LIFE IS COMPUTATION
Georg Seelig
Computational biology: Computer-based methods for understanding biology

Molecular computation: Understanding how molecular systems “compute”
A MOLECULAR PROGRAM: DEVELOPMENT

Biological programs are complicated, can we find alternative programming languages for molecular systems?
WHY DO WE NEED TO PROGRAM BIOLOGY?

“Smart drugs”: targeted therapeutics
WHAT DO WE NEED TO PROGRAM BIOLOGY?

Devices level: molecular sensors, logic and actuators

Programming languages and compilers for chemistry
Biology (often) uses protein. Currently we don’t know how to relate protein sequence to structure and function (Computational biology challenge!)
HOW CAN WE BUILD SENSORS AND ACTUATORS?

We understand DNA!
DNA as a building material: Silk, wood, DNA
HOW CAN WE BUILD MOLECULAR CIRCUITRY?

- Boolean logic (logic values 0/1 = low/high concentrations), AND, OR, NOT are sufficient for calculating Boolean functions
- Cascading (inputs and outputs have the same form)
- Signal restoration
- Modularity ("plug and play"), isolation and specificity (no load, crosstalk)

Transistor, 1947
Integrated Circuit, 1958 (2 transistors)
Microprocessor (1971) (2250 transistors)
let-7c AND mir-124a AND (mir-15a OR mir-10b) AND (mir-143 OR mir-122a)

INPUTS

TRANSLATION AND INPUT AMPLIFICATION

COMPUTATIONAL SUBCIRCUIT

SIGNAL RESTORATION

NOT IN CELLS!
A compiler for DNA logic circuits

**VHDL code**

```
architecture struct of comb_ckt is

component AND_GATE is  -- as entity of AND_GATE
    port( A: in std_logic;
        B: in std_logic;
        F: out std_logic
            );
    end component;

component OR_GATE is  -- as entity of OR_GATE
    port( X: in std_logic;
        Y: in std_logic;
        F1: out std_logic
            );
    end component;

    signal wire: std_logic;  -- signal just like wire
...
```

**boolean logic netlist**

```
```

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**DNA gate reaction mechanism**

```
```

**DNA sequences**

```
AAACACCAGAACCAGACCTGACTAAAATGCGCTGTA
CTATATTTTTAAAGCTACACTACTACAATATAG
ACCTCTTGAACAAACACTTTTTTCA
ATCATTTGCAAATCCCTTTAGAA
CAGCCGAAATAGTTTATTTG
CGTACCTGAAACCCTGAAAGCAGCAGCAGG
CAATACGGAATACCAACTAACAACTACGACGCTRA
TTTCTCCAATCGGAATGGAGAT
AGAAAGGATGCTCCAGATG
CAACAACCATCGGTTTTCTCT
AAACTCATATTTTTGGACAAACG
GAGATTGGACCAACTTTGAAGAACTGCG
TGACCCTGCGTTGCGCCGACG
GCTAACAGTAGCGGTCACTTTATAAGAGGAGG
ATGTTAGGCAATTAAACCTCCTTTACCCATAG
GTTAGATATGACGATGCAATTAGGGTT
ACTAGGAGATTAGACATATACTGGAAC
...
```
Enzyme-free nucleic acid logic circuits work reliably in a cell-free environment

Build components that work in a cell and characterize them quantitatively

Build multi-component circuits that are fully integrated with the cellular environment
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