Software Engineering for Molecular Programming

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How do we build more robust systems?

Software Safety & Reliability

Requirements Engineering

Software Engineering

NASA
Growth in Critical Systems

Pacemaker & Defibrillator
Guidant

Unmanned Helicopter
NASA-Ames Research Center

Space Telescope
NASA

MRI machine
http://i.cnn.net/cnn/2004/HEALTH/02/10/dyslexia.ap/story.dyslexia.ap.jpg

Medical Infusion Pump
http://www.terumo.co.th/image/medical2.jpg
Molecular programming

“Computing with soup
Molecular computing: DNA is sometimes called the software of life. Now it is being used to build computers that can run inside cells.” - The Economist, 3/3/2012
Molecular programming
(DNA nanotechnology)

Molecular programming creates and programs a wide variety of synthetic nanosystems that autonomously assemble themselves from molecular components.

Programming is done by carefully choosing the molecular strands & their concentrations such that they will achieve the desired shape, structure, function or dynamic behavior.

We are interested in the software engineering of these programmed systems.
Computing with DNA

Molecular computer: 130 DNA-strand calculates the floor of the Square Root of four-bit binary numbers (Qian and Winfree, 2011) Science Photo Library/Alamy.

Simulate digital signals with DNA logic circuits (AND, OR, NOT): Low (High)concentration/no fluorescence; Universal “seesaw” gate implements AND, OR by varying concentration of threshold gate (Qian and Winfree, 2011)

Binary Counter
Barish, Schulman, Rothemund, and Winfree, PNAS 2009


Self-assembled DNA box with a controllable lid, E. S. Andersen, et al., 2009. Many of the applications will be safety-critical
DNA origami pliers to detect presence of a target molecule

Figure 1. Atomic Force Microscope images of DNA origami pliers: (a) at initiation, DNA pliers are open in the cross form, (b) upon adding SA molecules to the solution, DNA pliers close to the parallel form, capturing the SA molecules in the pliers’ jaws; (c) at reset via addition of unset strands DNA pliers re-open, releasing SA molecules. Adapted by permission from Macmillan Publishers Ltd: ref. [12], copyright 2011.

Software engineering analysis tells you: Does the DNA system do what you want?

• Modeled the behavior of DNA pliers in solution.
• Identified an unexpected failure state.
• Verified by model checking that key properties are satisfied in the model--if the ratio of targets to detectors isn’t too low or too high:

1. Achieve capture when the target molecule (SA) is present
2. Avoid false positives when SA is not present
3. Identified error state (one SA in each jaw)

[ICSE’12, RE’12]
A molecular watchdog timer

Many envisioned DNA nanosystem applications will be safety-critical (ex. bio-sensors, drug delivery)

Problem:
Monitoring for when an expected event occurs in a DNA nanosystem is hard. Monitoring for the absence of an expected event is even harder.

Solution:
We’ve designed a robust, molecular watchdog timer & verified that the probabilistic model works as intended. [ASE’14]
Q: What good is Software Engineering?

A: A better way to make a new programmed system in DNA!

- Provides a process for incremental goal refinement/risk analysis
- Identifies missing requirements and incorrect operating assumptions
- Predicts performance
- Gives assurance that some failure modes are unlikely
- Yields requirements for more robust system
- Reduces number of experiments (aka tests & re-work) needed

Thanks!