The Intersection of Computer Science and Biology

Bioinformatics & the Next Software Revolution

(Sara-Jane Dunn's *"The next software revolution: programming biological cells"*)

Jackson Eshbaugh

The next *software revolution*

The Next Software Revolution

From Silicon to Biology

- The original technological revolution
  - On silicon, created so many new possibilities (including this presentation medium)
- The *next* technological revolution
  - **Biological**, will create so many new possibilities we can’t even dream of.
  - A living technological revolution

This is a *challenge*.

The Next Software Revolution

The Program Running in a Cell

The Next Software Revolution

Stem Cells

- Stem cells
  - Grow into other types of cells.
  - Normal cells can be “reprogrammed”—that is, turned back into stem cells
    - “Returned to the *naïve state*”
- Changing cell fate is still a process of trial and error.

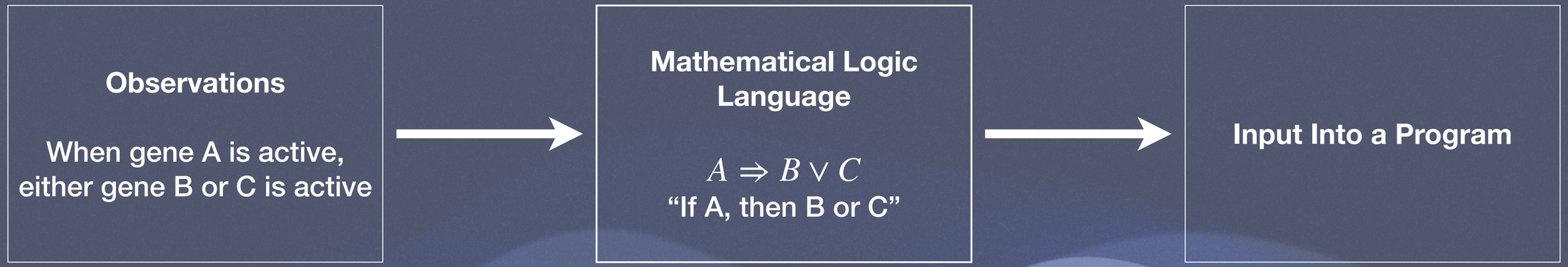
Ironically, *learning how this program runs*—which is a very tough question—starts with asking a very *simple question*:

What does this system actually have to do?

Since structure dictates function, we can use function to begin to envision structure.

The Next Software Revolution

A General Idea of how to Deobfuscate the Program



The Next Software Revolution

Sara-Jane Dunn’s Experiment

1. Starts with nearly 50 specifications generated from experimental observations.
2. Encodes these observations in the tool
3. The computer spits out a biological program (of gene interactions).
4. Predictions are generated by the program (testing in silico)
5. These predictions are tested in the lab.

The Experiment

“A common molecular logic determines embryonic stem cell self-renewal and reprogramming”

By Sara-Jane Dunn, Meng Amy Li, Elena Carbognin, Austin Smith & Graziano Martello

- **Purpose:** *To determine if a computer algorithm can predict the mechanism by which stem cells operate.*
- A cABN was created, fed the constraints that we talked about earlier, asked to predict different methods to achieve different goals under the general umbrella of inducing naïve pluripotency, then these results are tested in the lab.

77.4%

cABN predictions supported by experiment

“A common molecular logic determines embryonic stem cell self-renewal and reprogramming”

By Sara-Jane Dunn, Meng Amy Li, Elena Carbognin, Austin Smith & Graziano Martello

- Testing combinations of factors that could enhance stem cell resetting

A

Prediction

Factor 1	Factor 2	Factor 1 # steps	Factor 2 # steps	Factors 1+2 # steps	Syner-gistic effect?
Esrrb	Klf2	5	6	4	Y
Esrrb	Klf4	5	6	4	Y
Esrrb	Tbx3	5	7	3	Y
Klf4	Tbx3	6	7	4	Y
Klf2	Tbx3	6	7	4	Y
Klf2	Klf4	6	6	5	Y*
Esrrb	Tfcp2l1	5	6	5	N

7

3

Experiment

Factor 1	Factor 2	Factor 1 Fold Over WT	Factor 2 Fold Over WT	Factors 1+2 Fold over WT	Syner-gistic effect?
Esrrb	Klf2	11	13	49	Y
Esrrb	Klf4	11	12	42	Y
Esrrb	Tbx3	11	4	29	Y
Klf4	Tbx3	12	4	26	Y
Klf2	Tbx3	13	4	25	Y
Klf2	Klf4	13	12	16	N*
Esrrb	Tfcp2l1	11	2	10	N

4x

50x

“A common molecular logic determines embryonic stem cell self-renewal and reprogramming”

By Sara-Jane Dunn, Meng Amy Li, Elena Carbognin, Austin Smith & Graziano Martello

- This research is exactly what Sara-Jane described in her TED Talk.
- Real World Applications
  - Using a network like this to inform how to reset a sample of cells and then differentiate them to grow implants that the body is less likely to reject.

The Next Software Revolution

In Closing…

- This is just one building block. More testing is needed (on all scales—from genetics to the flow of information between cells)
- We need to build new tools in order to fully realize this new revolution
  - We need new programming languages that compile not to machine code, but instead to genetic code (DNA & biochemistry)
- We need to bring together all types of scientists, and they need a common language in order to communicate effectively in the field.

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