The Biological Layer Abstraction and Standards Hierarchy

Applying Abstraction to Biology

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CSAIL Student Workshop 2006

Synthetic Biology

Simple systems can be built without using abstraction principles or standards.

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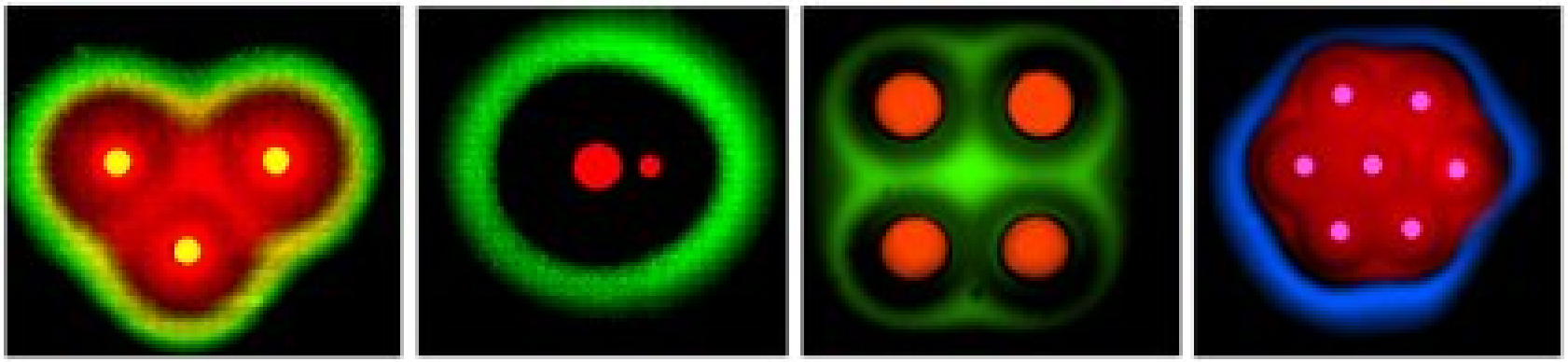
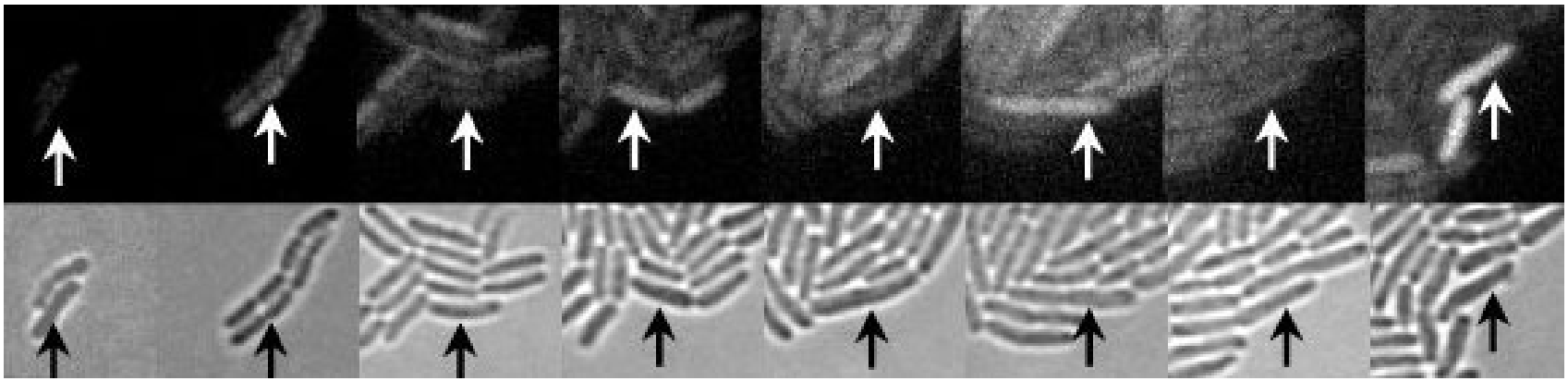


The Repressilator

An oscillator built from biological repressors



The Repressilator

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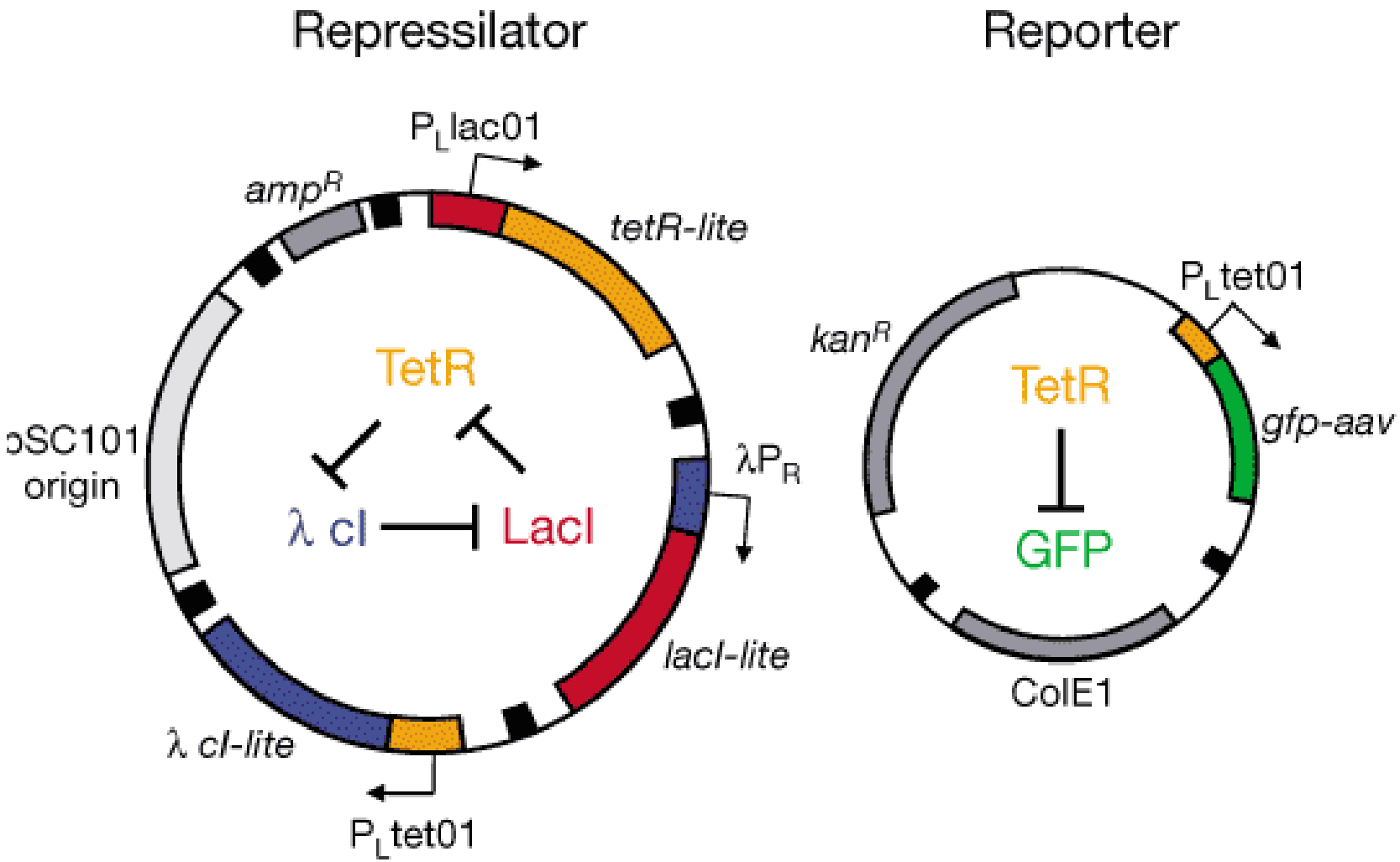

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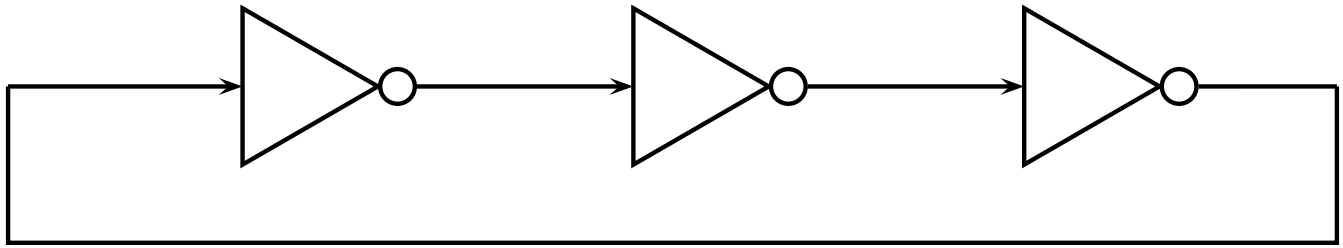
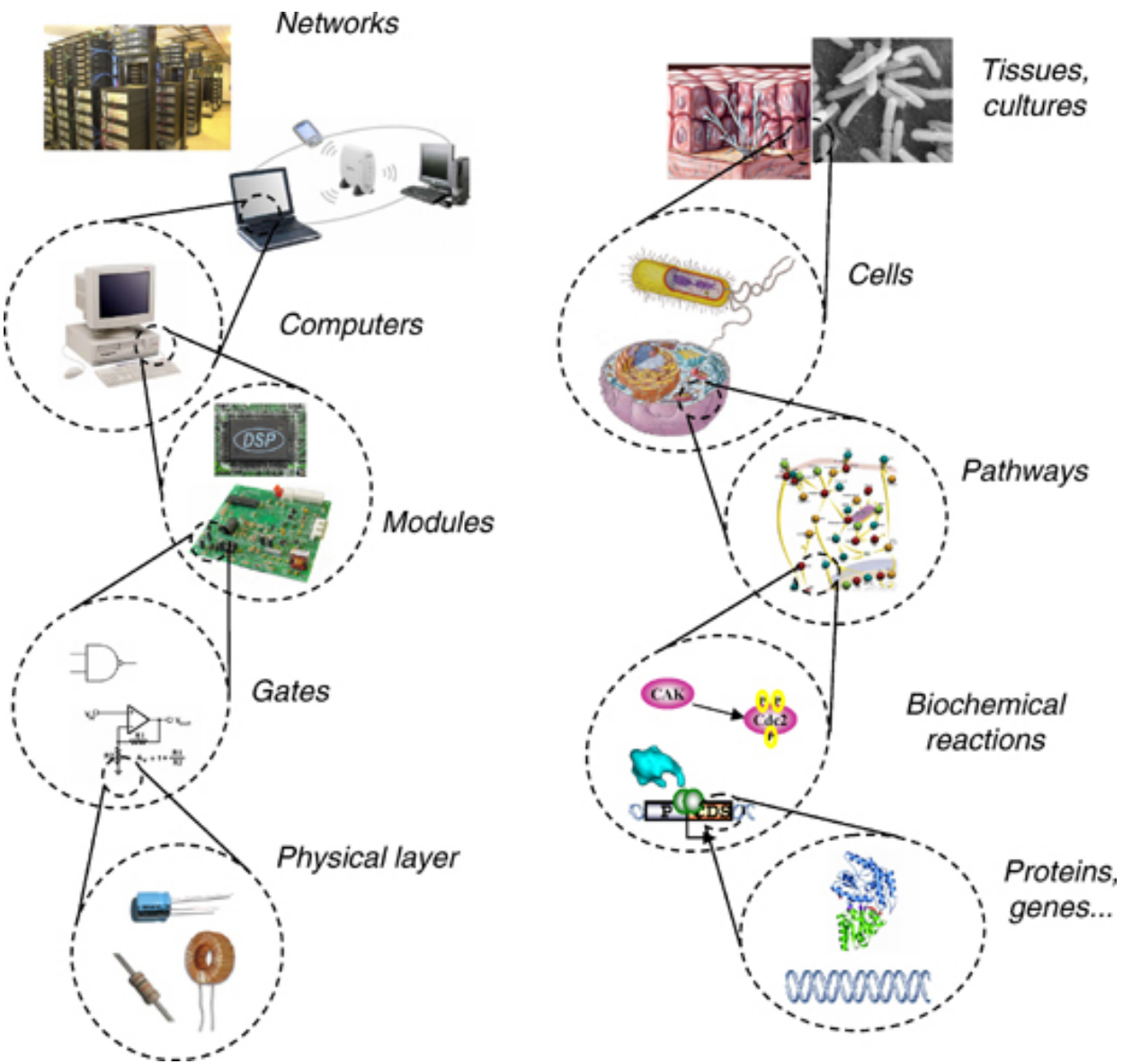
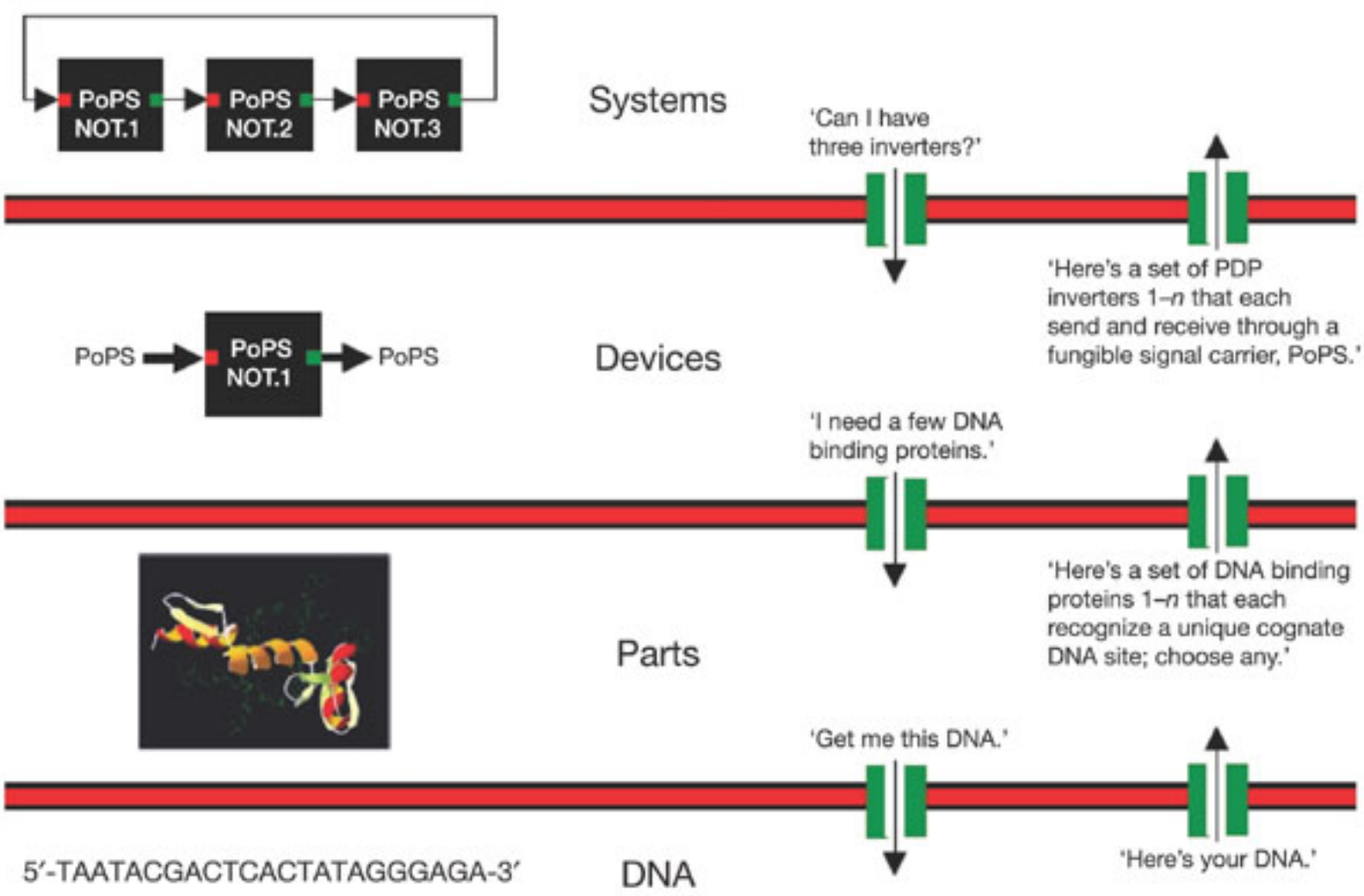


Hierarchy Inspired By Computer Engineering



Source: E. Andrianantoandro, S. Basu, D. Karig, R. Weiss. Synthetic biology: new engineering rules for an emerging discipline. Mol. Sys. Biol. 2006

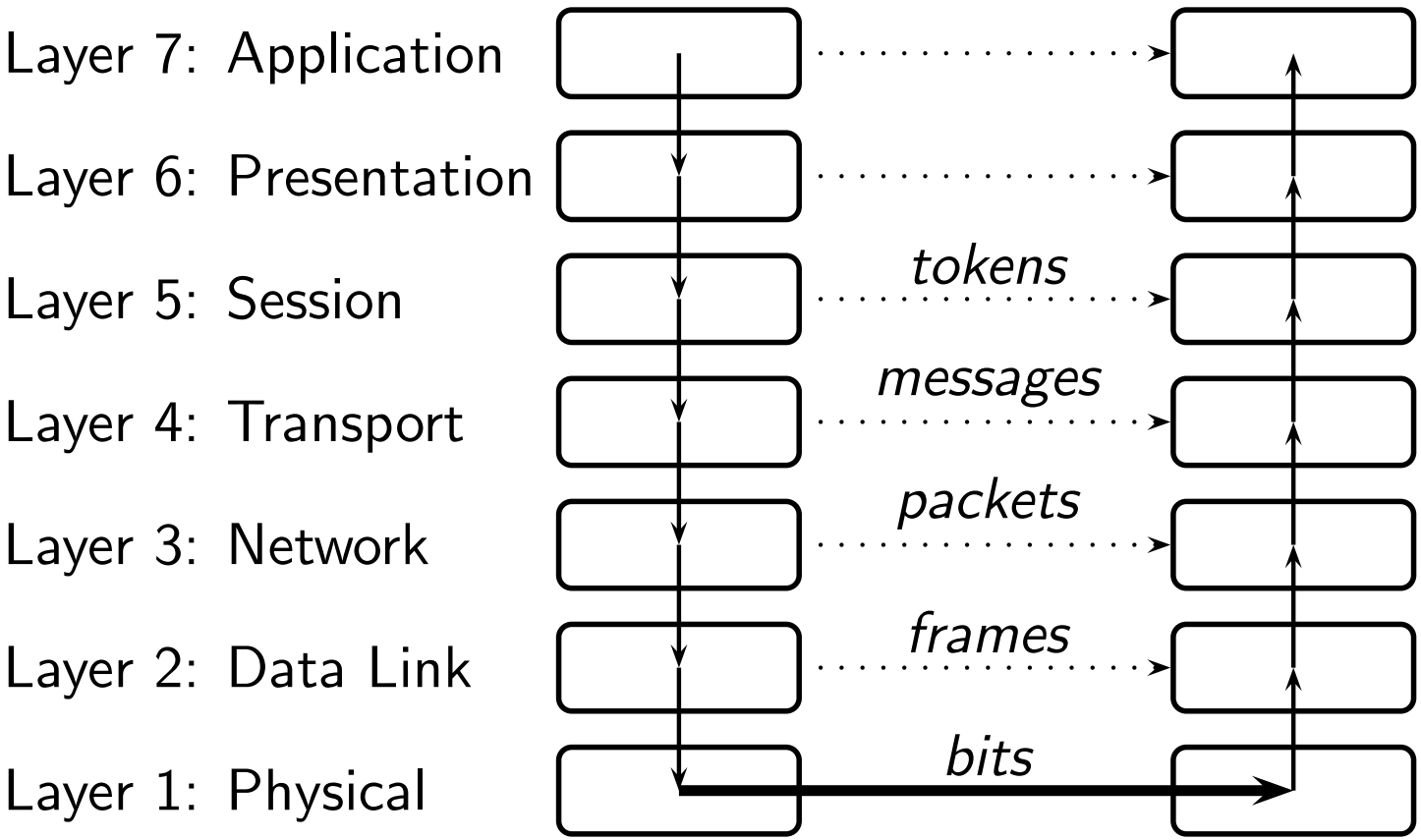
Another Abstraction Hierarchy



Source: D. Endy. Foundations for engineering biology. Nature 2005

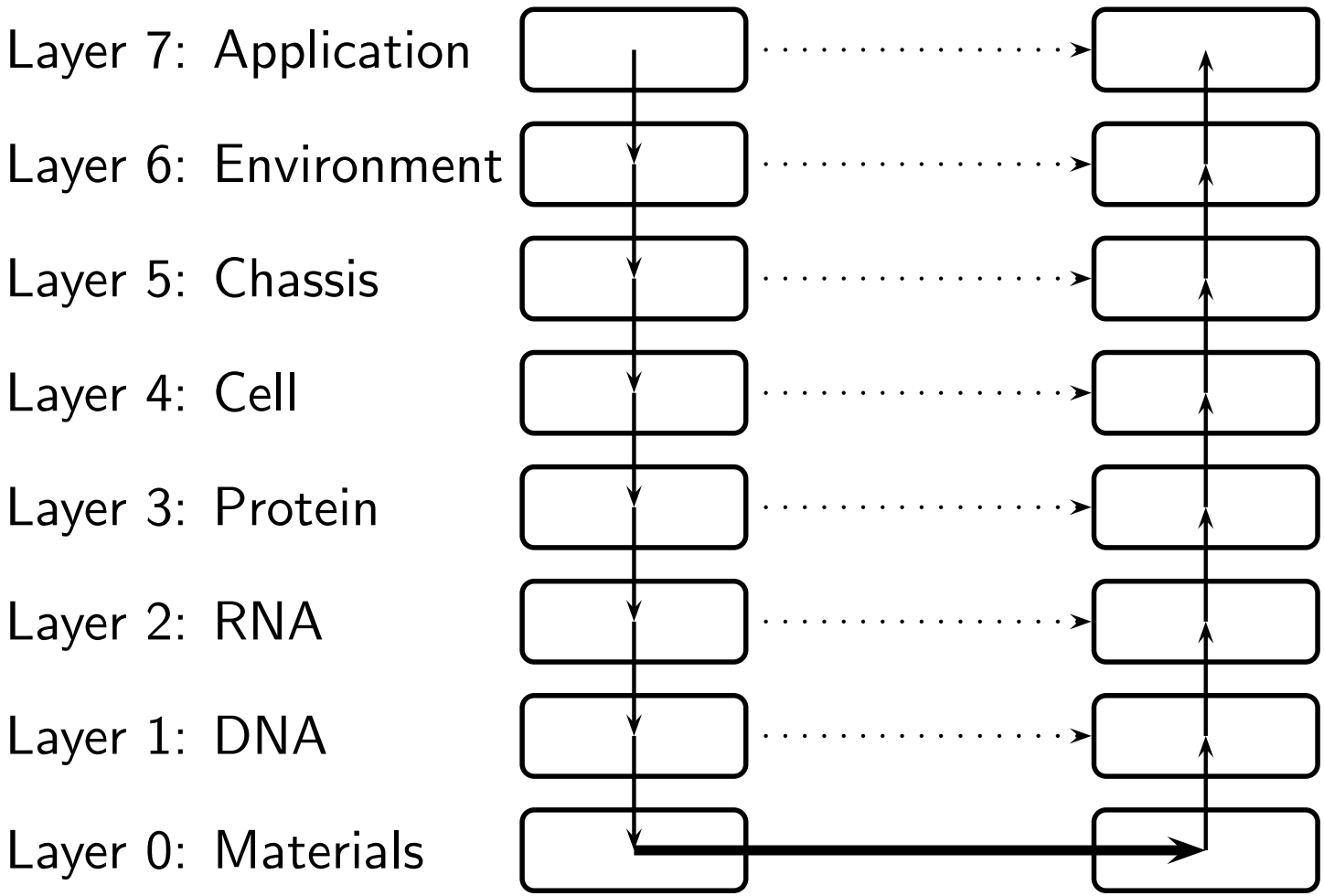
The ISO OSI Network Model

Information is passed down and up the layer stack.



The Biological Layer Model

Layers and interlayers specify standard interfaces.



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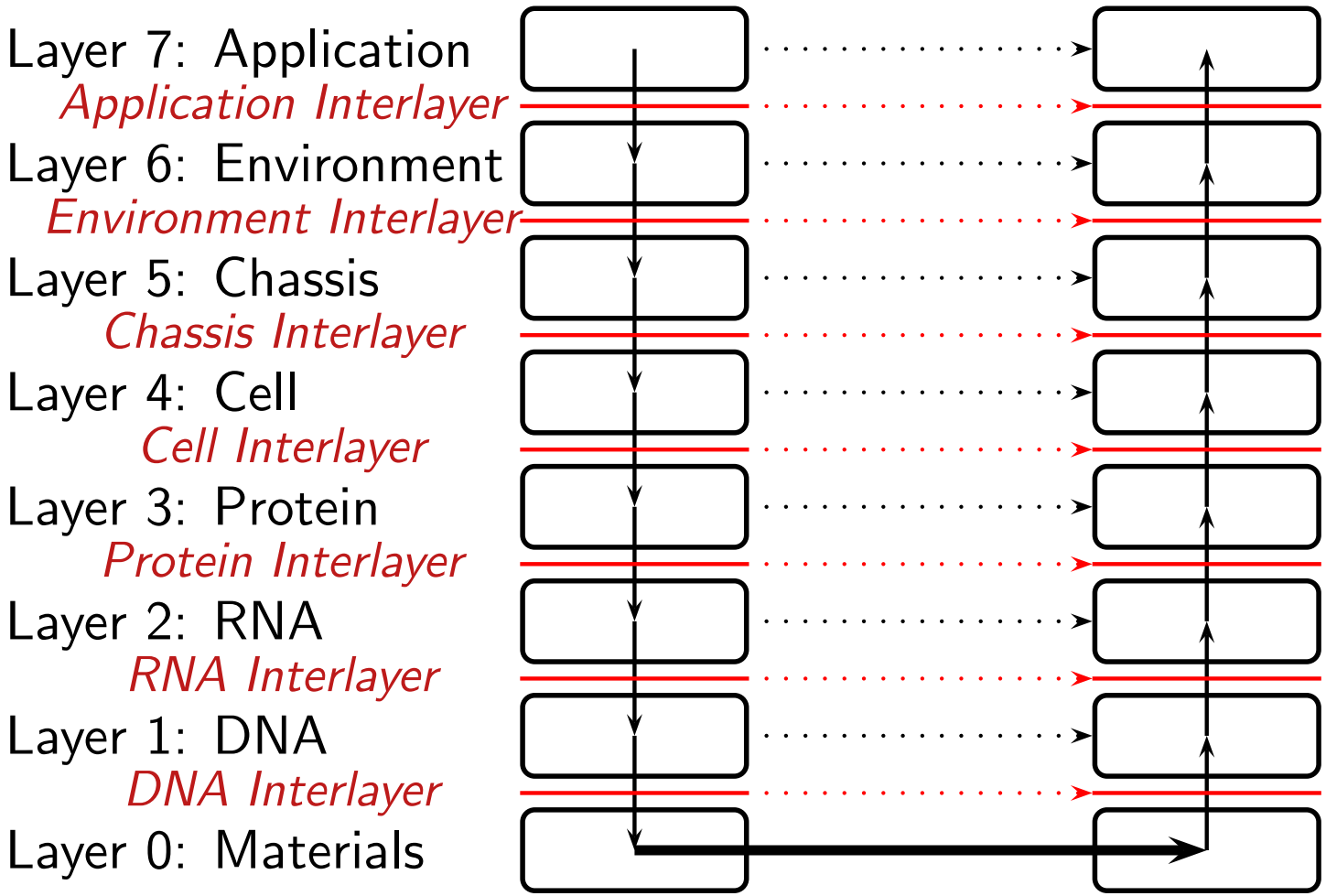
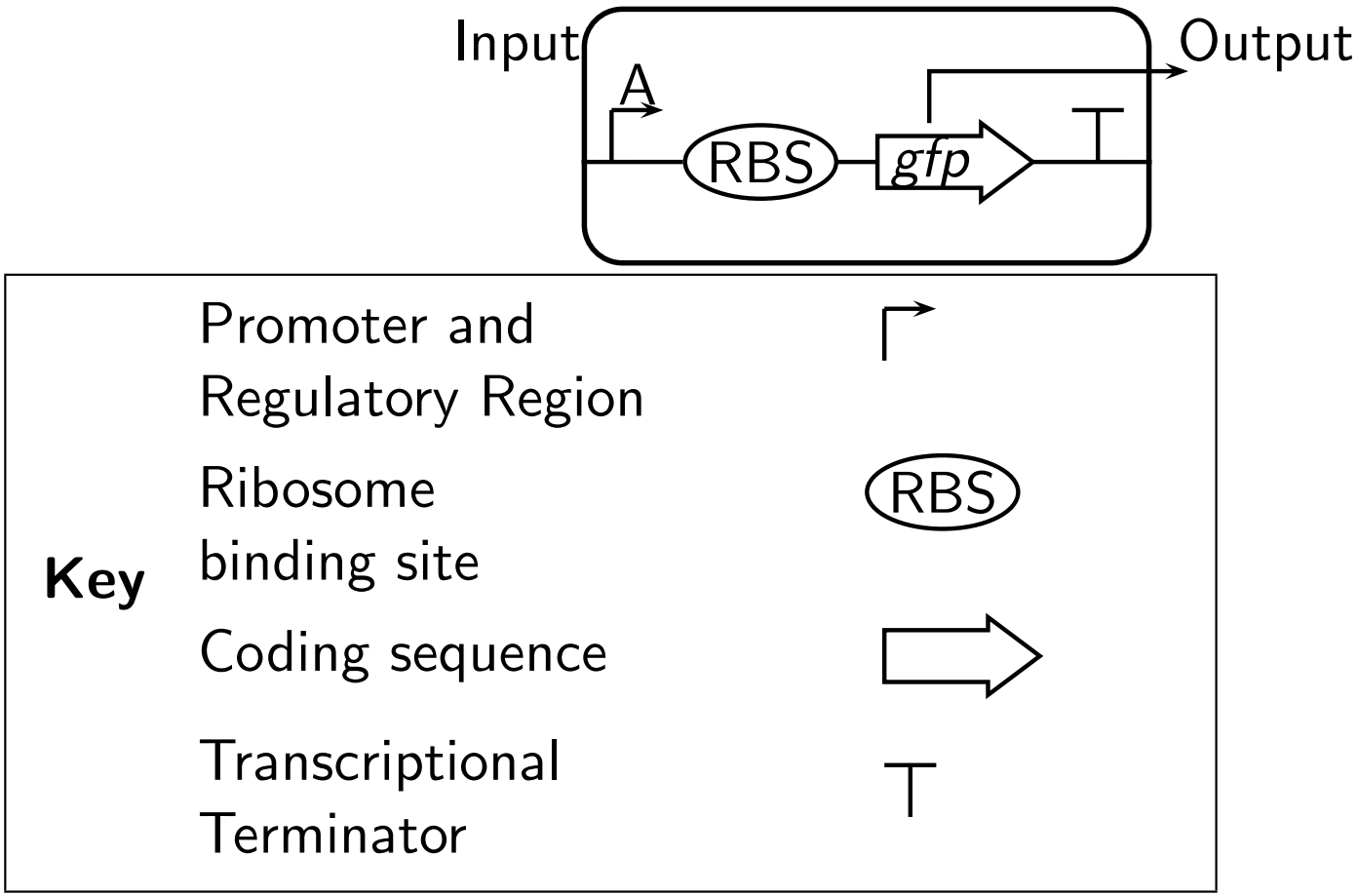


Example Biological Network

The module produces green fluorescent protein (gfp) when protein A is present.



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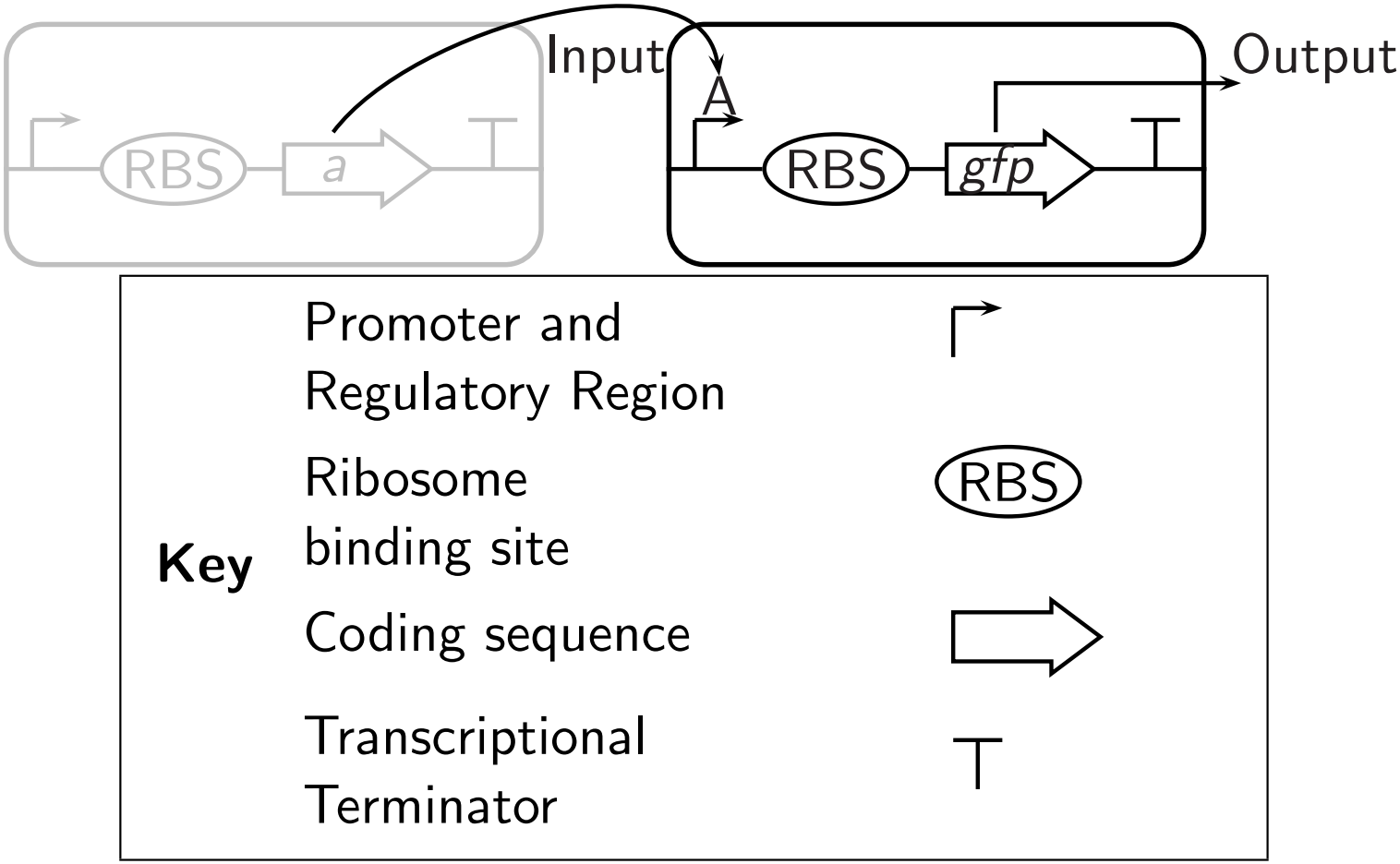

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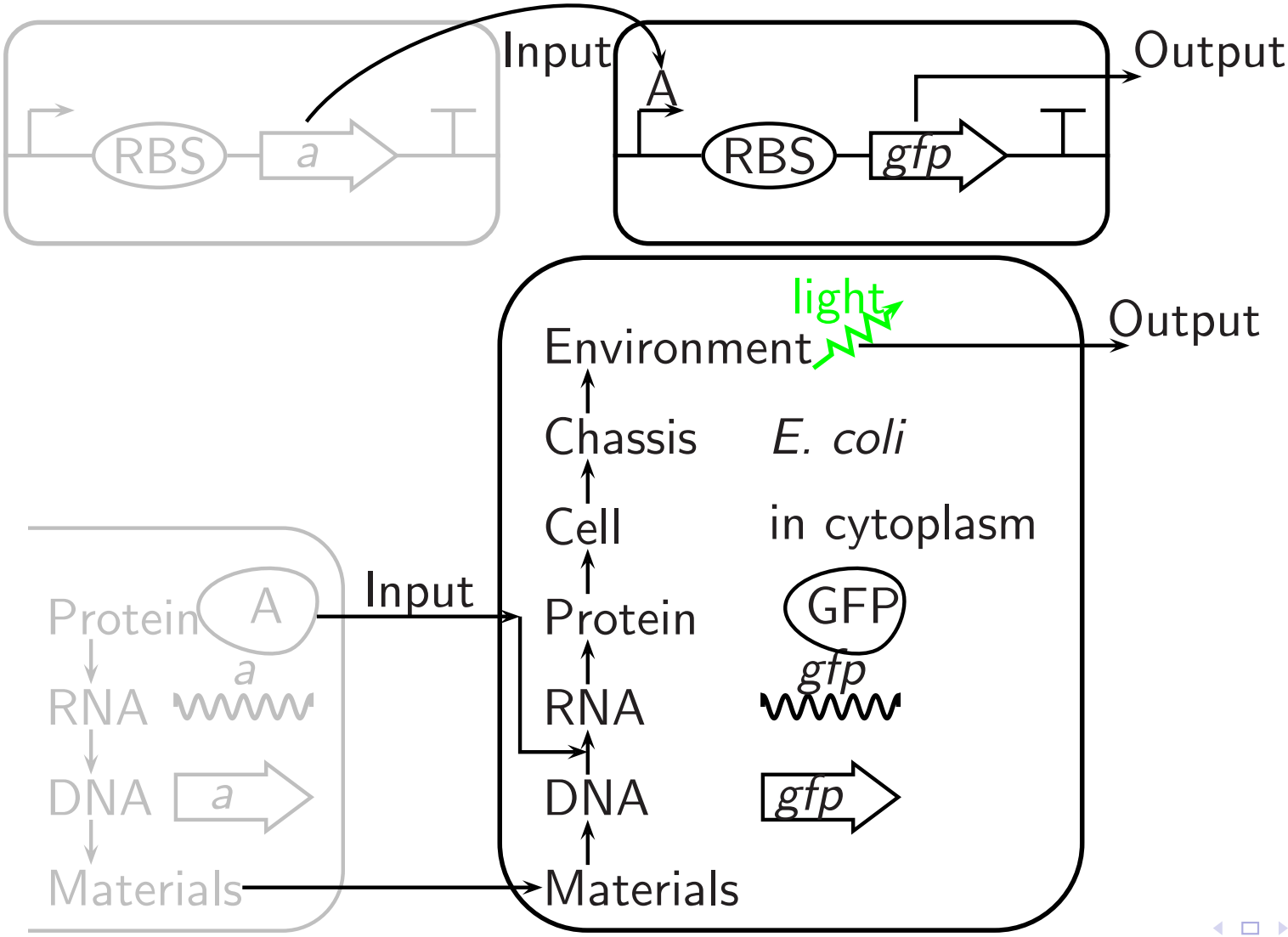
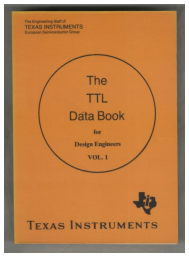


Two General Types Of Standards

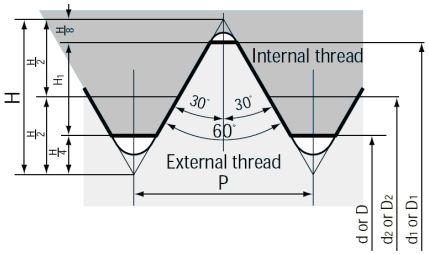
Definition

Functional Standard: Allows connecting the functions of modules.



Definition

Structural Standard: Allows physically connecting modules.



Defining Parts/Devices/Systems

Definition

Part: A part is anything that conforms to a structural standard. It is the *physical* object.

Definition

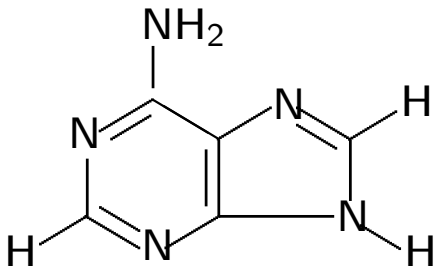
Device: A device is a part that also conforms to functional standards for all inputs and outputs. It is the *conceptual* view of a part.

Definition

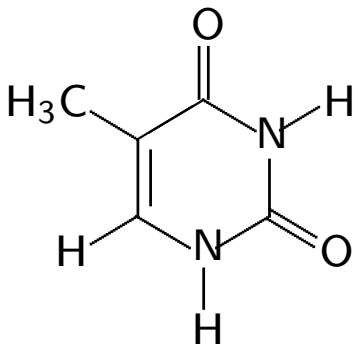
System: A system is a device with application layer standards. It is the design *specification*.

Layer 0: Materials

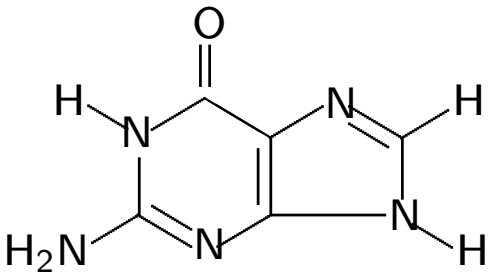
Nucleotides



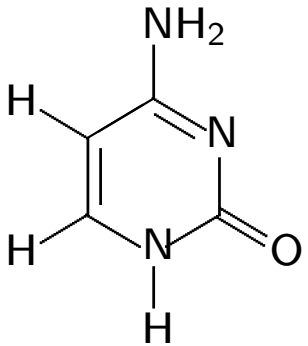
Adenine



Thymine

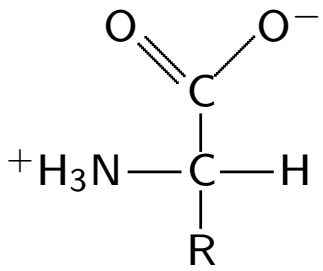


Guanine

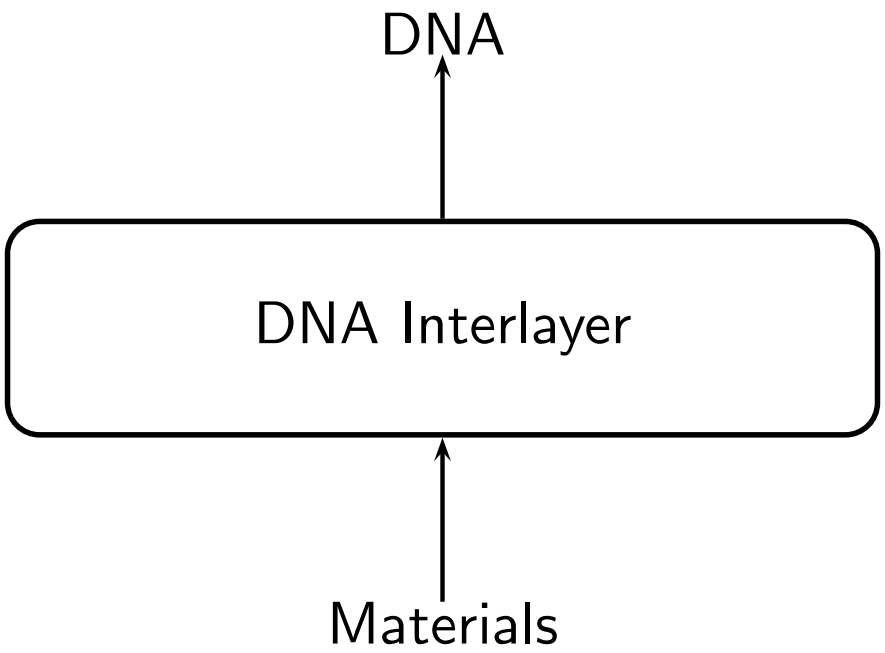


Cytosine

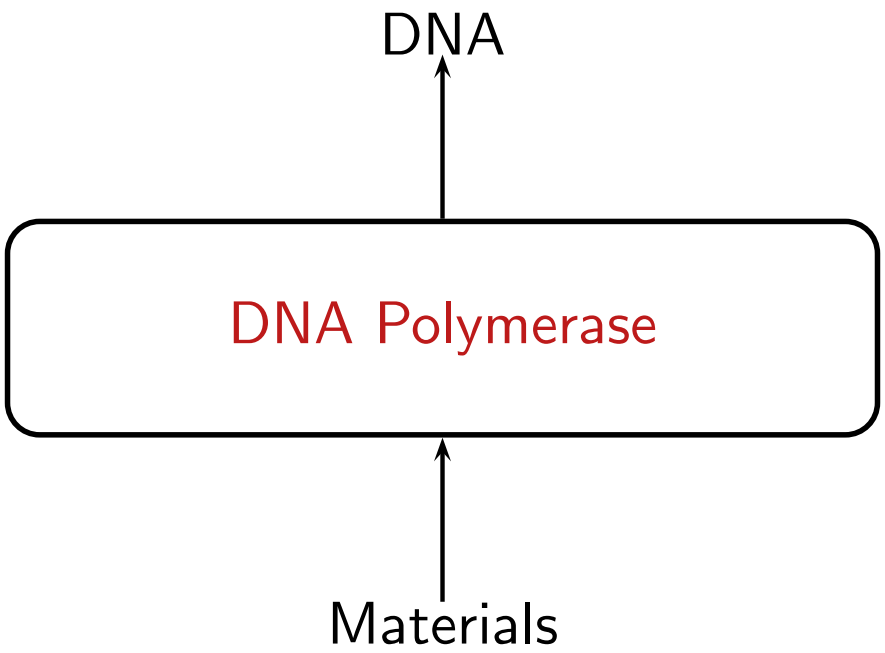
Amino Acids



Interlayer: DNA



Interlayer: DNA



Layer 1: DNA

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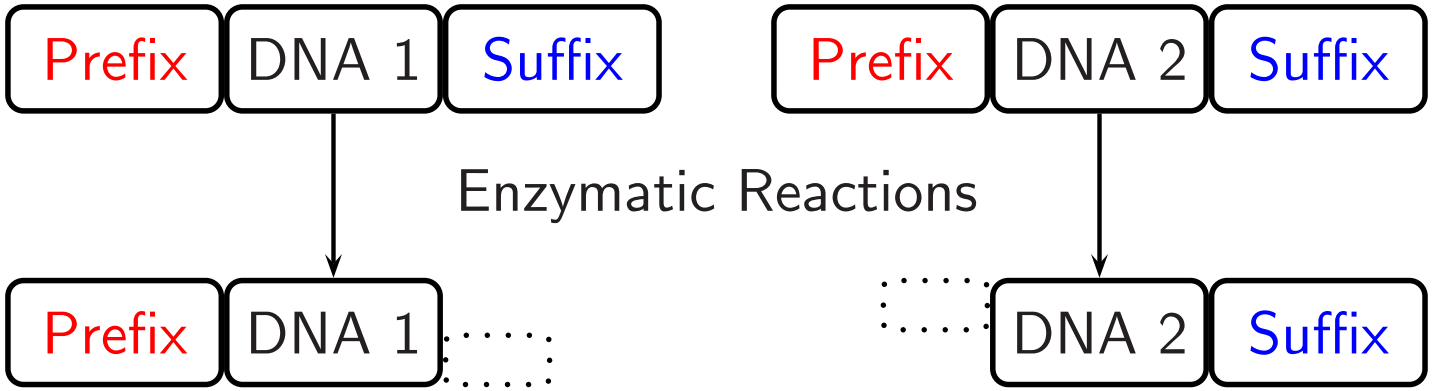
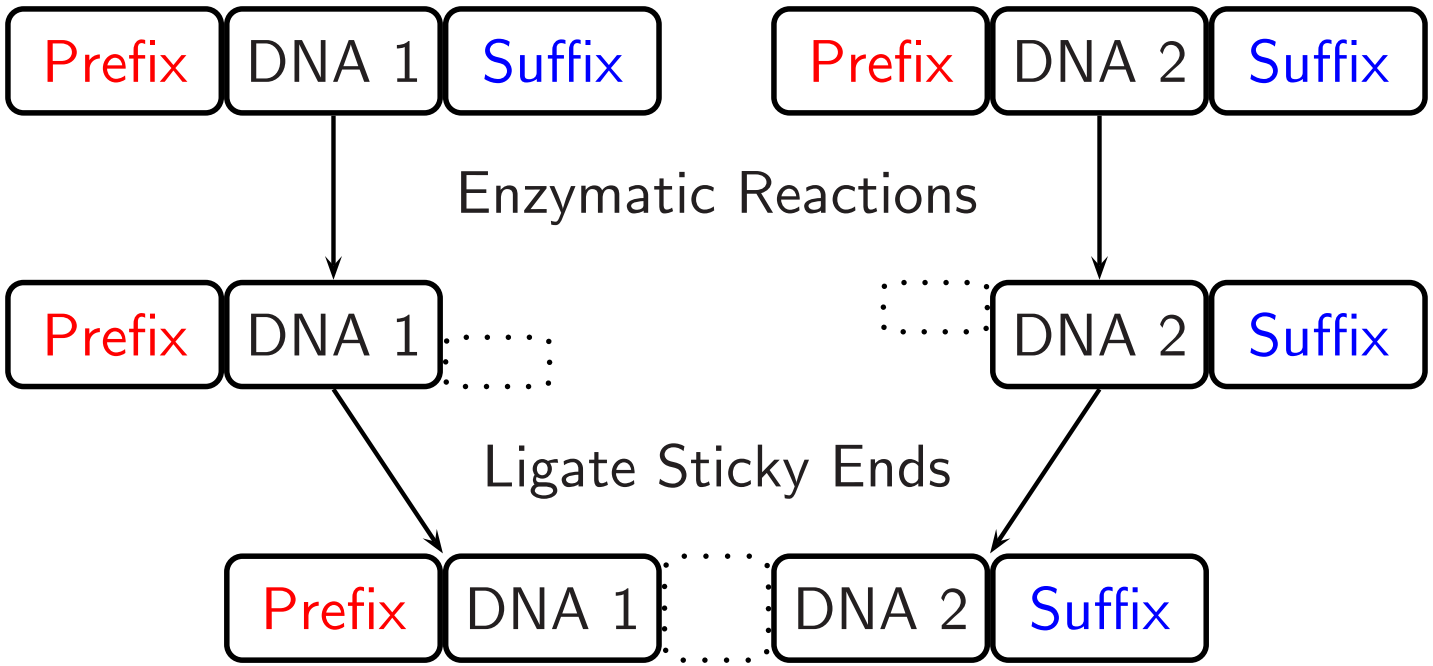
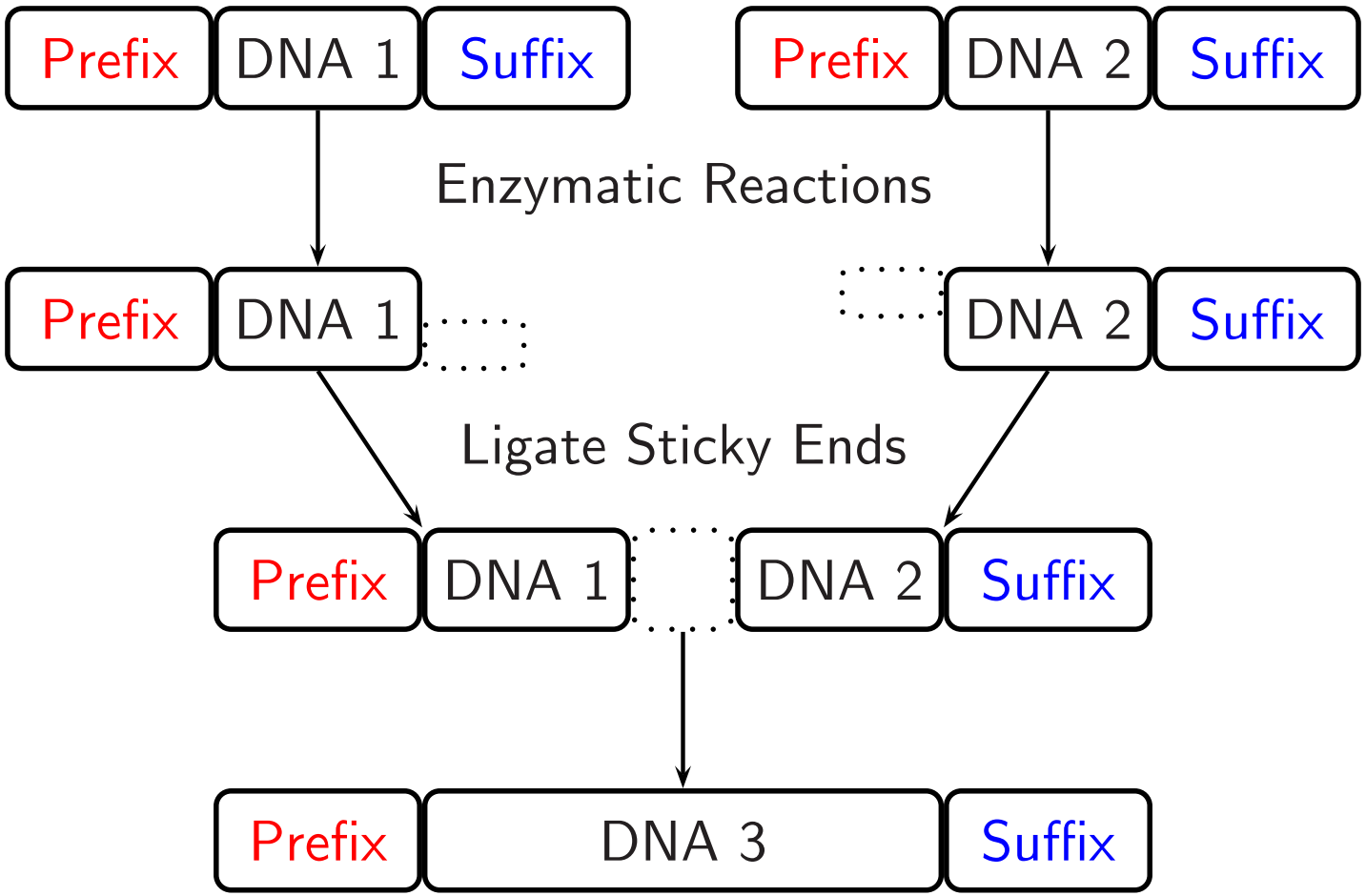

Prefix
DNA 1
Suffix
Prefix
DNA 2
Suffix
Enzymatic Reactions
Prefix
DNA 1
DNA 2
Suffix

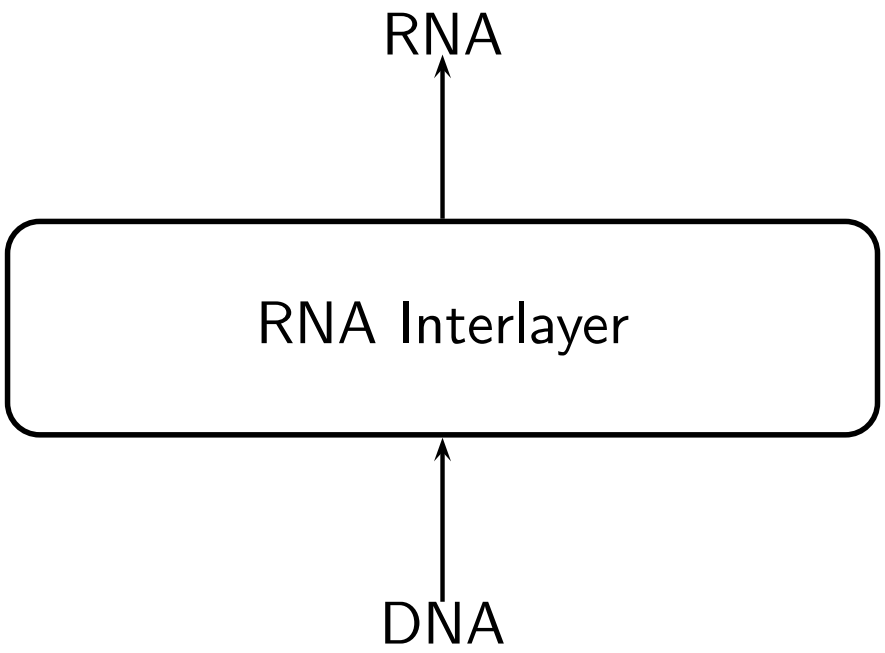
Layer 1: DNA


Prefix
DNA 1
Suffix
Prefix
DNA 2
Suffix
Enzymatic Reactions
Prefix
DNA 1
DNA 2
Suffix
Ligate Sticky Ends
Prefix
DNA 1
DNA 2
Suffix

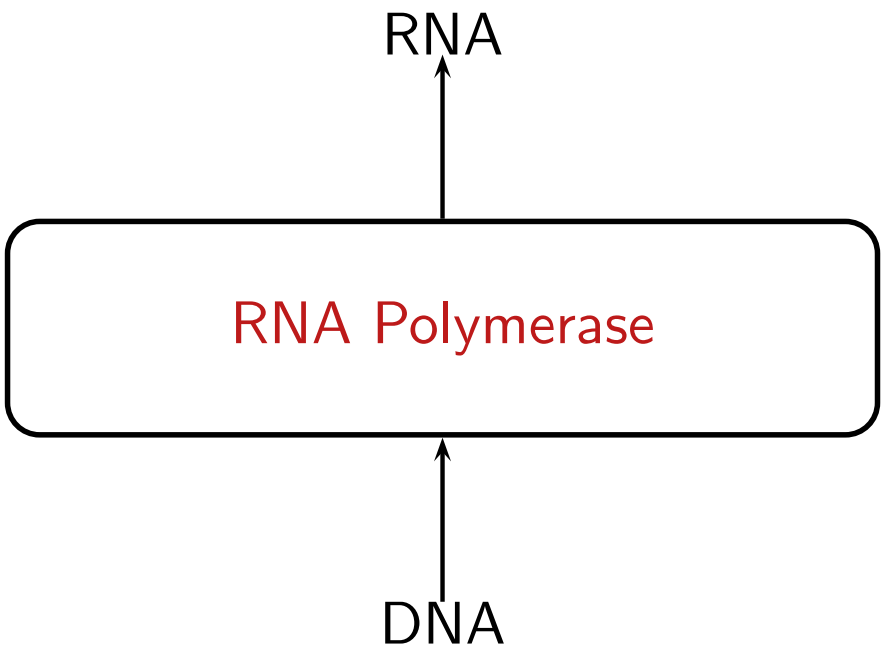
Layer 1: DNA


Prefix
DNA 1
Suffix
Prefix
DNA 2
Suffix
Enzymatic Reactions
Prefix
DNA 1
DNA 2
Suffix
Ligate Sticky Ends
Prefix
DNA 1
DNA 2
Suffix
Prefix
DNA 3
Suffix

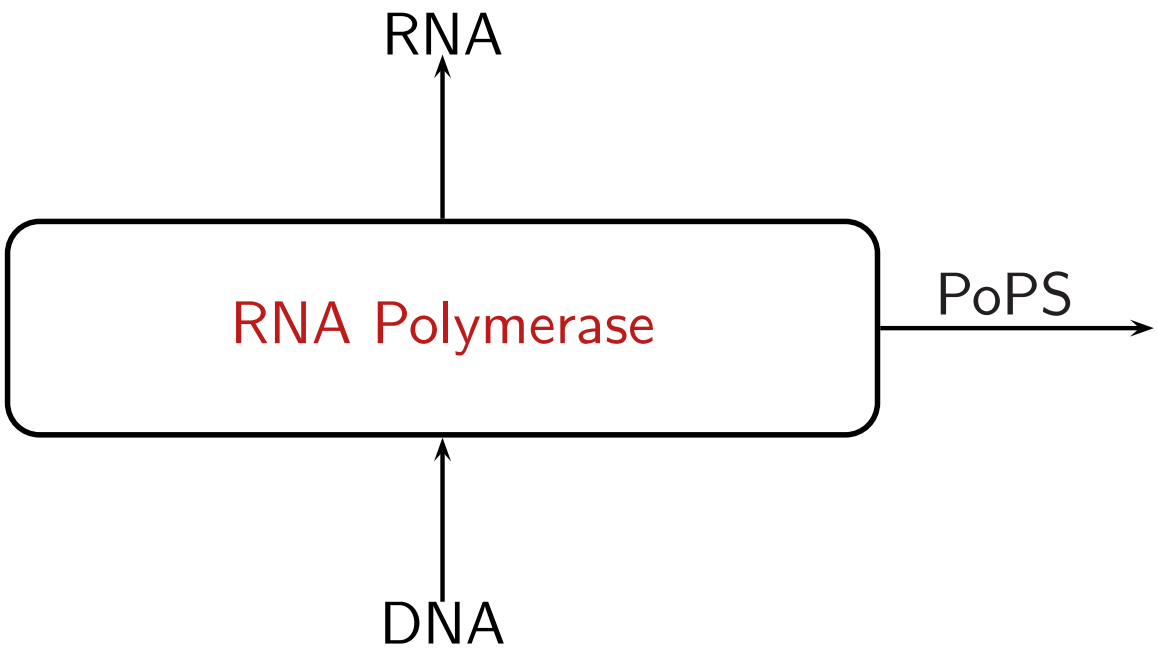
Interlayer: RNA



Interlayer: RNA

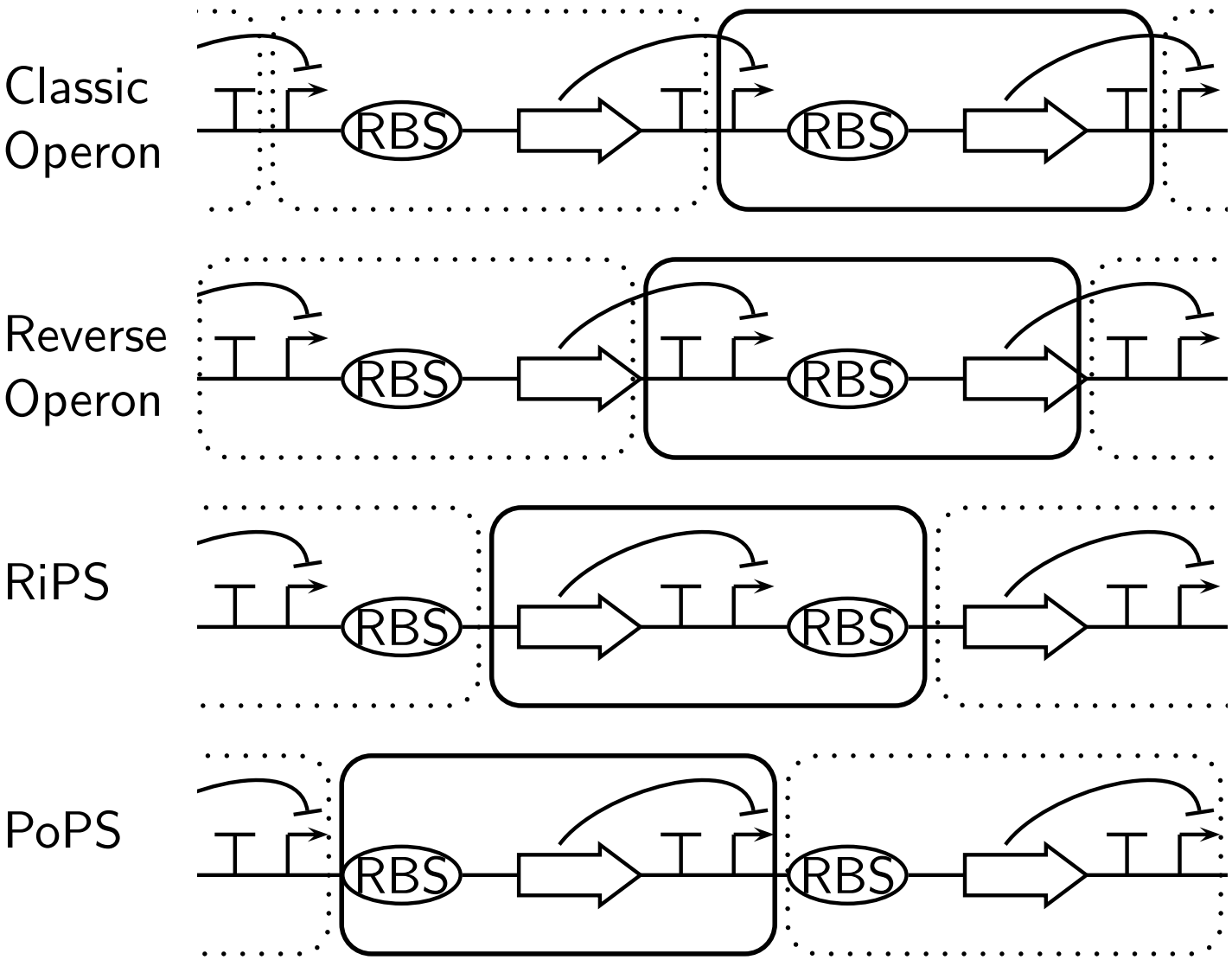


Interlayer: RNA



Interlayer: RNA

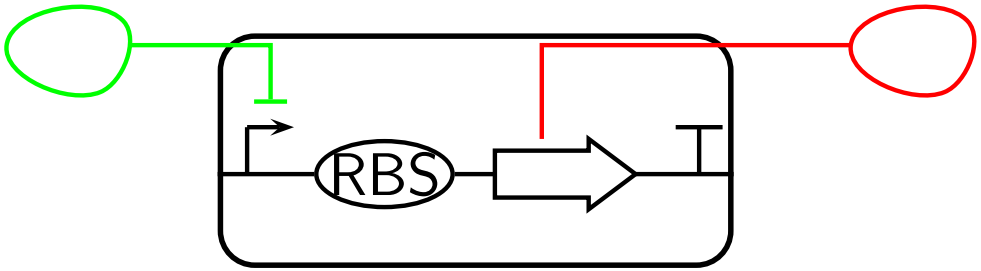
Example: PoPS (RNA Polymerases Per Second)



Interlayer: RNA

Example: PoPS (RNA Polymerases Per Second)

Operon

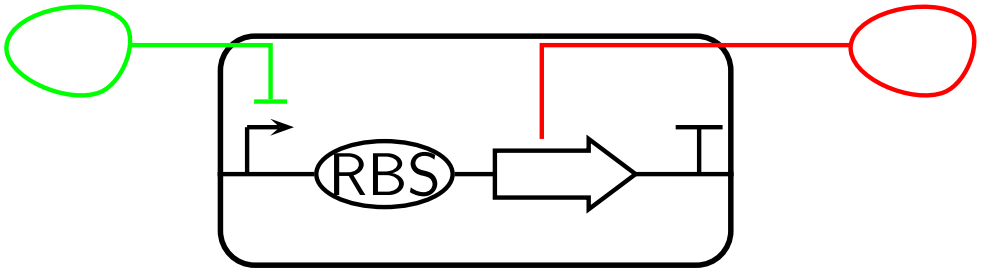


Protein Layer

Interlayer: RNA

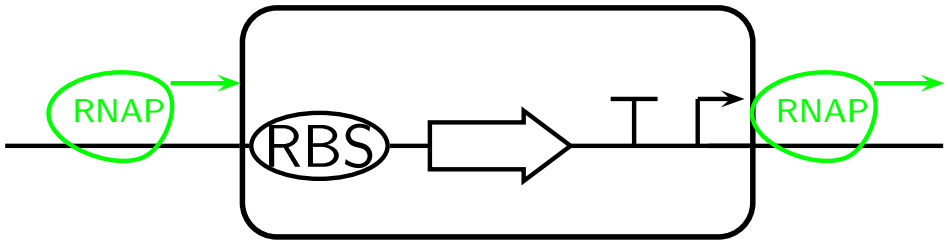
Example: PoPS (RNA Polymerases Per Second)

Operon



Protein Layer

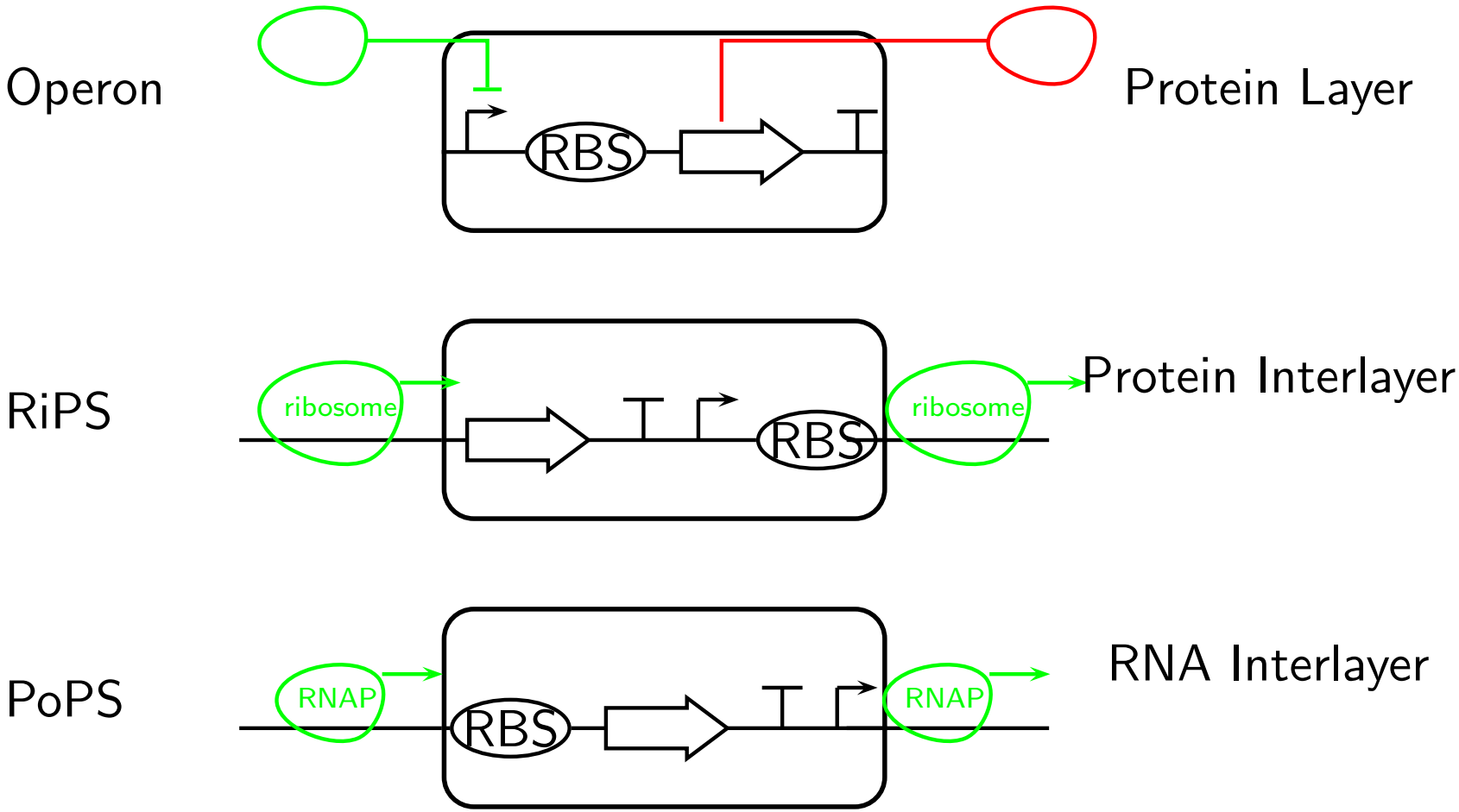
PoPS



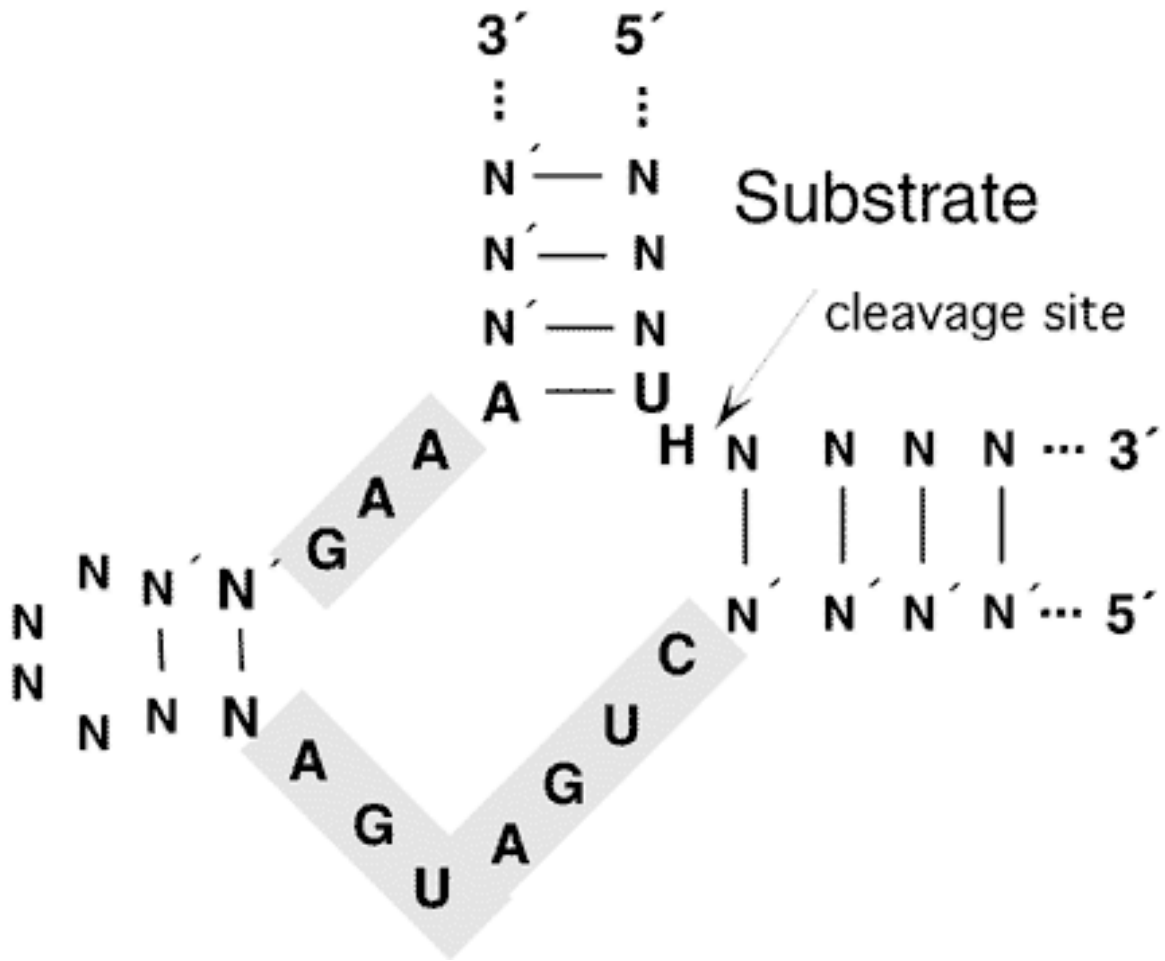
RNA Interlayer

Interlayer: RNA

Example: PoPS (RNA Polymerases Per Second)



Layer 2: RNA

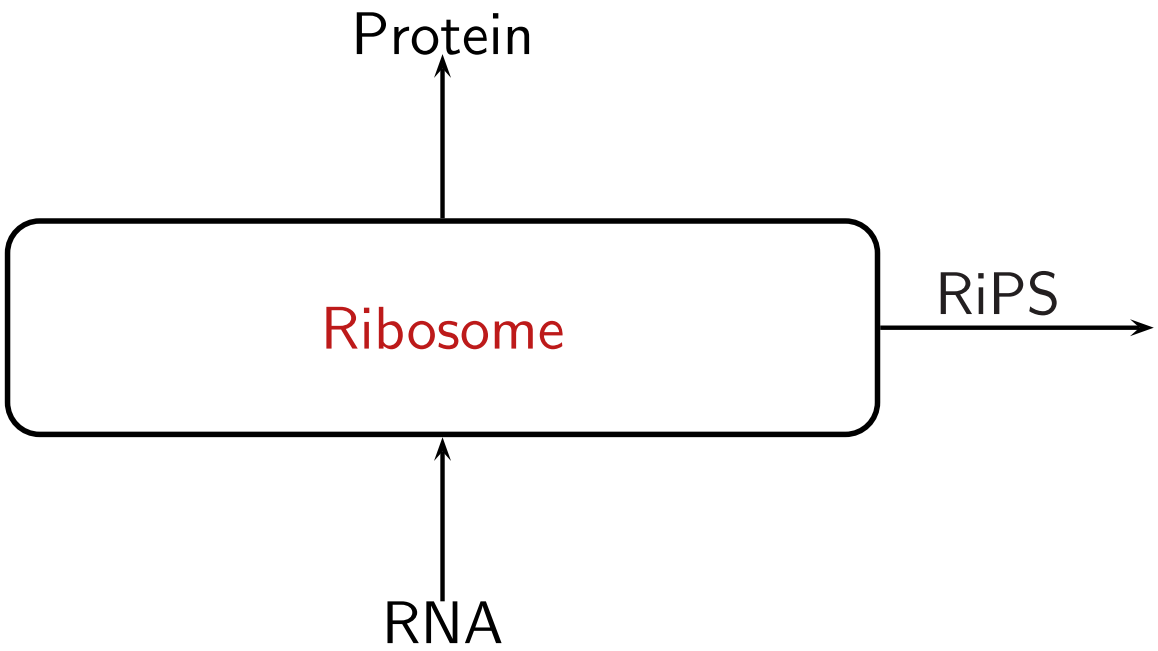


Hammerhead ribozyme

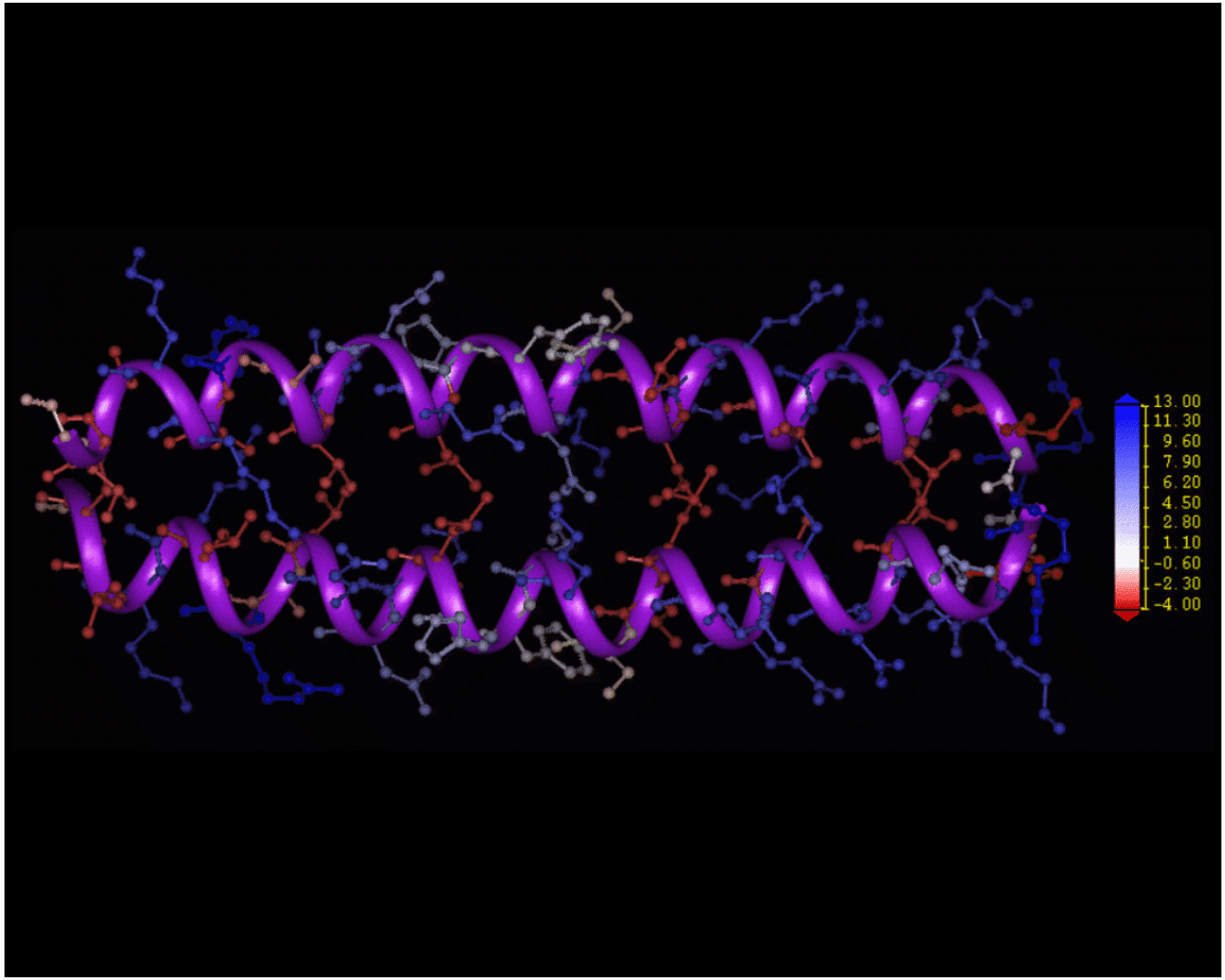
http://www.mpibpc.gwdg.de/inform/MpiNews/cientif/jahrg5/9.99/fig1g.gif

Interlayer: Protein

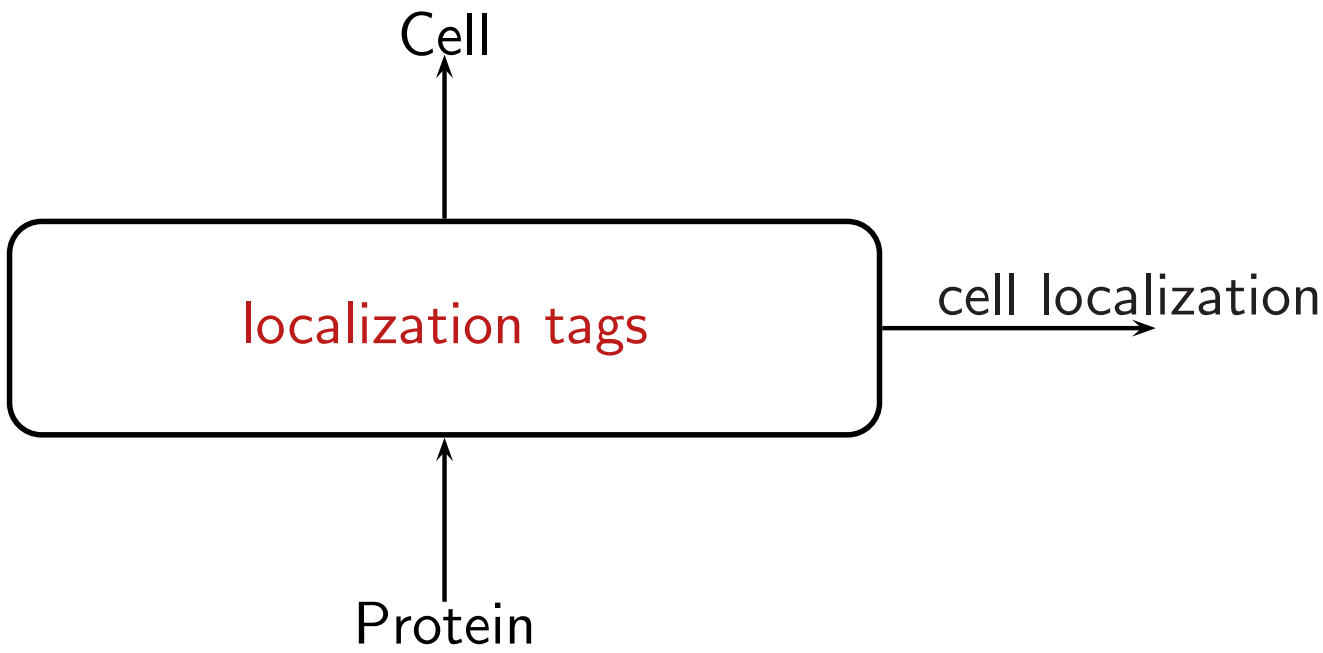
Example: RiPS (Ribosomes Per Second)



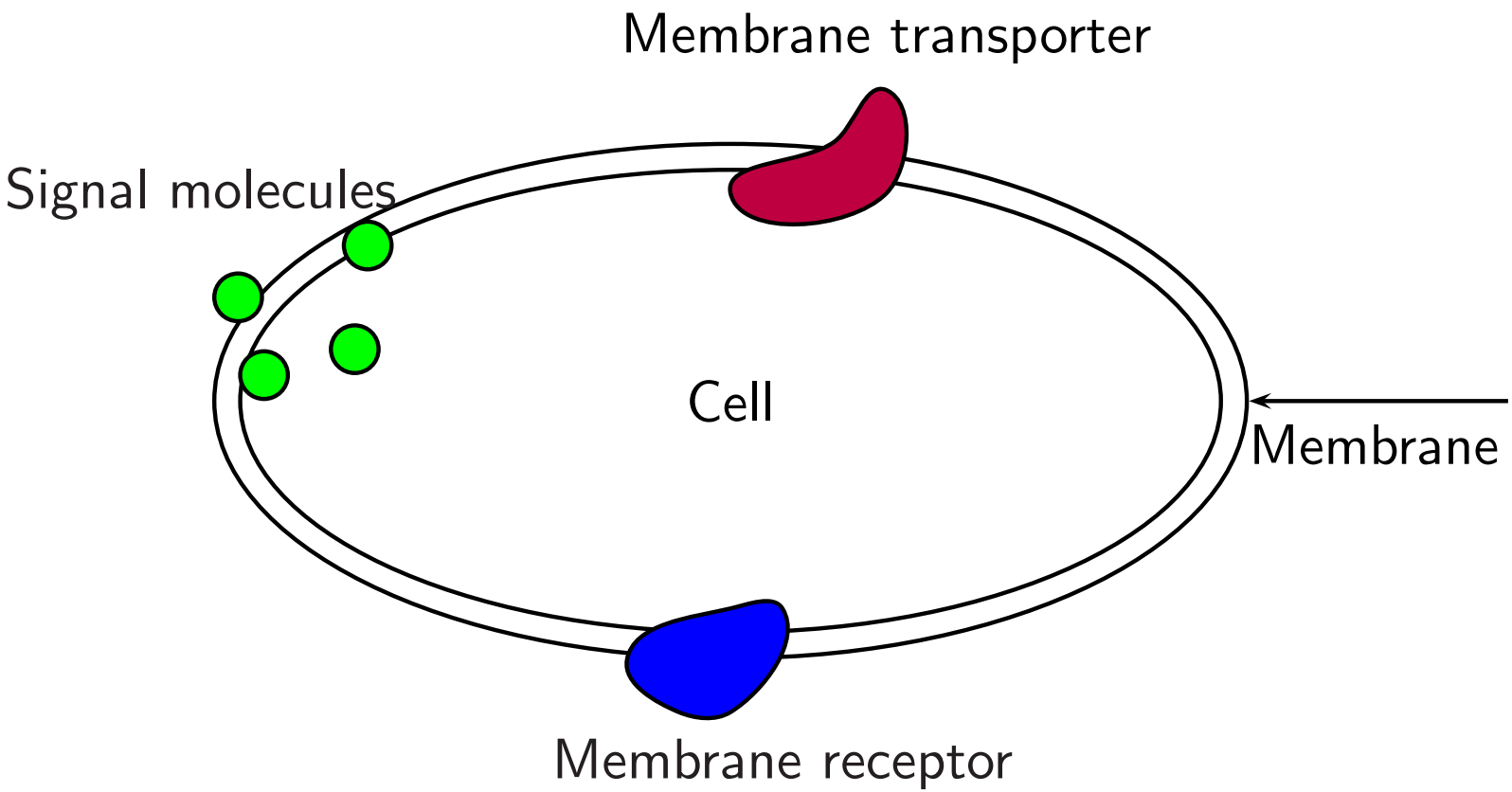
Layer 3: Protein



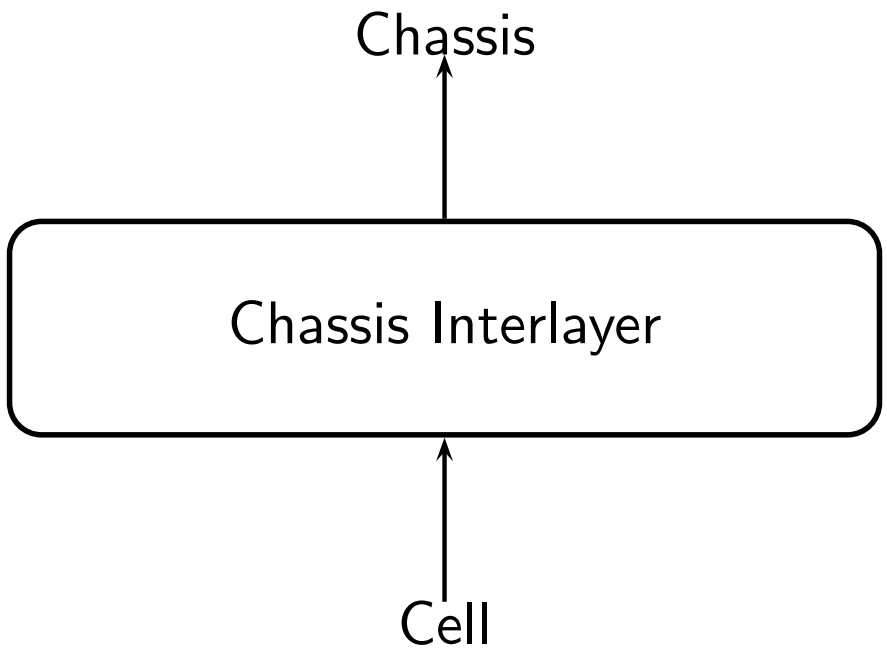
Interlayer: Cell



Layer 4: Cell


Membrane transporter
Signal molecules
Cell
Membrane
Membrane receptor

Interlayer: Chassis



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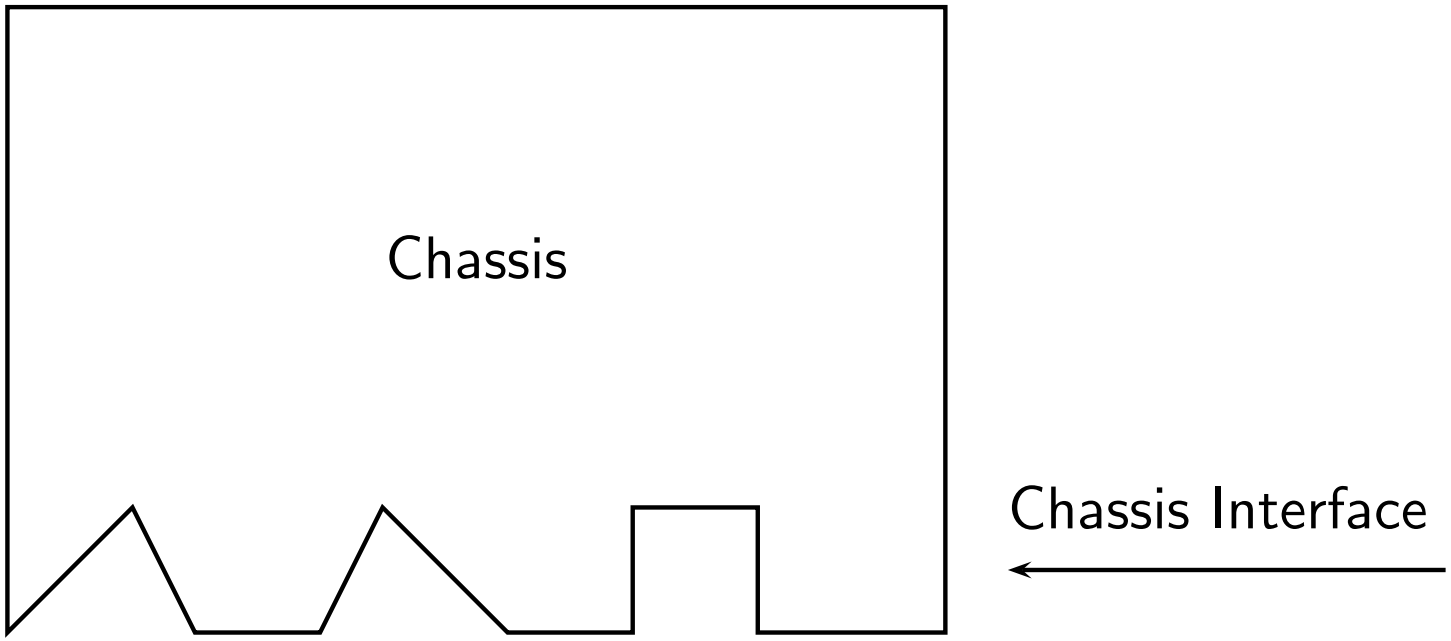

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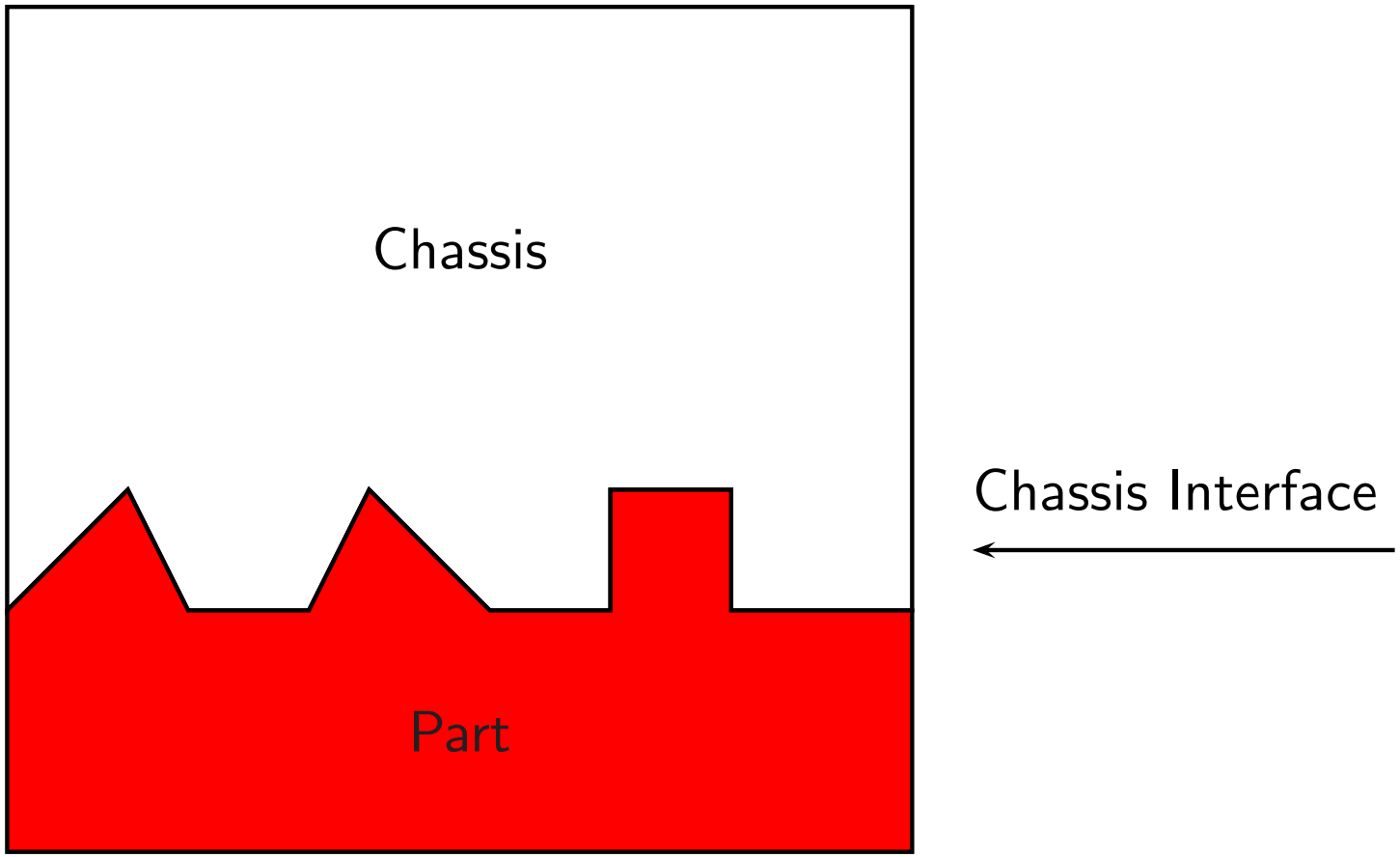

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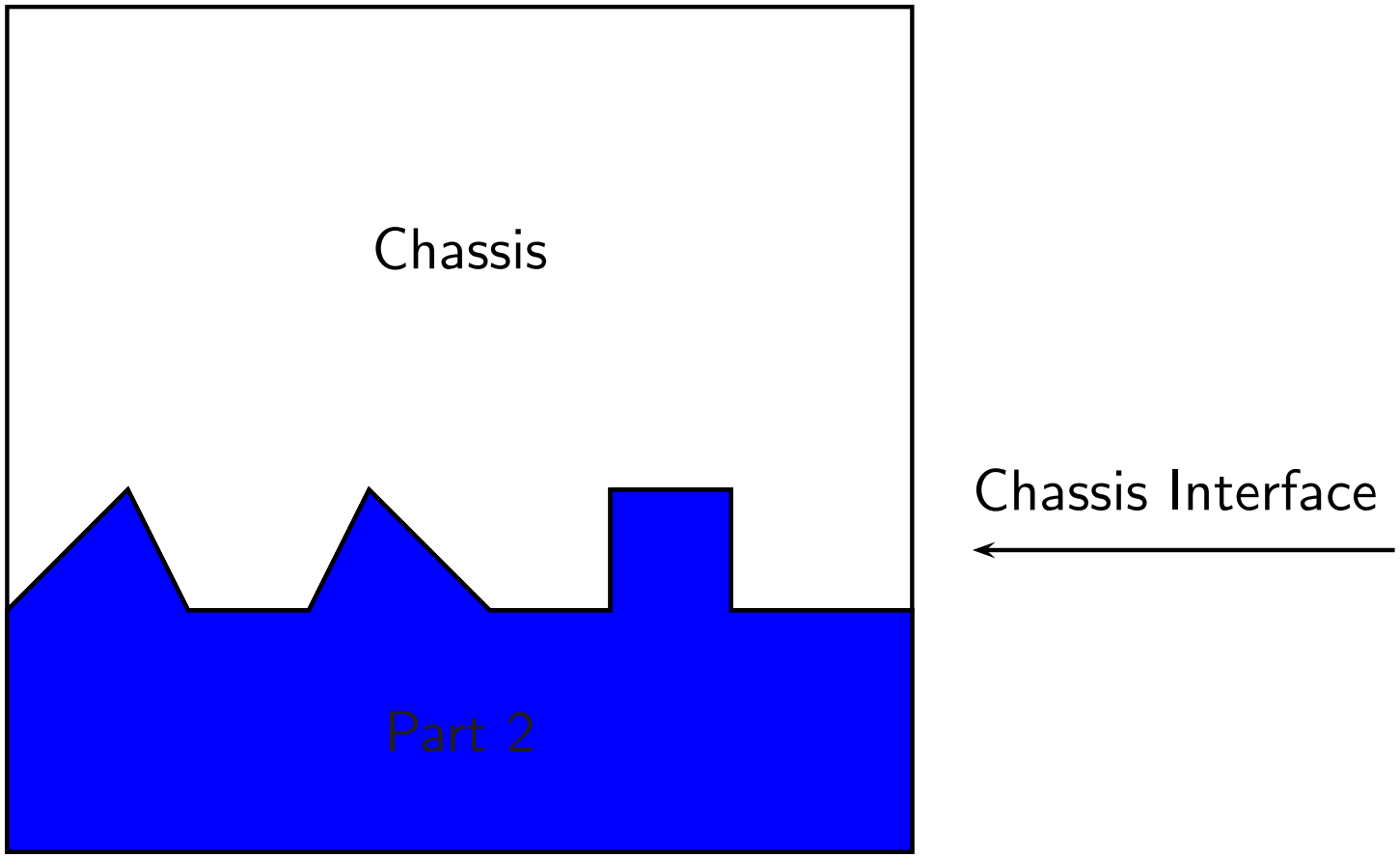
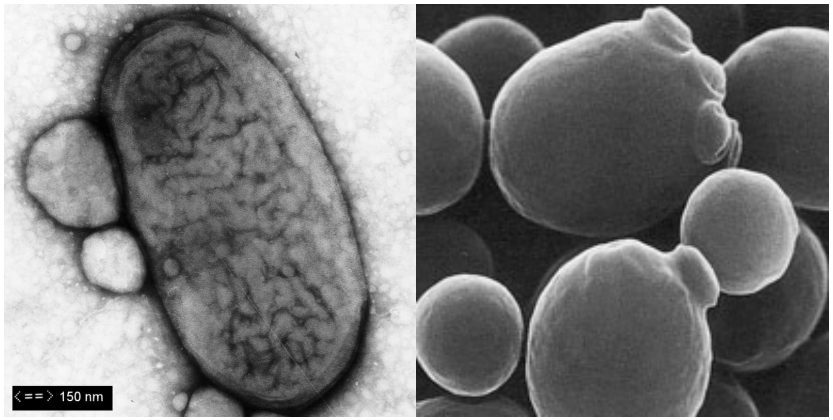


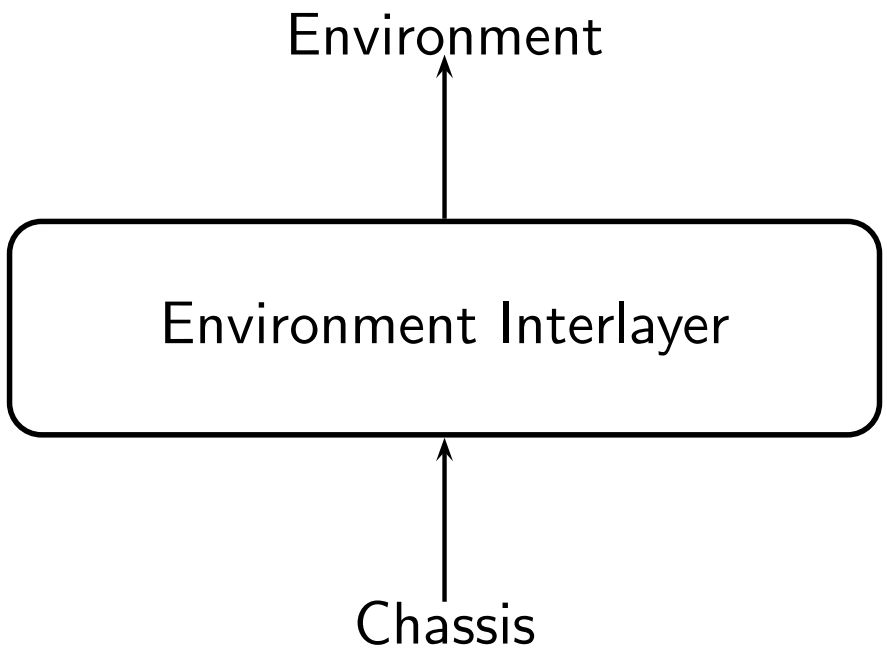
Layer 5: Chassis



Desirable chassis properties:

- Well-understood chassis
- Simple (no unnecessary functions)
- Powerful enough to supply needed operating power

Interlayer: Environment

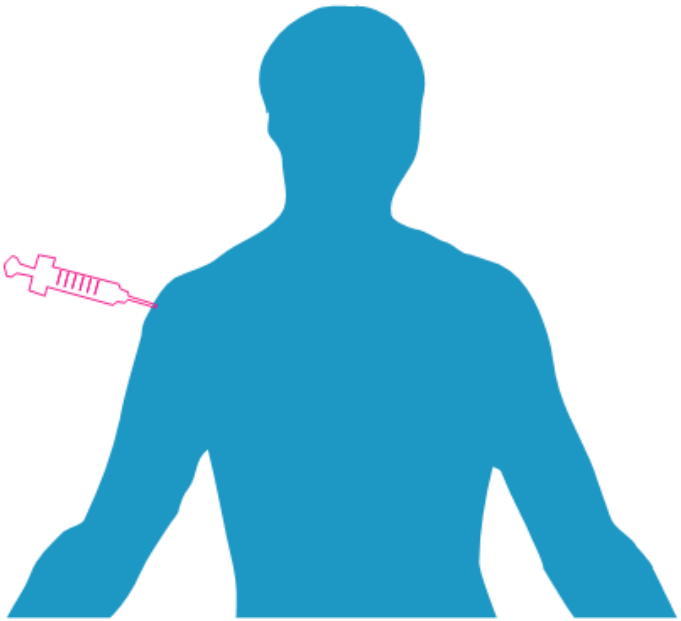


Interlayer: Environment

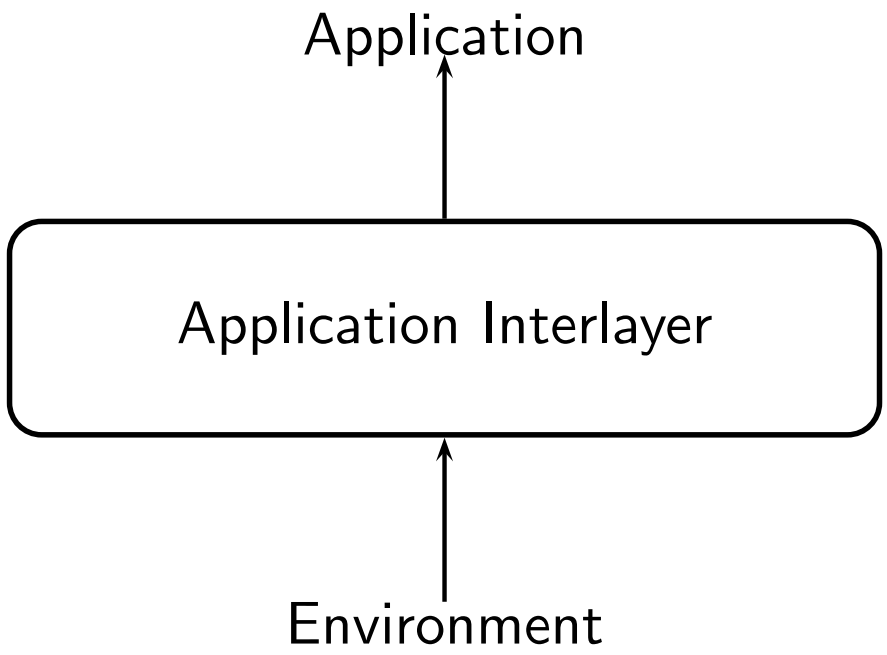
Examples

Layer 6: Environment

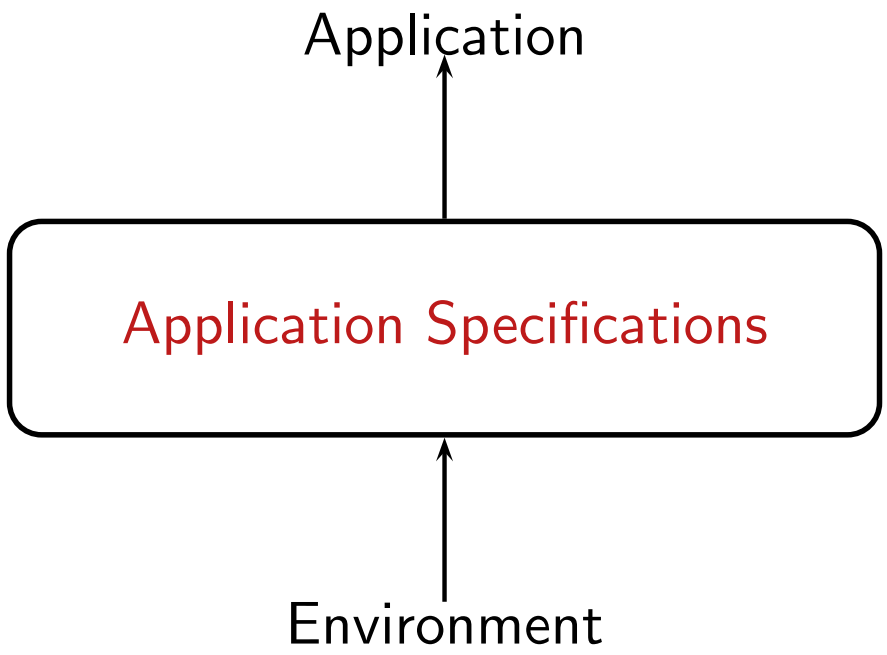
Examples



Interlayer: Application



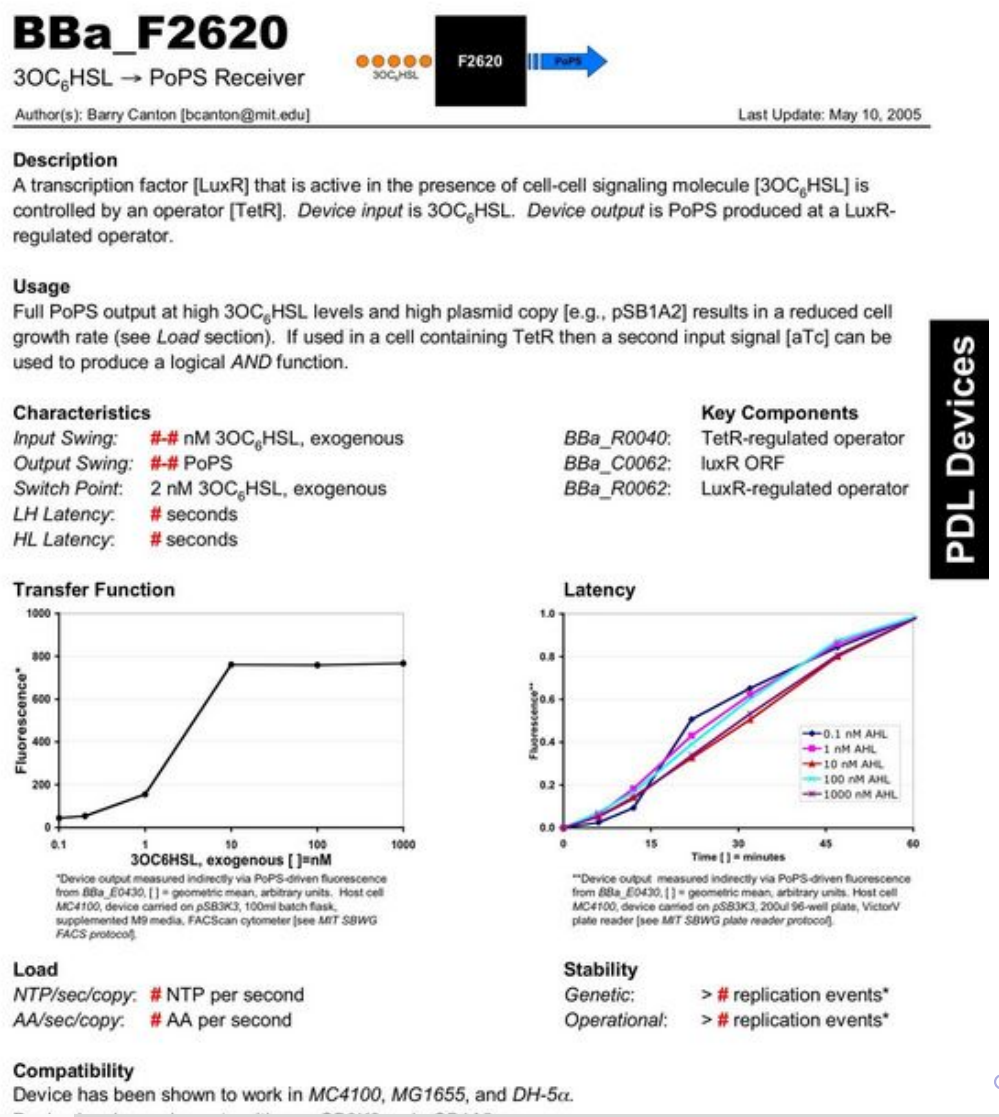
Interlayer: Application



Interlayer: Application

Standard specifications facilitate implementation reuse.

- transfer functions
- genetic or phenotypic (in)stability
- noise, cell variation
- dynamic response, timings
- safety, release risk



BBa_F2620

$3OC_6HSL \rightarrow$ PoPS Receiver

Author(s): Barry Canton [bcanton@mit.edu] Last Update: May 10, 2005

Description

A transcription factor [LuxR] that is active in the presence of cell-cell signaling molecule [$3OC_6HSL$] is controlled by an operator [TetR]. *Device input* is $3OC_6HSL$. *Device output* is PoPS produced at a LuxR-regulated operator.

Usage

Full PoPS output at high $3OC_6HSL$ levels and high plasmid copy [e.g., pSB1A2] results in a reduced cell growth rate (see *Load* section). If used in a cell containing TetR then a second input signal [aTc] can be used to produce a logical *AND* function.

Characteristics

Input Swing: #-# nM $3OC_6HSL$, exogenous
Output Swing: #-# PoPS
Switch Point: 2 nM $3OC_6HSL$, exogenous
LH Latency: # seconds
HL Latency: # seconds

Key Components

BBa_R0040: TetR-regulated operator
BBa_C0062: luxR ORF
BBa_R0062: LuxR-regulated operator

PDL Devices

Transfer Function

Fluorescence* 0 200 400 600 800 1000
0.1 1 10 100 1000
3OC6HSL, exogenous [ ]=nM

*Device output measured indirectly via PoPS-driven fluorescence from *BBa_E0430*, [ ] = geometric mean, arbitrary units. Host cell *MC4100*, device carried on *pSB3K3*, 100ml batch flask, supplemented M9 media, FACScan cytometer [see *MIT SBWG FACS protocol*].

Latency

Fluorescence** 0.0 0.2 0.4 0.6 0.8 1.0
0 15 30 45 60
Time [ ] = minutes
0.1 nM AHL
1 nM AHL
10 nM AHL
100 nM AHL
1000 nM AHL

**Device output measured indirectly via PoPS-driven fluorescence from *BBa_E0430*, [ ] = geometric mean, arbitrary units. Host cell *MC4100*, device carried on *pSB3K3*, 200ul 96-well plate, VictorV plate reader [see *MIT SBWG plate reader protocol*].

Load

NTP/sec/copy: # NTP per second
AA/sec/copy: # AA per second

Stability

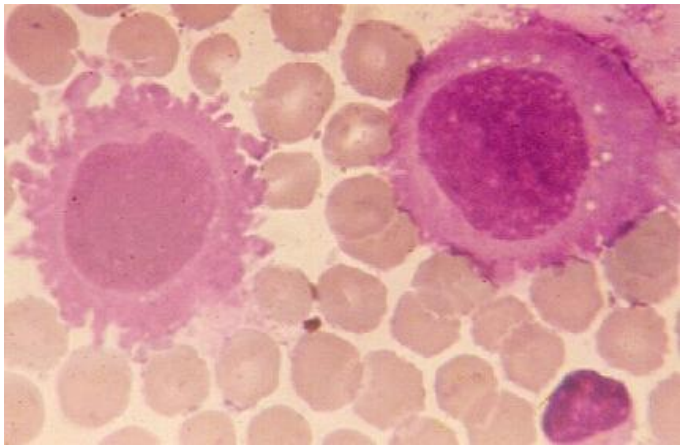
Genetic: > # replication events*
Operational: > # replication events*

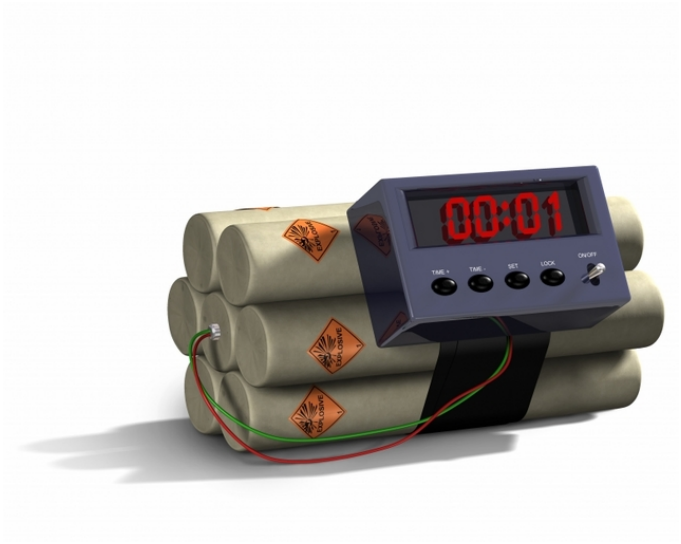
Compatibility

Device has been shown to work in *MC4100*, *MG1655*, and *DH-5α*.

Layer 7: Application

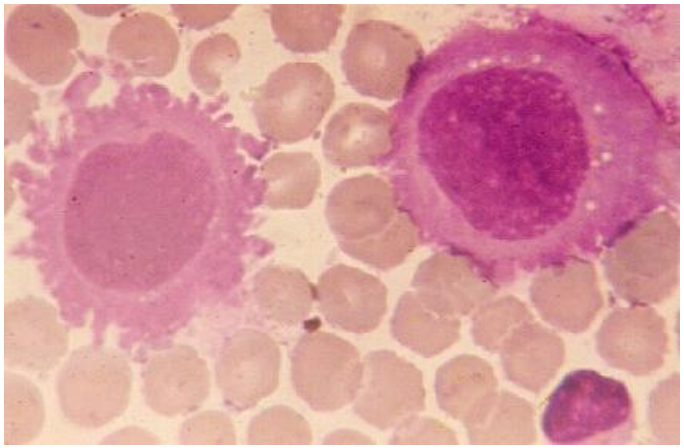
Examples

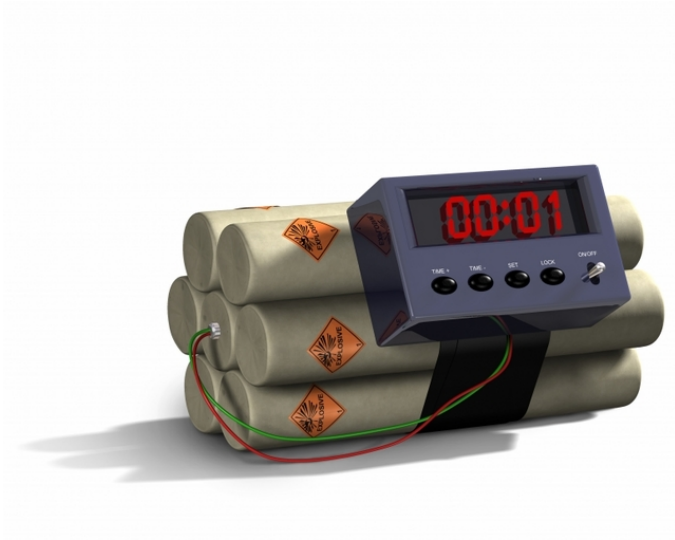




Layer 7: Application

Examples





RED ALERT

The Biological Layer Model

An abstraction and standards hierarchy for synthetic biology

Layer 7: Application

Application Interlayer

Layer 6: Environment

Environment Interlayer

Layer 5: Chassis

Chassis Interlayer

Layer 4: Cell

Cell Interlayer

Layer 3: Protein

Protein Interlayer

Layer 2: RNA

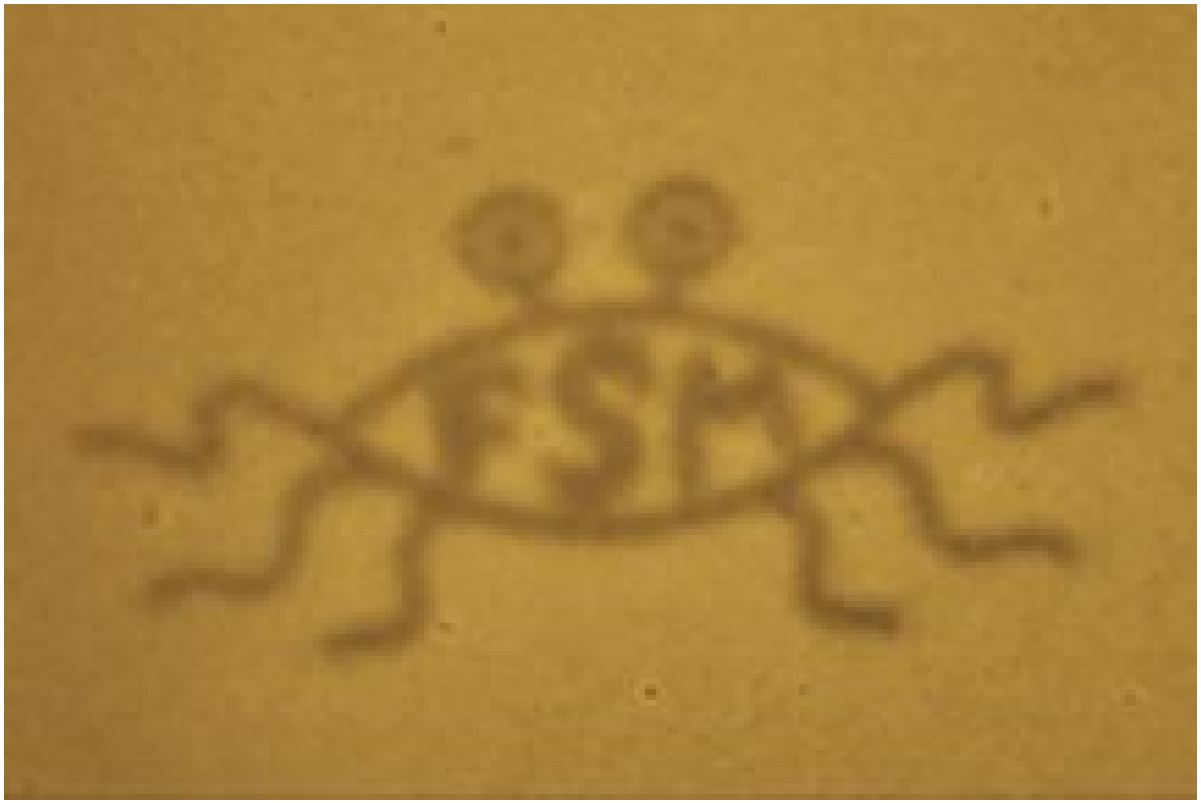
RNA Interlayer

Layer 1: DNA

DNA Interlayer

Layer 0: Materials

Intelligent Design Exists!



`http://syntheticbiology.org/`

Making life better...one part at a time.