Living Software

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Crawling Neutrophil Chasing a Bacterium

Human Cell (Neutrophil)

Bacterium (S. aureus)

Red Blood Cells

How does it do it?

[www.biochemweb.org/fenteany/research/cell_migration/neutrophil.html]
Cells Compute

- No survival without computation!
  - Finding food
  - Avoiding predators

- How do they compute?
  - Proteins: what kind of circuits?
  - Genes: what kind of software?

Protein Networks = Circuits?

The p53-Mdm2 and DNA Repair Regulatory Network

Figure 6B: The p53-Mdm2 and DNA repair regulatory network (version 2p - May 19, 1999)

Gene Networks = Software?

Control diagram of a sea urchin gene


B
if \((F = 1 \text{ or } E = 1 \text{ or } CD = 1) \text{ and } (Z = 1)\)
\[
\alpha = 1
\]
else
\[
\alpha = 0
\]
if \((P = 1 \text{ and } CG_1 = 1)\)
\[
\beta = 2
\]
else
\[
\beta = 0
\]
if \((CG_1 = 1 \text{ and } CG_2 = 1 \text{ and } CG_3 = 1)\)
\[
\gamma = 2
\]
else
\[
\gamma = 1
\]
\[
\xi(t) = B(t) + G(t)
\]
\[
\eta(t) = \beta^{\alpha}(t)
\]
if \((\xi(t) = 0)\)
\[
\zeta(t) = Otx(t)
\]
else
\[
\zeta(t) = \xi(t)
\]
if \((\alpha = 1)\)
\[
\eta(t) = 0
\]
else
\[
\eta(t) = \xi(t)
\]
\[
\phi(t) = \gamma^{\eta(t)}
\]
Repression functions of modules F, E, and DC mediated by Z site
Final step up of system output
Positive input from modules B and G
Synergistic amplification of module B output by CG, P subsystem
Switch determining whether Otx site in module A, or upstream modules (i.e., mainly module B), will control level of activity
Repression function inoperative in endoderm but blocks activity elsewhere
Final output communicated to BTA
Biological Algorithms

Protein Production and Secretion

[Voet, Voet & Pratt Fundamentals of Biochemistry Wiley 1999. Ch10 Fig 10-22.]

Viral Replication

[Adapted from: B. Alberts et al. Molecular Biology of the Cell 3rd Ed. p.279.]

LDL-Cholesterol Degradation

Understanding by Direct Engineering

- If we could manipulate molecules as well as nature, what would we do?
  - Nanomaterials Engineering
  - Genetic Engineering

- How does nature do it?

[Folding DNA to create nanoscale shapes and patterns, Paul W. K. Rothemund, Nature Vol 440 | 16 March 2006]

[A synthetic oscillatory network of transcriptional regulators, Michael B. Elowitz & Stanislas Leibler, NATURE | VOL 403 | 20 JANUARY 2000]
Understanding by Reverse Engineering

**Biological Organism**

Software: \( \sim 3\text{MB} \) (yeast) - \( \sim 650\text{MB} \) (human)

Hardware:
- \( \sim 10^{10} \) protein molecules (~5000 species)
- \( \sim 10^{12} \) other organic (~250 species)

[www.foresight.org/Nanomedicine/Ch03_1.html]

**Technological Organism**

- \( \sim 1\text{MB} \) (?)
- \( \sim 10^5 \) transistors (?)

[www.tamagotchi.com]

Every known living autonomous entity has at least 150KB of software (M. genitalium); and usually a lot more.
Reverse Engineering an Organism

- Understanding the principles
  - What does a Tamagotchi compute?
Reverse Engineering an Organism

- Understanding the principles
  - What does a Tamagotchi compute?

- Understanding the mechanism
  - How are the parts connected to the cyberpet on the screen?
Reverse Engineering an Organism

- Understanding the principles
  - What does a Tamagotchi compute?

- Understanding the mechanism
  - How are the parts connected to the cyberpet on the screen?

- Understanding the behavior
  - How does it react to stimuli?

“How often do I have to exercise my Tamagotchi?”
Every Tamagotchi is different. However we do recommend exercising at least three times a day.”
Reverse Engineering an Organism

- Understanding the principles
  - What does a Tamagotchi compute?

- Understanding the mechanism
  - How are the parts connected to the cyberpet on the screen?

- Understanding the behavior
  - How does it react to stimuli?

- Understanding the interactions with the environment
  - How did it evolve from the Japanese culture and economy?
Reverse Engineering an Organism

- Understanding the principles
  - What does a Tamagotchi compute?

- Understanding the mechanism
  - How are the parts connected to the cyberpet on the screen?

- Understanding the behavior
  - How does it react to stimuli?

- Understanding the interactions with the environment
  - How did it arise from the Japanese culture and economy?

- Understanding the math
  - What differential equations does it obey?

\[
\frac{dTamagotchi}{dt} = ???
\]
Reverse Engineering an Organism

- Understanding the principles
  - What does a Tamagotchi compute?

- Understanding the mechanism
  - How are the parts connected to the cyberpet on the screen?

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- Understanding the math
  - What differential equations does it obey?

- Now what?
Reverse *Software* Engineering

- Understanding the hardware is not enough
  - *Everything* interesting a Tamagotchi does is defined by its software
  - The hardware is completely generic: e.g. ~same as in a digital watch

- Understanding the software, and how it controls the hardware
  - Dumping the raw code (*genomics*)
  - Taking stack traces (*transcriptomics*)
  - Taking core dumps (*proteomics*)
  - Monitoring the heap size and power supply (*metabolomics*)
  - Sniffing the network packets (*systems biology*)
A Cell is:

- Living chemistry

Roche Applied Sciences biochemical pathways wall chart

Yes, but chemistry is there to implement function
A Cell is:

- Living chemistry
- A living machine

Yes, but machinery needs control

[Schematic diagram of the flagellar motor

[Keiichi NAMBA, Osaka University, JAPAN NANONET BULLETIN - 11th Issue - February 5, 2004]
A Cell is:

- Living chemistry
- A living machine
- A living computer

Yes, but cellular circuits need to be built and reconfigured from blueprints

Epidermal Growth Factor Receptor pathway map

A Cell is:

- Living chemistry
- A living machine
- A living computer
- Living software

Without understanding the software of life, ultimately, we cannot understand/repair cells.

Even if we understood all the chemistry, mechanics, and circuitry.

Portion of the sea urchin embryo endomesoderm gene regulatory network

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Conclusions

- Biology and Computing will ultimately converge
  - Nanomachines are the ultimate hardware
  - “How does a cell work” has to be answered at many levels and ultimately at the “software” (dynamic control) level