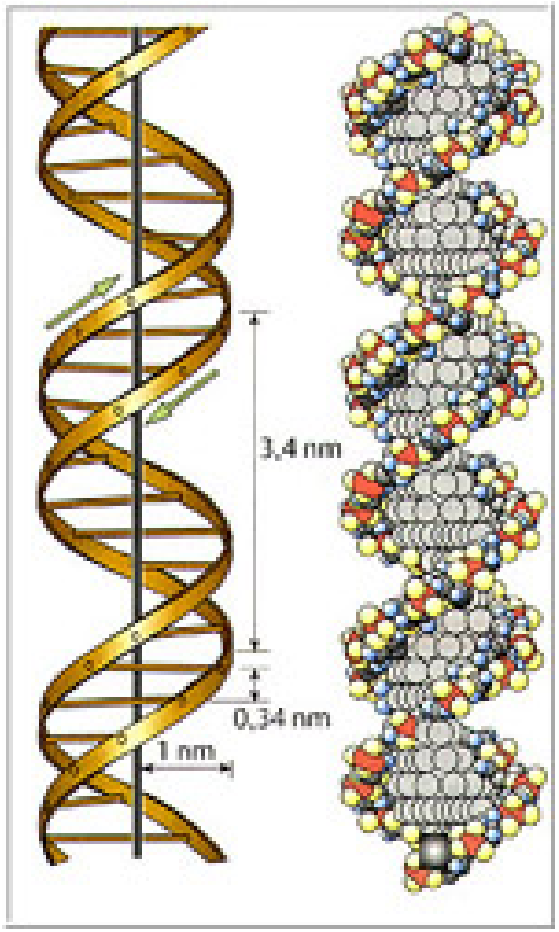


image (c) T. Maxwell

DNA replication enables inheritance

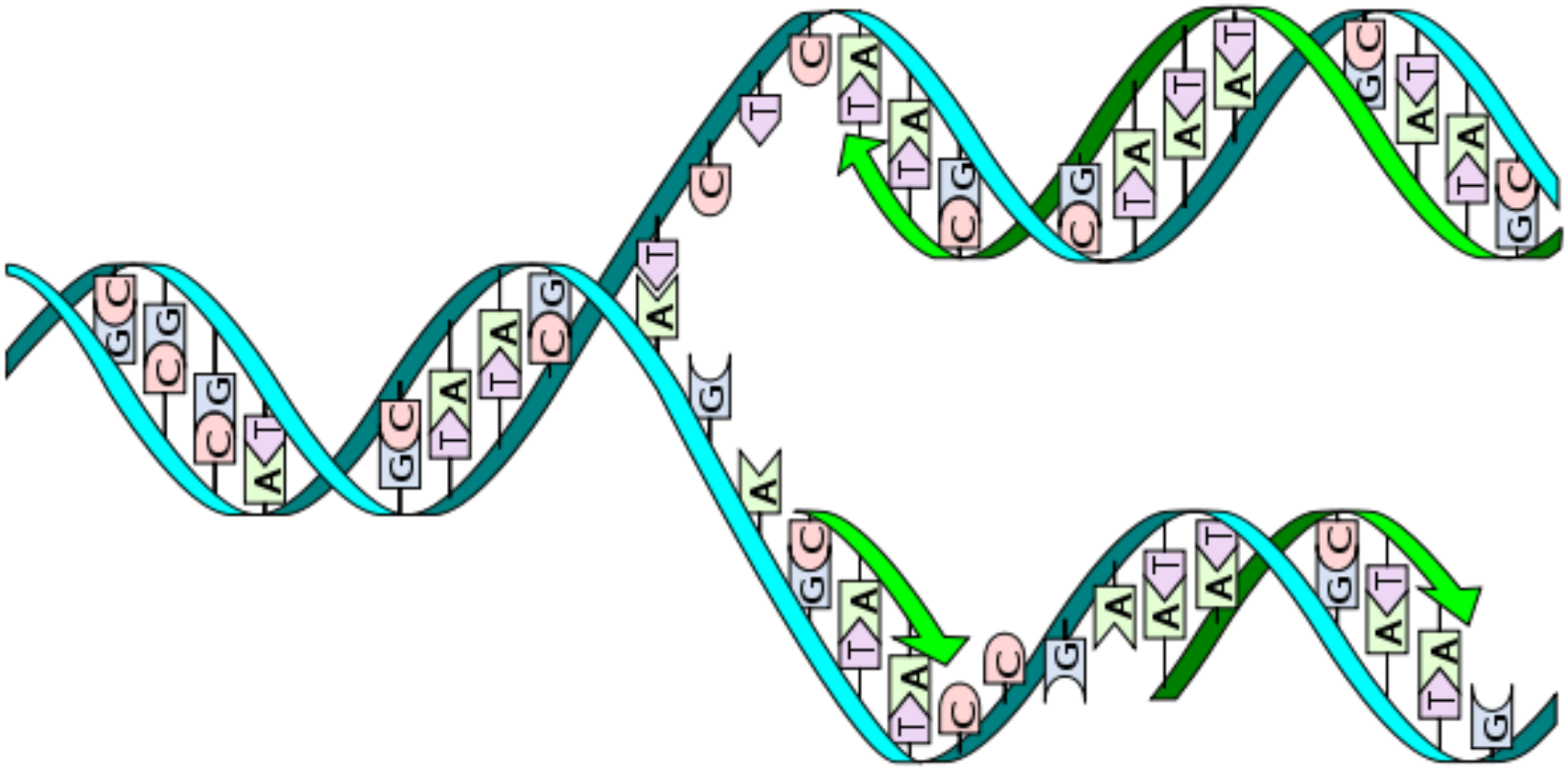


image (c) wikimedia

Central dogma of molecular biology

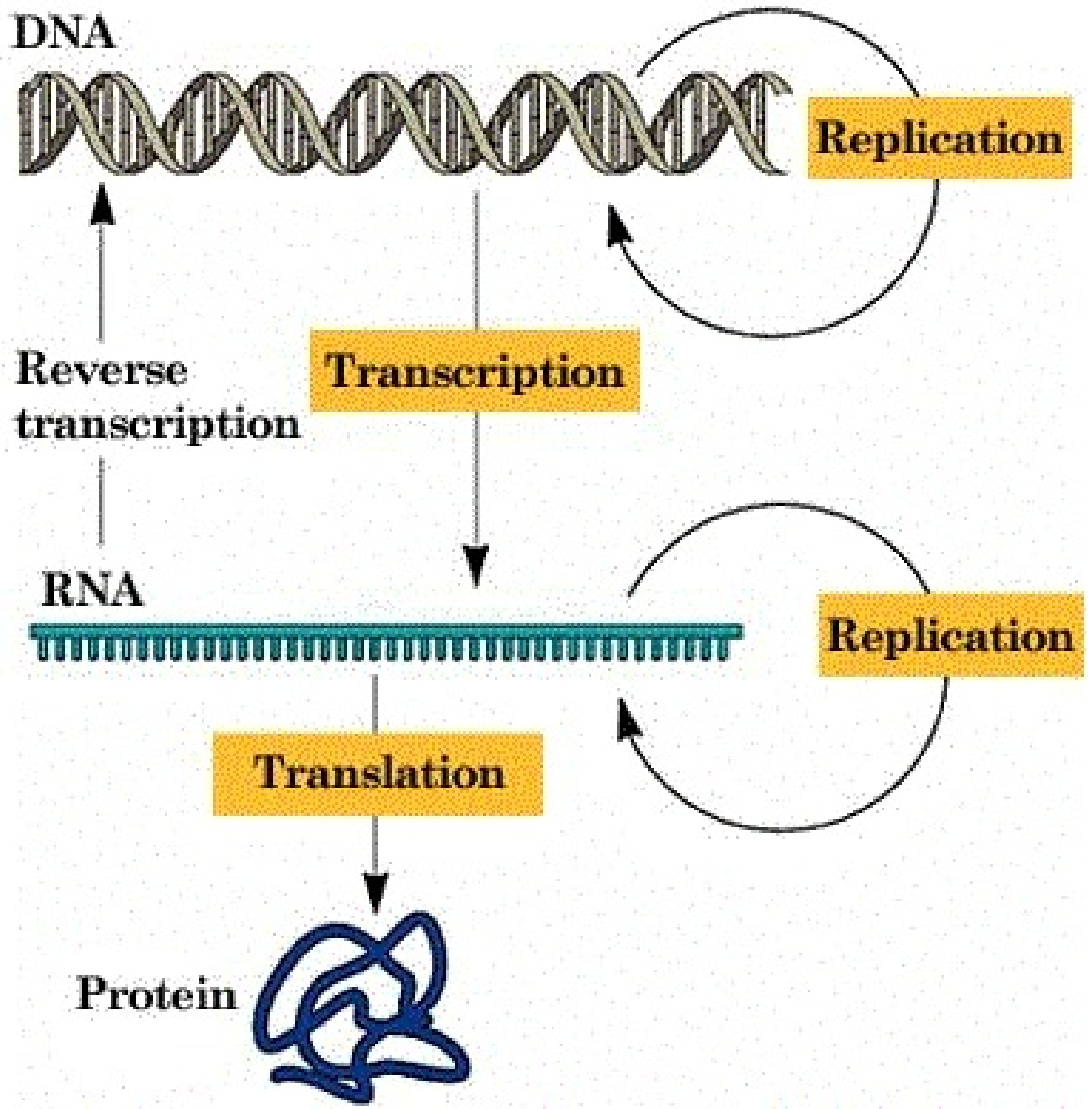


image (c) SCF IIT Delhi

Microarray concept

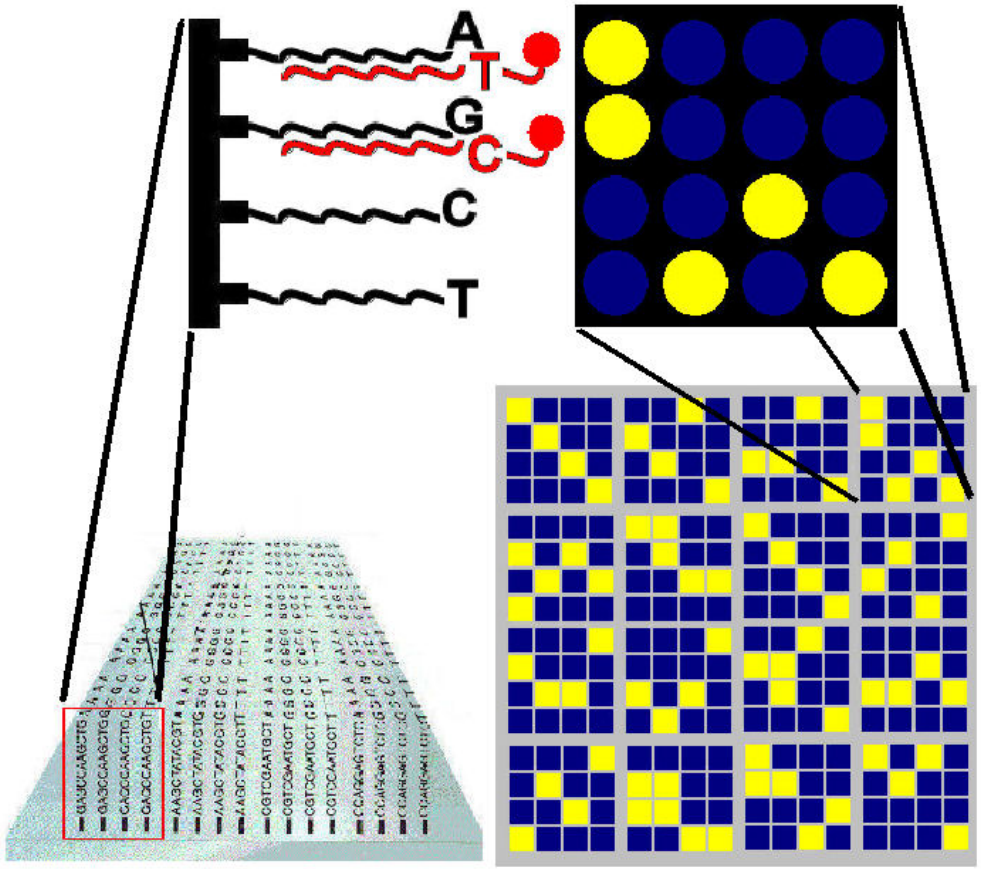


image (c) Steven M. Carr

affymetrix chip

image (c) Molecularstation.com

Sequencing by hybridization

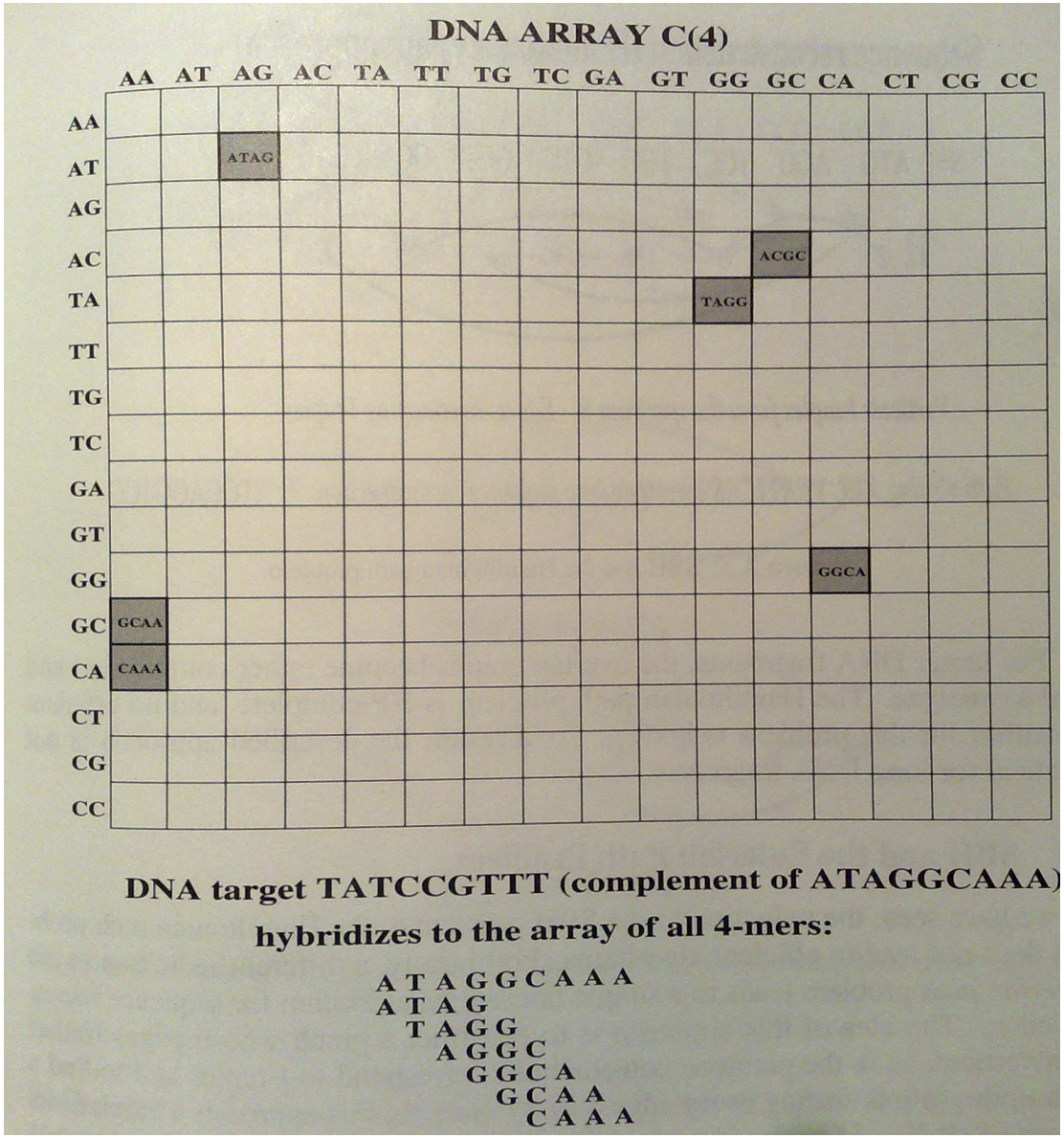


image (c) P. Pevzner

SBH - natural approach

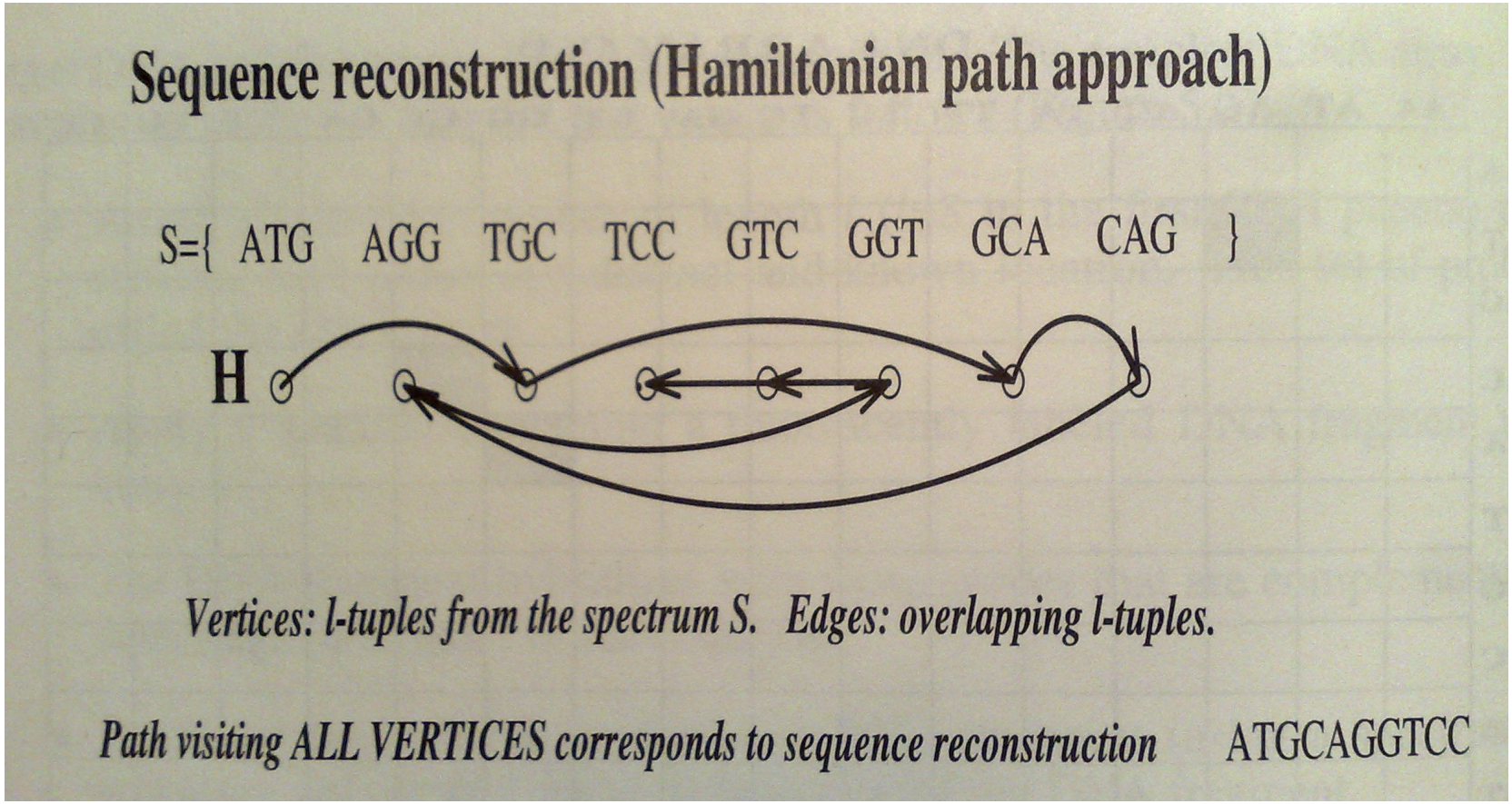


image (c) P.Pevzner

SBH - multiple solutions

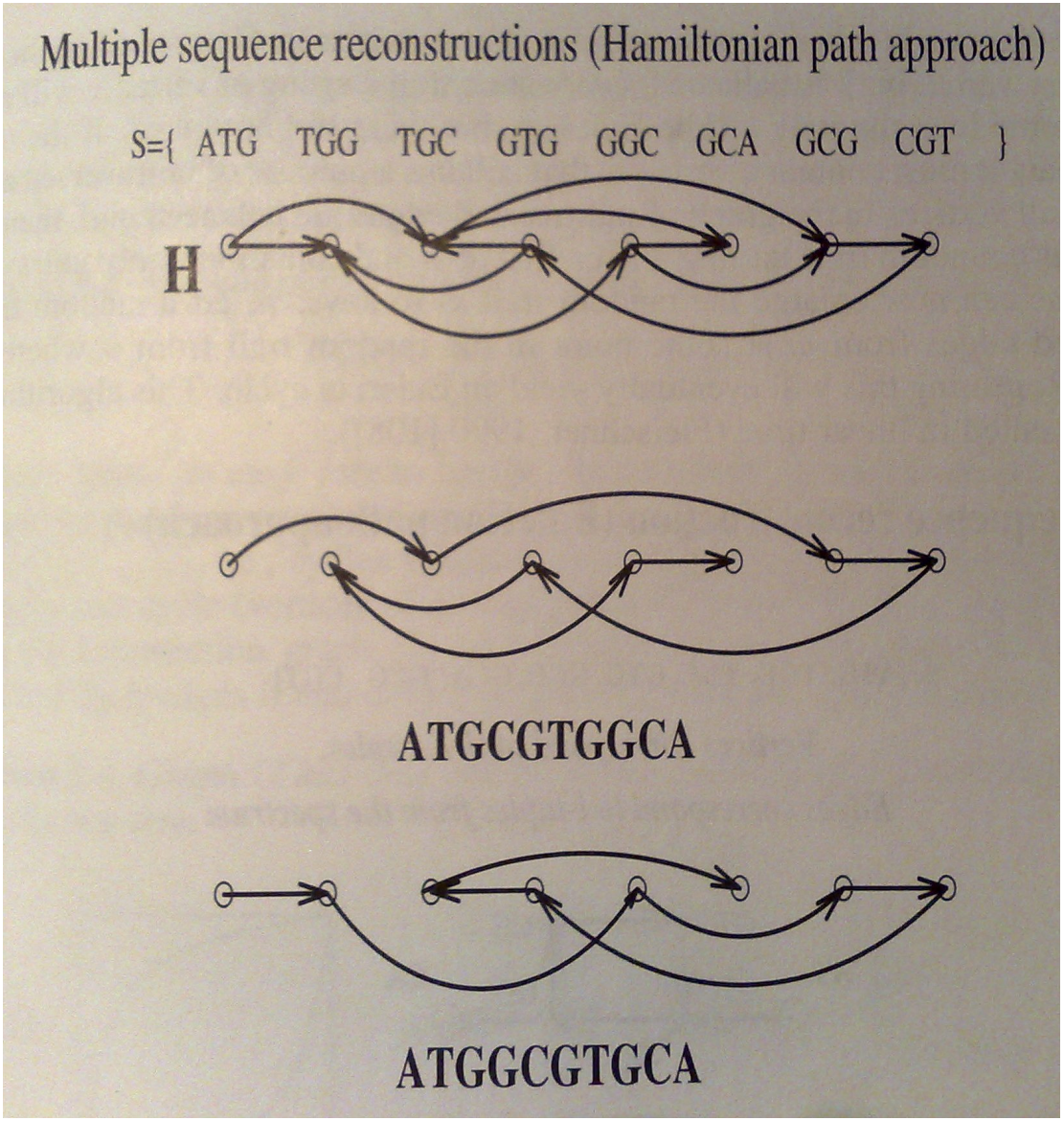


image (c) P.Pevzner

Hamiltonian and Eulerian graphs

Finding Hamiltonian paths is NP-complete, while finding Eulerian paths is easy.

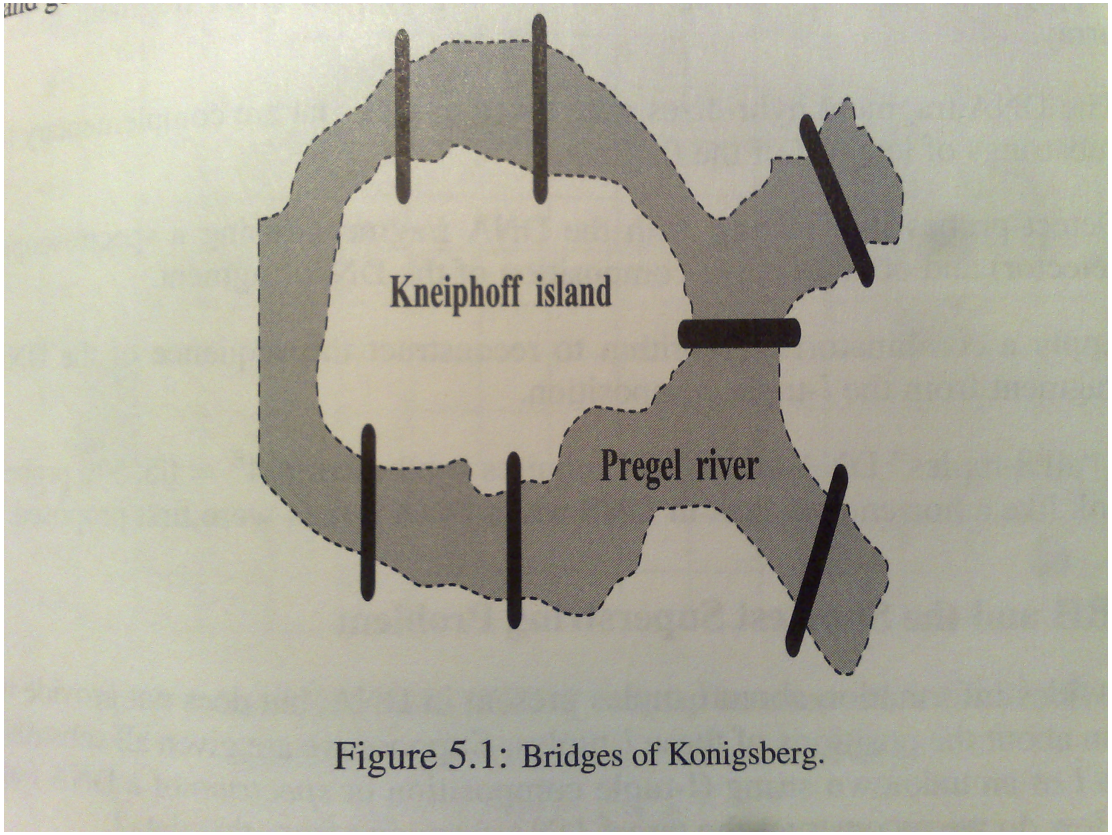


Figure 5.1: Bridges of Konigsberg.

image (c) P.Pevzner

SBH - Eulerian formulation

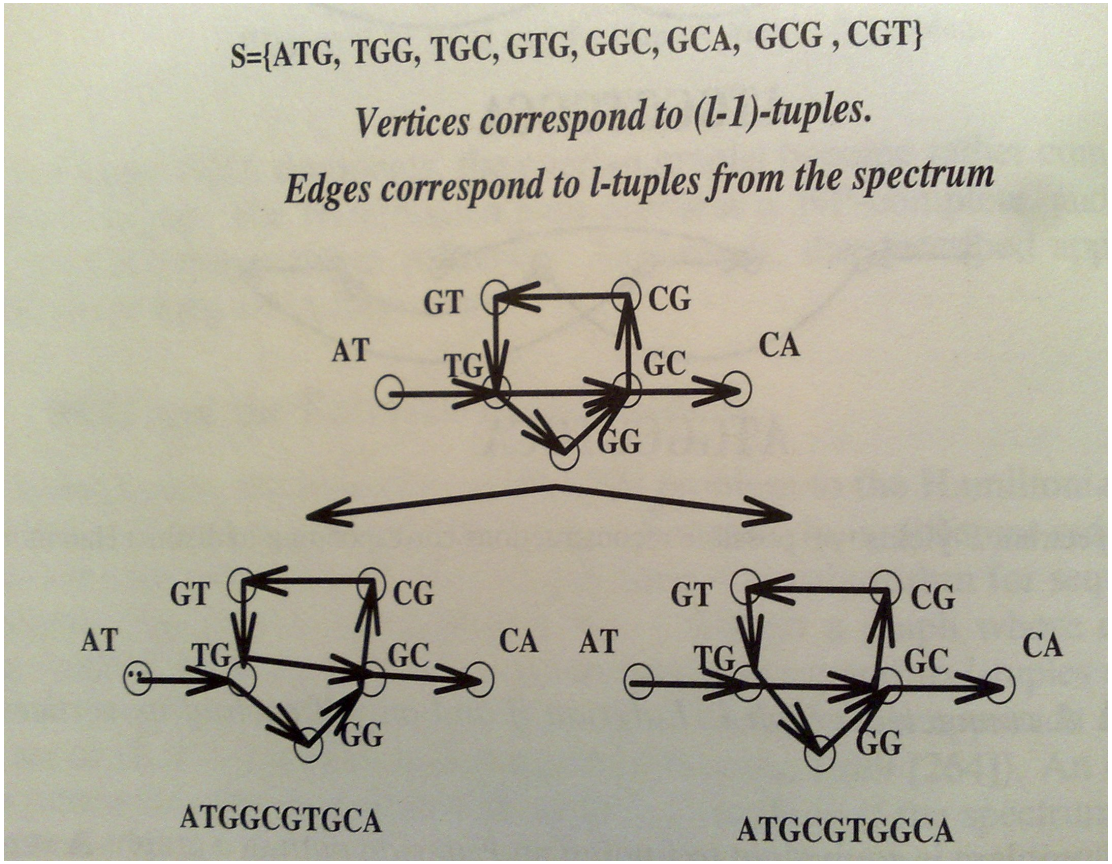


image (c) P.Pevzner

Other uses of microarrays

- SBH not practical due to hybridization errors, superseded by Next generation sequencing
- Gene arrays for RNA abundance quantification
- Snip arrays for detecting mutations (disease screening, paternity tests)
- aCGH arrays for detecting copy number variation
- biochips for quick pathogen detection

Designing unique probes

- We are given a set of n different DNA sequences (targets) $\mathcal{S} = \{s_1 \ldots s_n\}$
- We need to design a set $\mathcal{P} = \{p_1 \ldots p_n\}$ of n sequences (probes) of length k, such that for each $i \in \{1 \ldots n\}$, probe p_i hybridizes with sequence s_i and does not hybridize with any other sequence $s_{j,j \neq i}$.
- Depending on the amount of sequence identity and parameter k, there might be no valid solutions or exponentially many solutions
- Instead of searching for probes of the same length, one might search for probes of the same *melting temperature*

$$t_m = 4 \cdot \#GC + 2 \cdot \#AT$$