Lecture 1.3

Introduction:
Strings that encode Life

Historical Perspective

- …   – 1900 Pre-Mendelian period
- 1900 – 1940 Pre-DNA period
- 1940 – 1990 DNA period
- 1990 – 2003 Genomic period

►2003 – …   Post-genomic era

Ambitions

- Systems biology
  - Complete set of all molecules of an organism
  - Complete set of interactions between these parts
  - Modeling of life
- Synthetic biology
  - *Mycoplasma laboratorium* is a minimal genome organism obtained by removal 100 genes from 482 genes of the smallest organism grown in culture, *M. genitalium*
- Evolution

Practical goals

- Medicine and agriculture

  Gene therapy with no side effects

- Synthetic biology – engineering new products

  Since natural biological systems are so complicated, we would be better off re-building the natural systems that we care about, from the ground up, in order to provide engineered surrogates that are easier to understand and interact with.

  Example: Biofuel in a minimal genome – Mycoplasma laboratorium

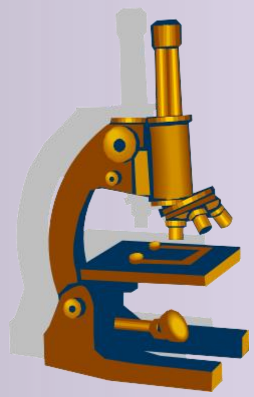
The post-genomic era

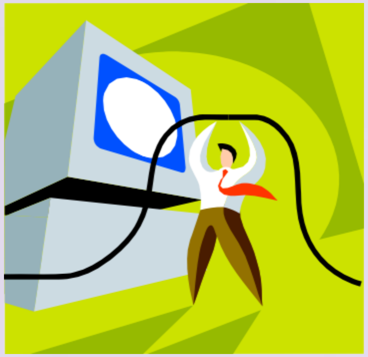
– Let me now comment on the question "what next". Up to now we were working on the descriptive phase of molecular biology. ... But the real challenge will start when we enter the synthetic biology phase of research in our field.

We will then devise new control elements and add these new modules to the existing genomes or build up wholly new genomes. This would be a field with the unlimited expansion potential and hardly any limitations to building "new better control circuits" and ..... finally other "synthetic" organisms, like a "new better mouse". ... I am not concerned that we will run out exciting and novel ideas…Waclaw Szybalski

Perspectives

- Computational tools instead of a microscope
- Very long period …

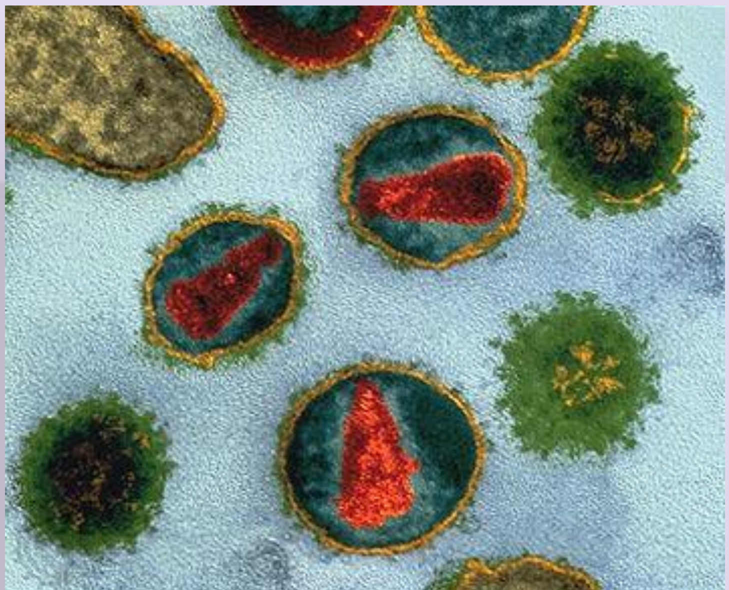




Problems can be solved algorithmically

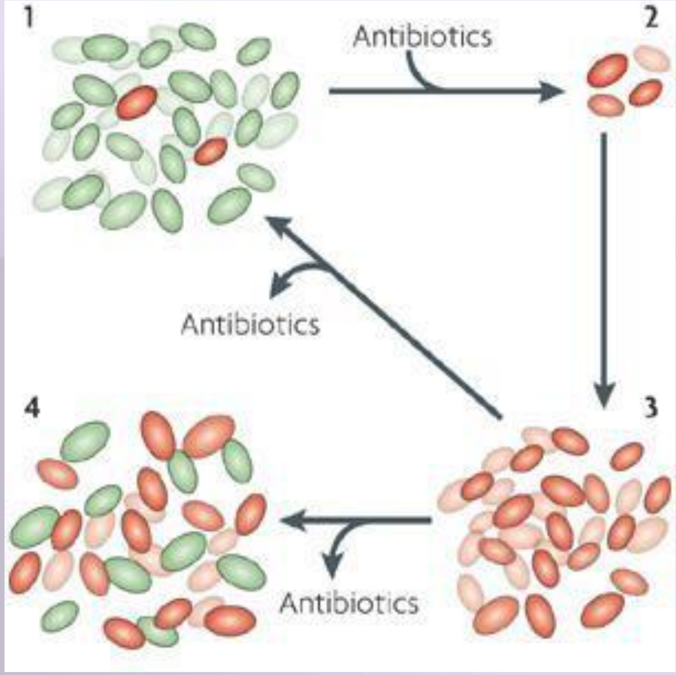
Problem 1.HIV virus: high mutation rate

Subject: The plan - Re: request for alignment of HIV sequences



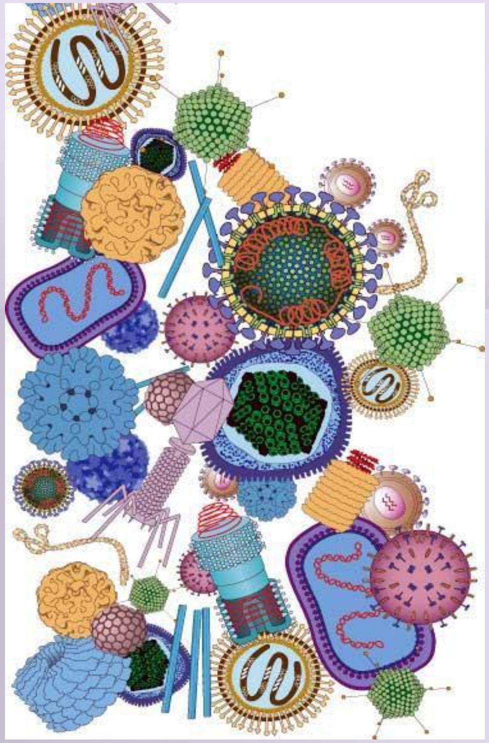
Find local regions of high similarity to design HIV drugs

Problem 2. Antibiotics resistance



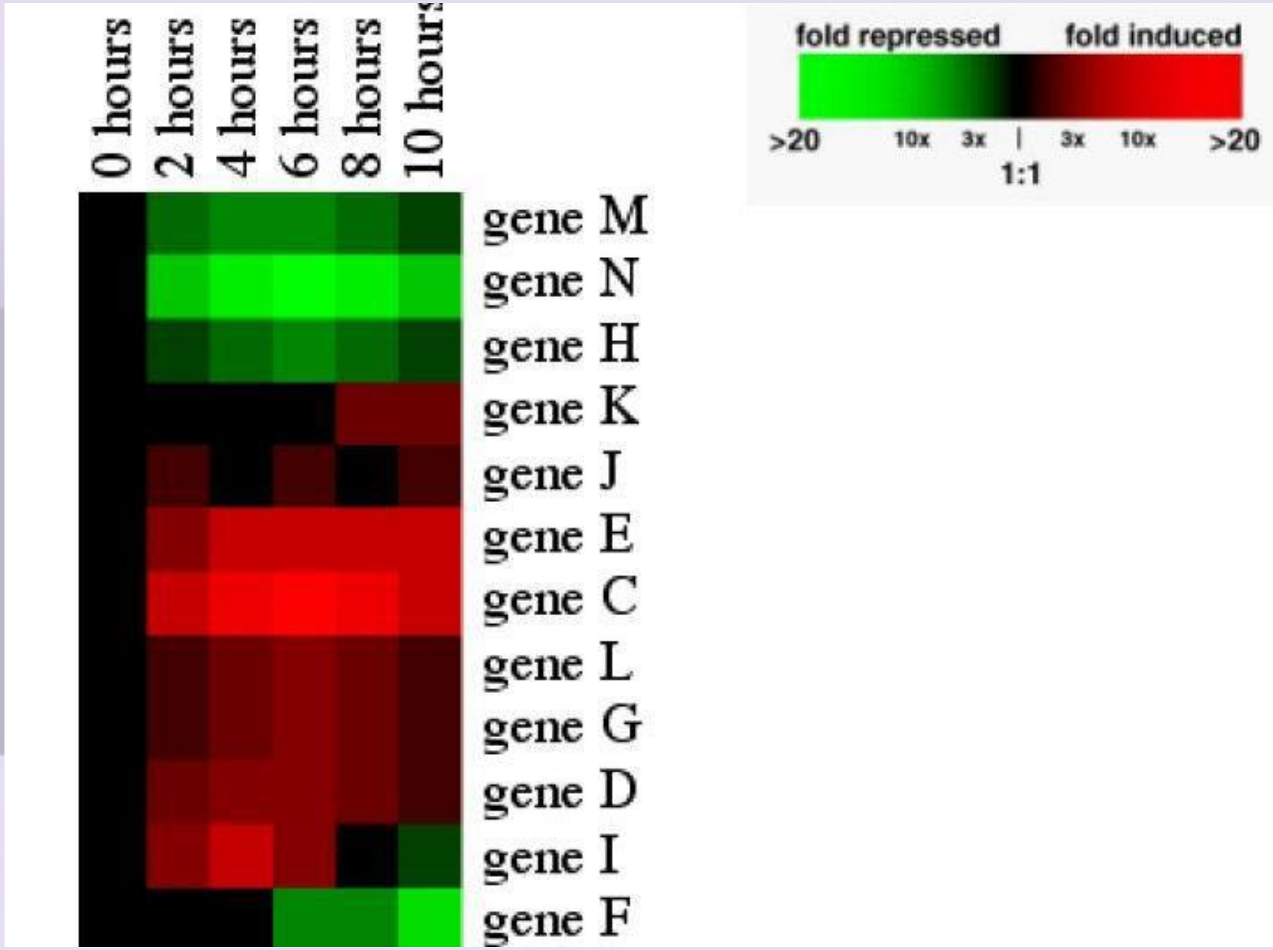
Design a new type of antibiotics which will kill all pathogenic bacteria, and no mutant strain will survive and proliferate?

Problem 3. Sequence redundancy in viral databases



Remove the redundant sequence information from the database of viral genomes

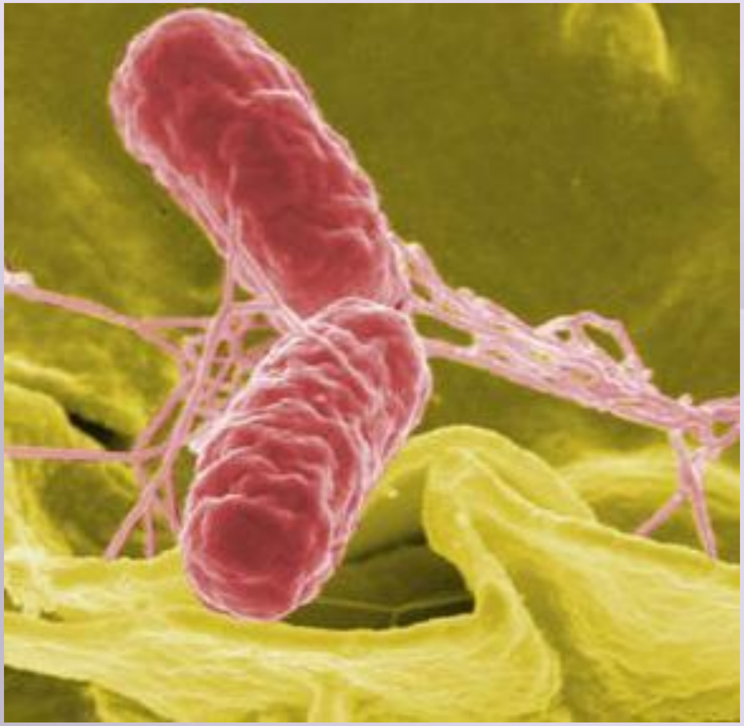
Problem 4. Expression patterns



Identify the group of genes with similar expression patterns

Time series comparison

Problem 5. Lethal E.coli



The pathogenic strain contains O-islands, and the normal strain contains K- islands, with different frequency of nucleotides.

Detect an early mutation of a normal E. coli into a pathogenic strain

O157-H7 modification of E. Coli (in undercooked beef) causes occasionally lethal hemorragic colitis

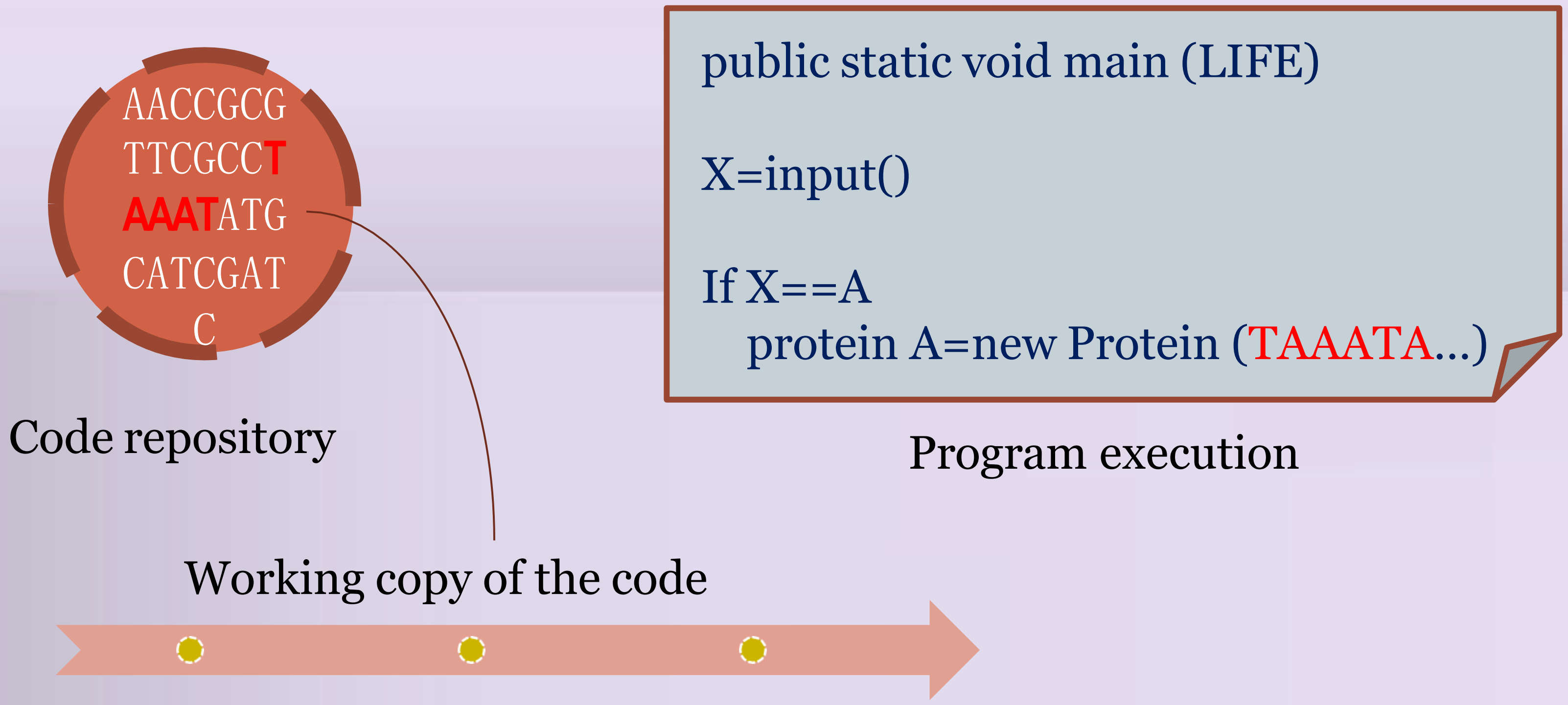
Living cells as computational devices

Code repository

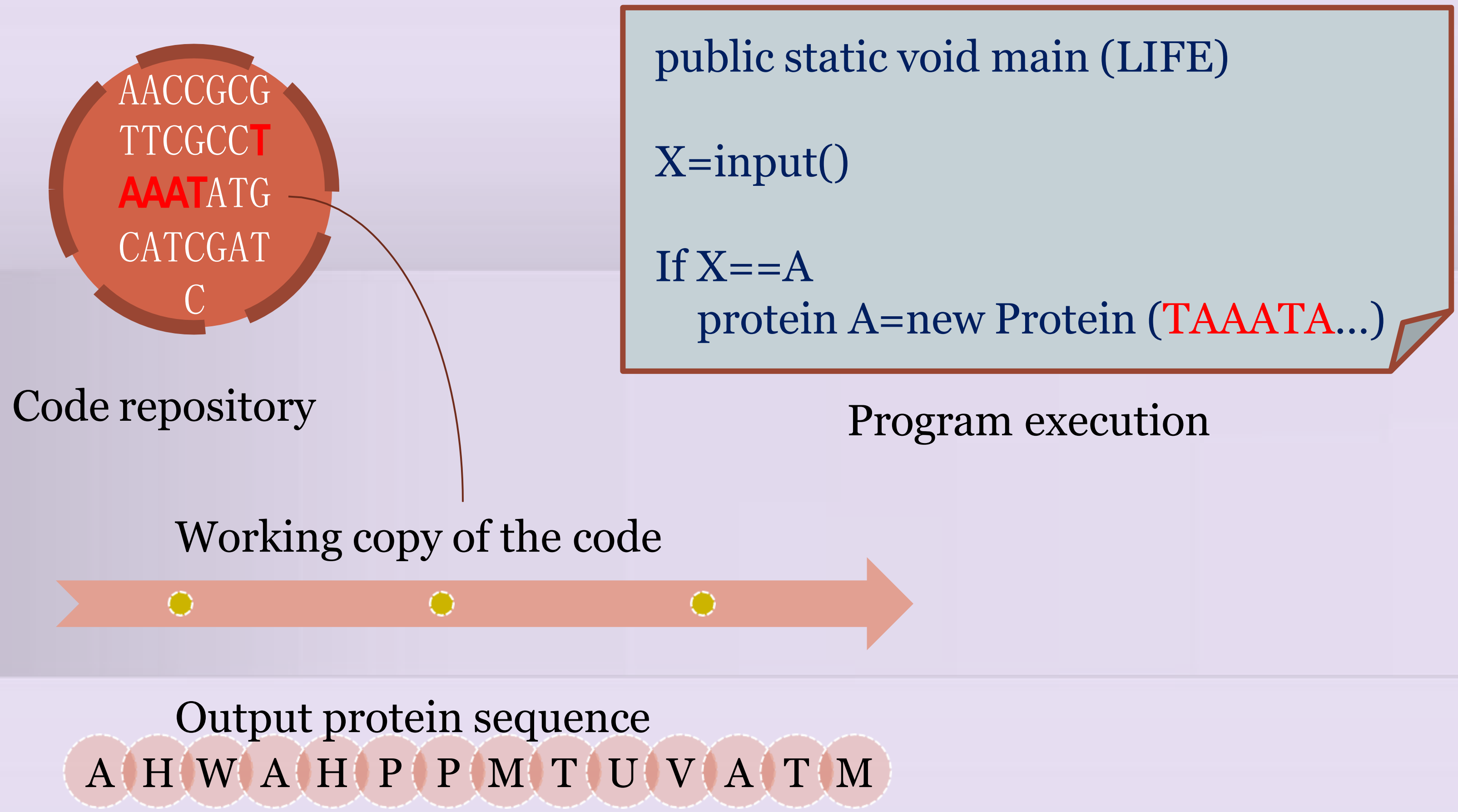
```
public static void main (LIFE)

X=input()

If X==A
   protein A=new Protein (TAAATA…)
```

Program execution

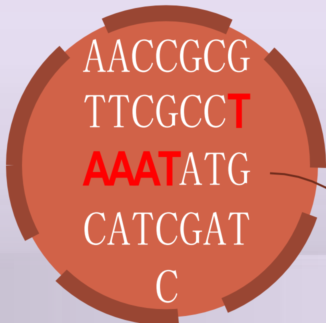
Living cells as computational devices



Living cells as computational devices



Living cells as computational devices



Code repository

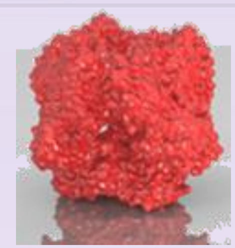
```
public static void main (LIFE)

X=input()

If X==A
   protein A=new Protein (TAAATA...)
```

Program execution

Working copy of the code

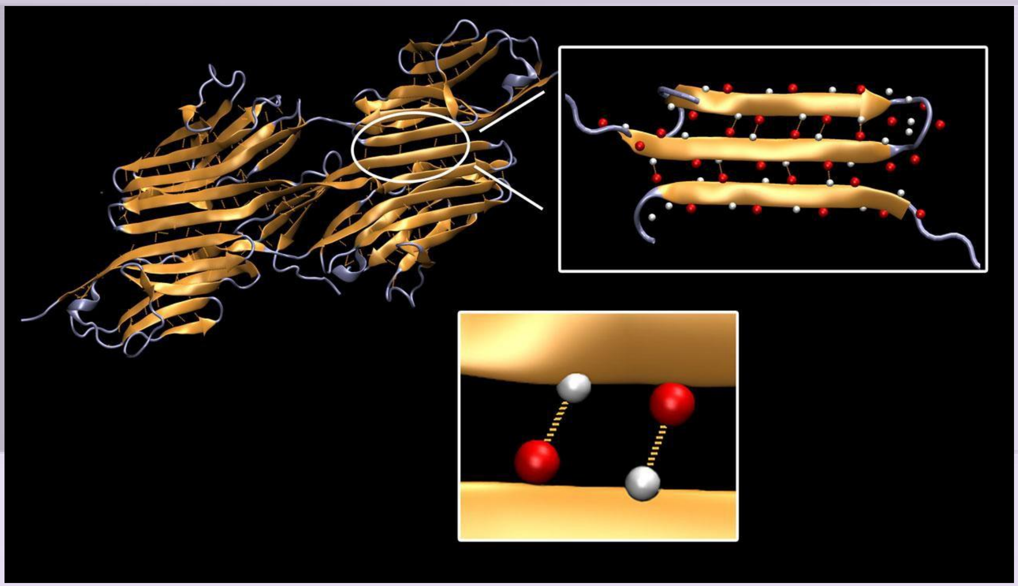
Sequence-dependent folding

Output protein sequence



Imagine: engineering projects at Oberlin

public static void main
(SPIDER_SILK)



Implement a living system that produces a biodegradable plastic

Implement bacteria that produces spider-silk protein

...