History of Topology

Semester I, 2009-10

Graham Ellis
NUI Galway, Ireland

History of Topology Outline

- Lecture 1:
  What is topology?
  Euler circuits in graphs
- Lecture 2:
  Topological invariants:
  Euler-Poincaré characteristic
- Lecture 3:
  One recent application of topology in biology

Some Elementary Biology

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  e.g. offspring of a blue eyed mother and brown eyed father has 3/4 chance of having brown eyes.
- In 1889 Hugo de Vries gave Mendel's inheritance mechanism the name *gene*. Had little understanding of the physical nature of a gene.

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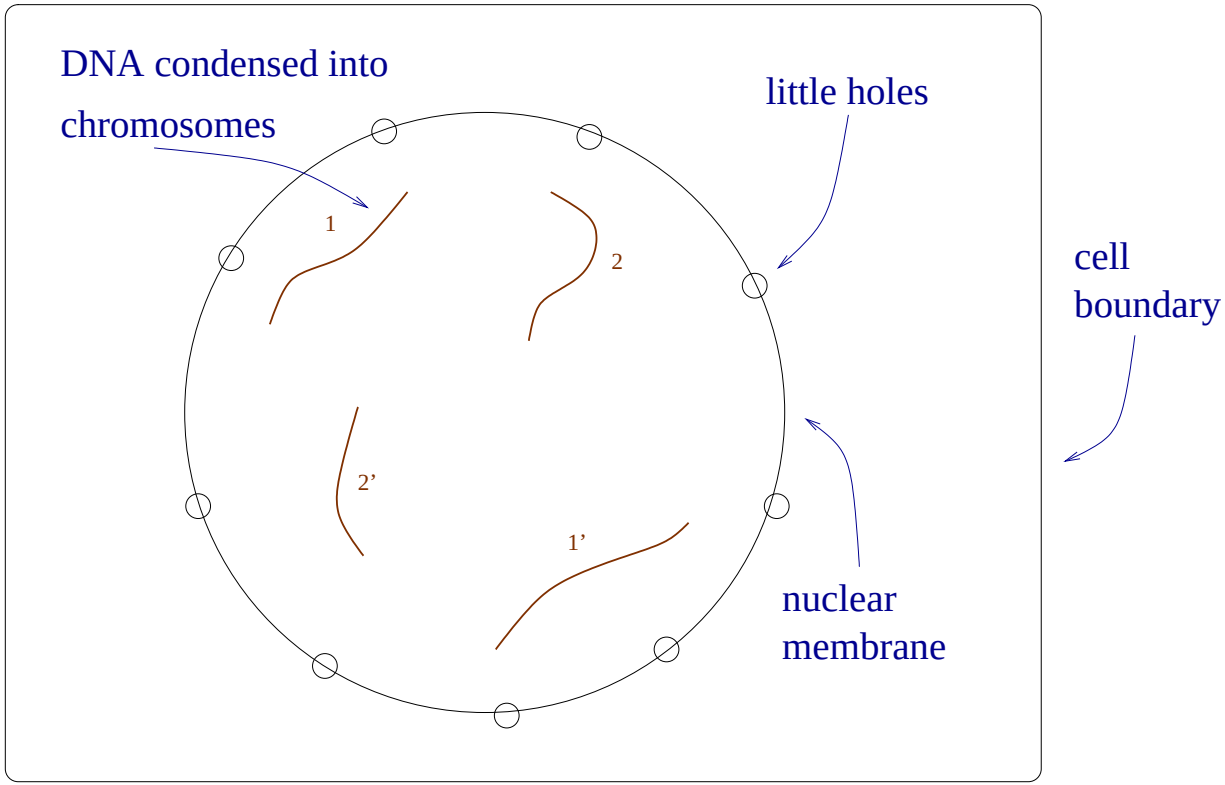
- In 1953 Crick and Watson demonstrated the molecular structure of DNA.

A typical (animal) cell

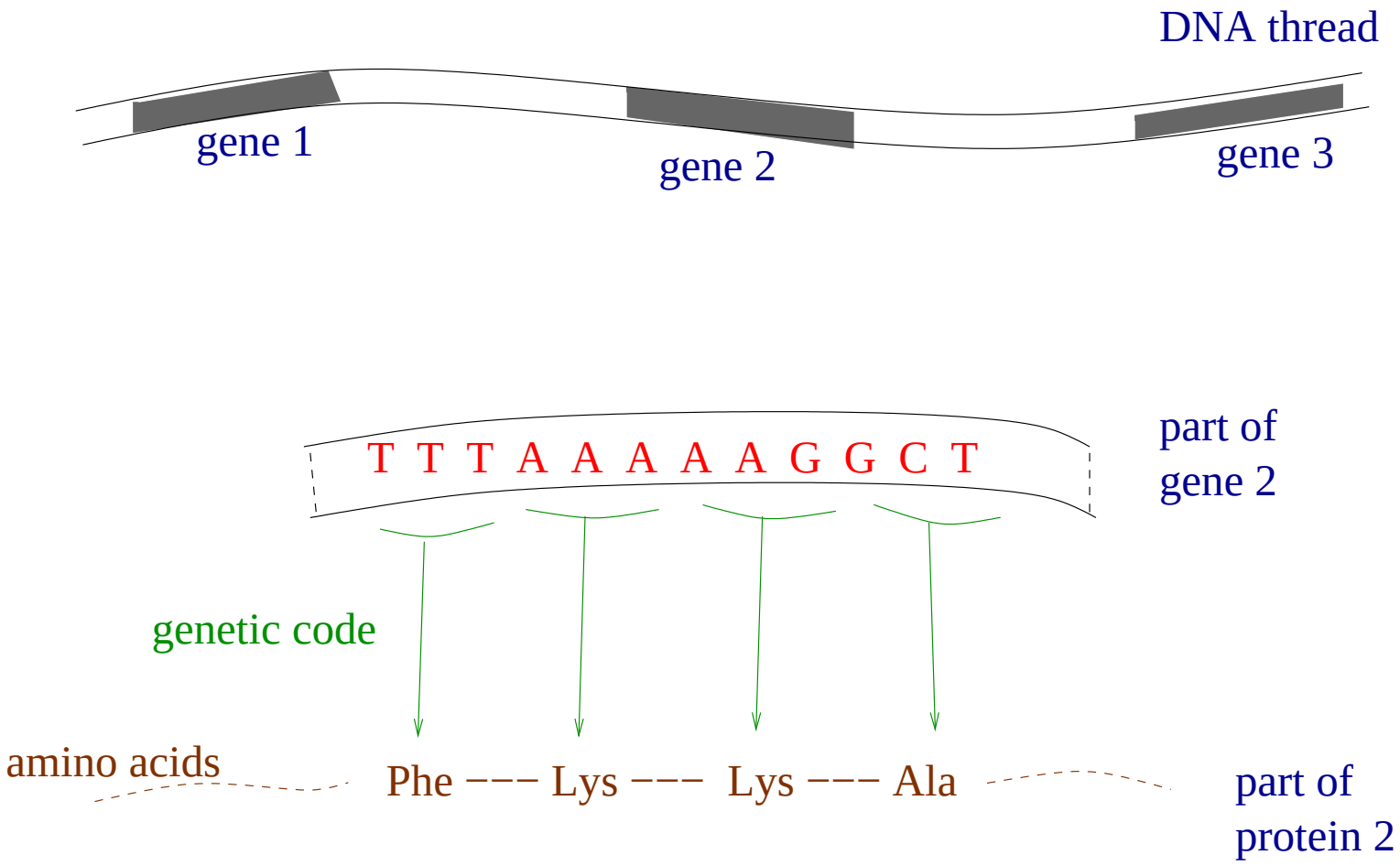


Chromosomes contain a mixture of protein and DNA. They often come in pairs.

Humans cells contain 46 chromosomes in 22 homologous pairs plus the non-homologous X and Y chromosomes that determine sex.

What is DNA?

DNA is a string of four different nucleotides: **A**denine, **G**uanine, **C**ytosine and **T**hymine.



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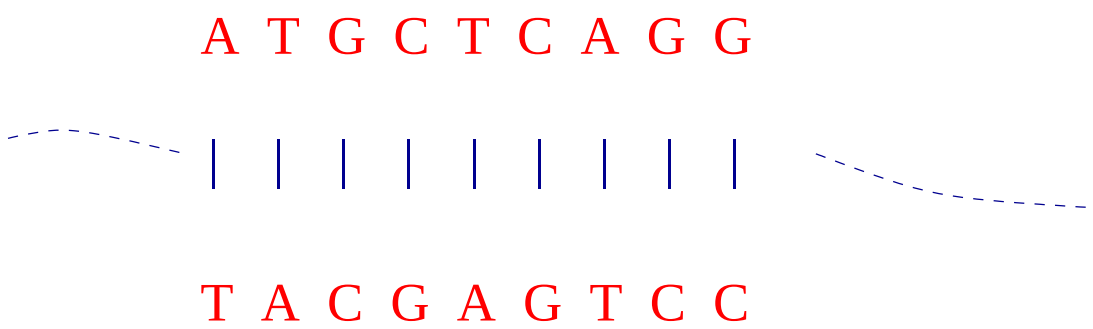

Question

Given a long strand of physical DNA, how can a biologist determine the sequence of letters

$$\ldots ACCGATTGCAGTAGC \ldots$$

representing the DNA?

Answer

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Given a long single stranded target thread, the target will bind (or hybridize) to precisely those probes which are the Crick-Watson complement of fragments of the target thread.

Hybridization

For example, the probe

$$ACCGTGGA$$

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since the probe's Crick-Watson complement is

$$TGGCACCT.$$

The upshot

Using arrays of probes of a given length L, biologists can determine all the letter sequences of length L contained in a target DNA thread.

A mathematical question

How can we determine a DNA letter sequence from a knowledge of all L-letter fragments of the sequence?

Example of the question

Suppose that a DNA array analysis of a piece of single-standed target DNA, using probes of length $L = 3$, shows that the length 3 fragments of the target DNA are precisely:

$$F = \{ATG, TGG, TGC, GTG, GGC, GCA, GCG, CGT\}$$

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What can we say about the target DNA?

Some topology

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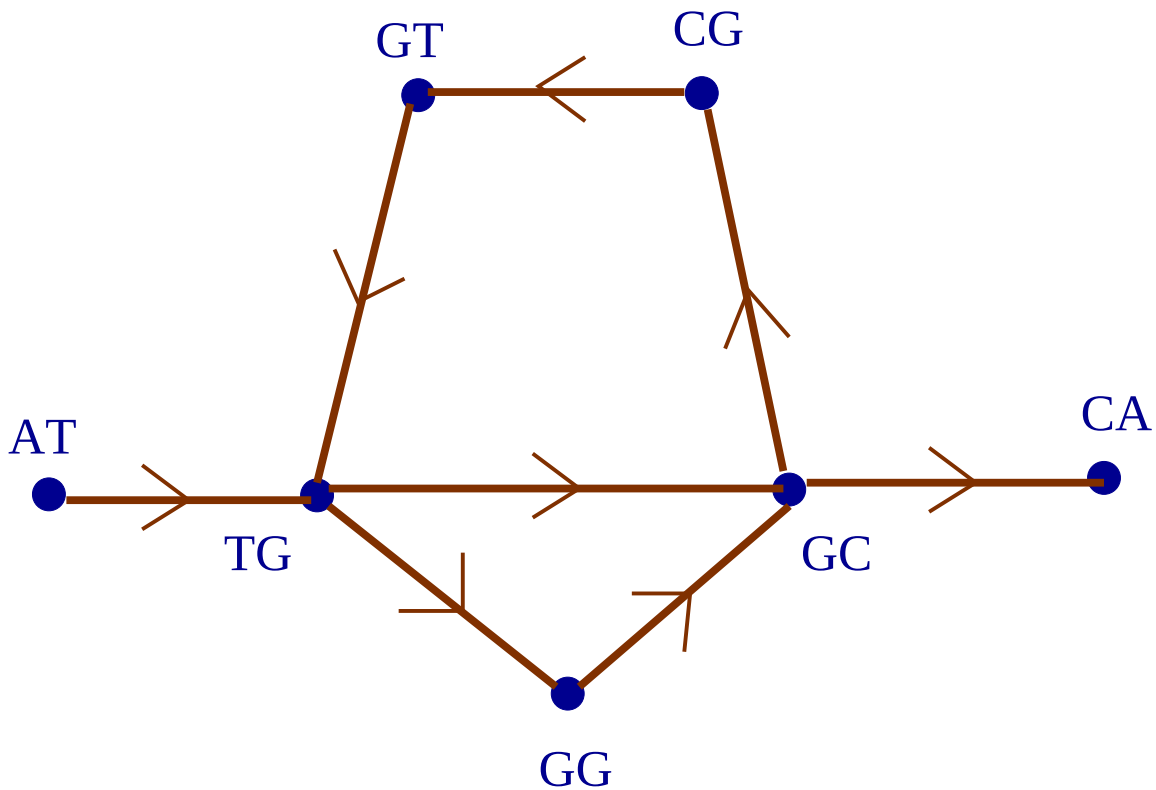
Moreover, we'll place an arrow on the edge going from XY towards YZ.

Some topology

For $F = \{ATG, TGG, TGC, GTG, GGC, GCA, GCG, CGT\}$ the graph's eight edges are as follows.



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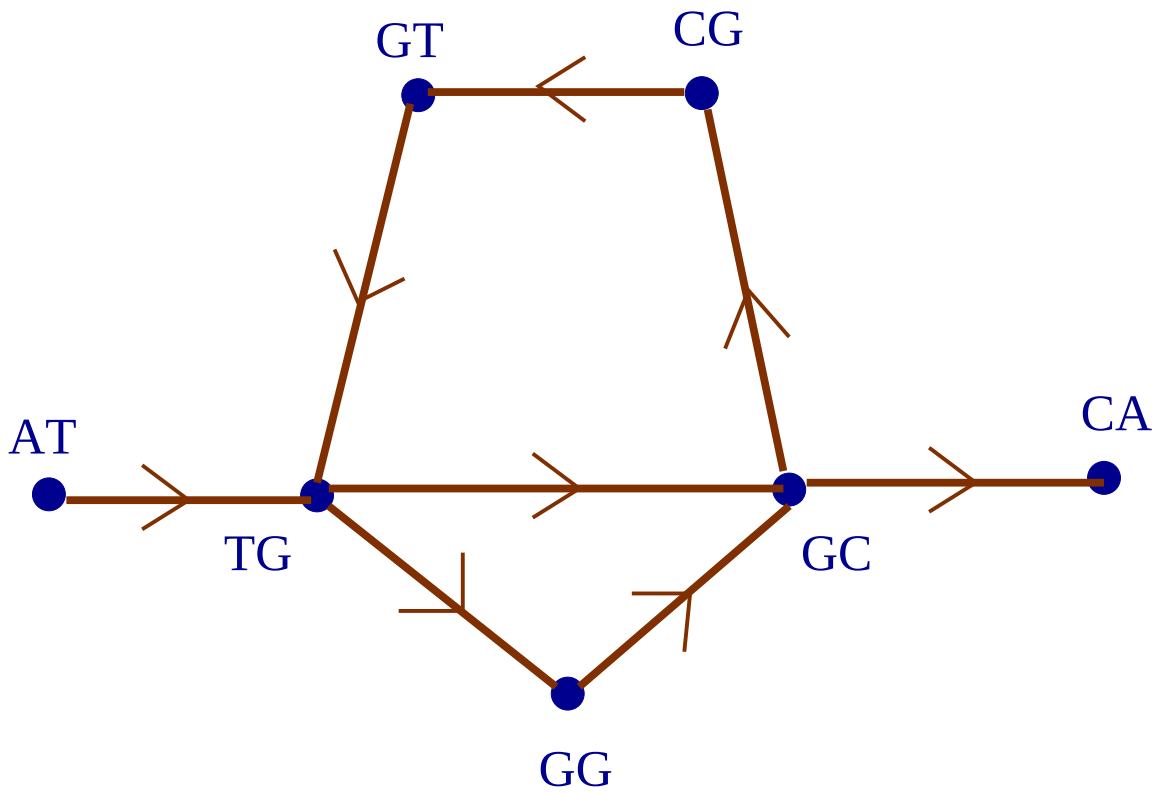
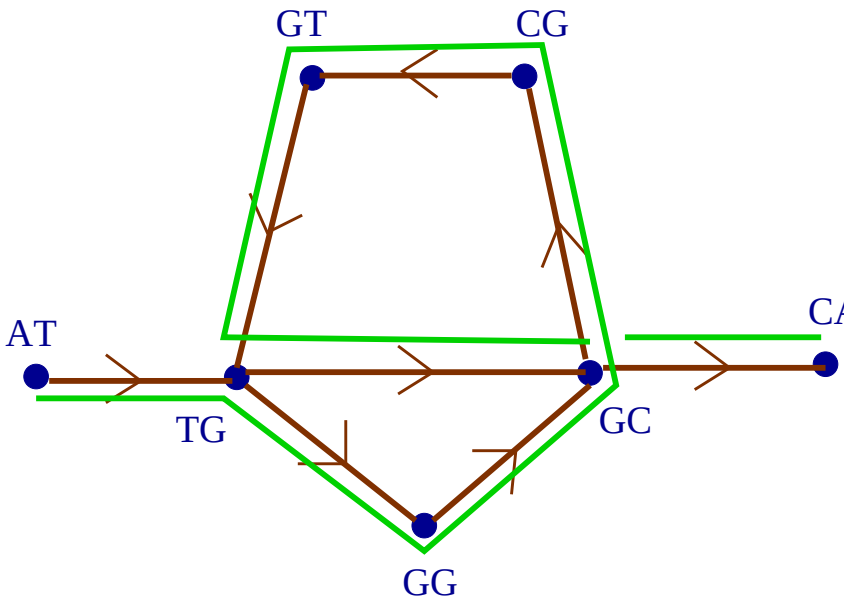


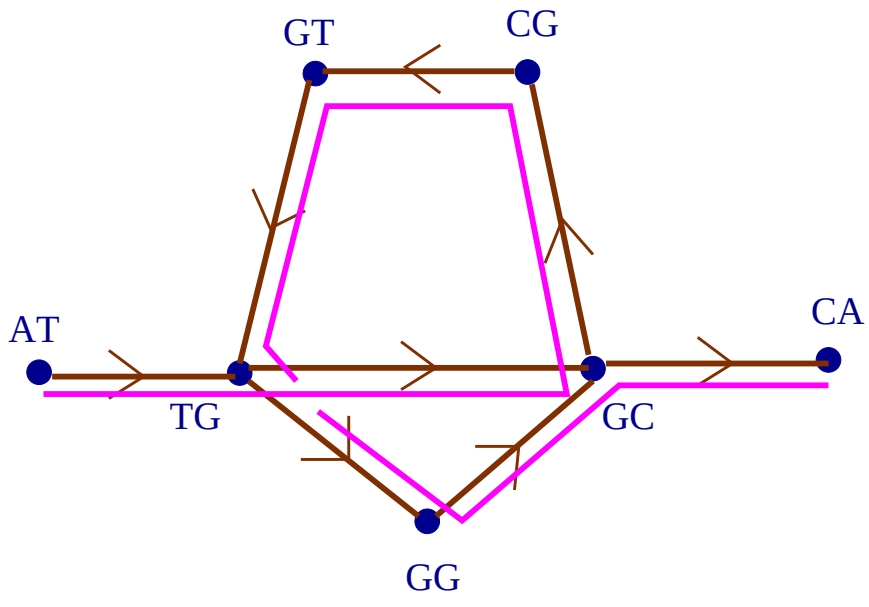
The target DNA corresponds to an Euler path in this graph (where the path direction is given by the arrows in the graph).

Some topology

There are just two possible Euler paths.



ATGGCGTGCA



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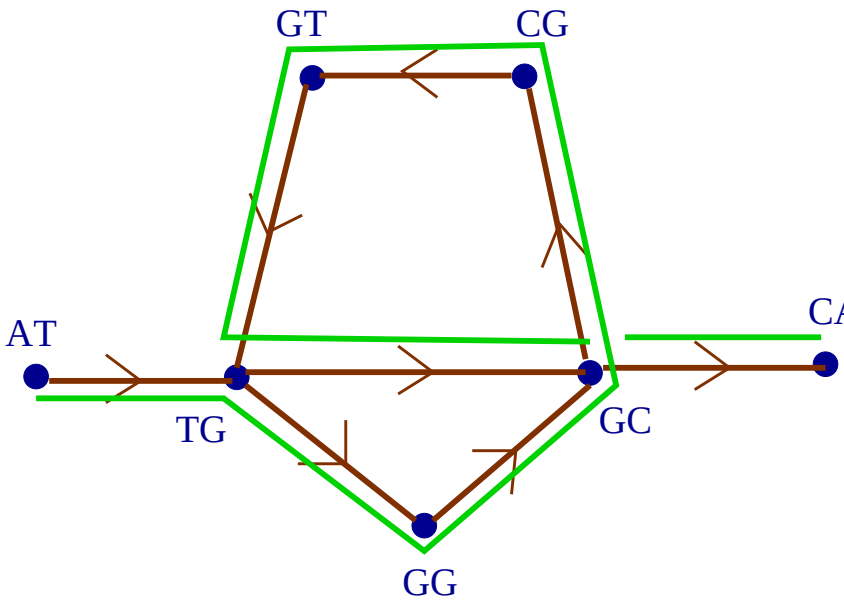

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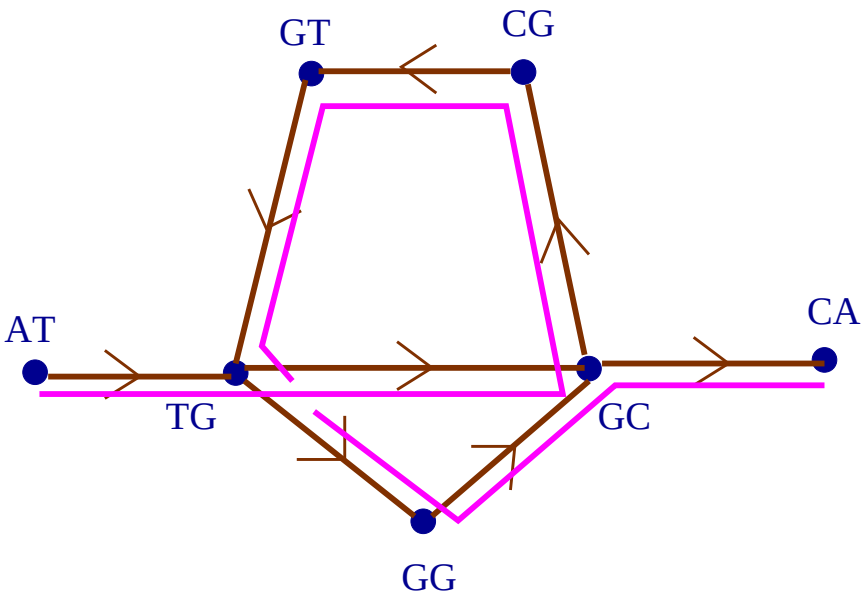

ATGCGTGGCA

So the possible sequences for the target DNA are: ATGGCGTGCA and ATGCGTGGCA.

Some topology

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Answer: Euler's proof of his theorem explains how to produce an Euler path.

Reference

P.A. Prevzner, *L*-tuple DNA sequencing: computer analysis, *Journal of Biomolecular Structure and Dynamics* 7 (1989), 65-73.