Colloquia Review: Decision Making Molecular Networks as presented by Milan Stojanovic

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1 Introduction

Professor Milan Stojanovic was kind enough to visit the University of New Mexico Computer Science Colloquia on Thursday, February 20th to give a presentation on his and Professor Darko Stefanovic's research in the field of molecular decision making networks. What follows is a brief summary and review of the topics discussed.

2 Overall Goal

The process described has a fairly simple goal; to provide response to a chemical stimulus. This response can take many forms, and only a few were discussed during the lecture. All of the responses involve a fundamental change in molecular form of the reagents present in the solution. The change in form can be a simple change in the secondary structure of the molecule or it can be as drastic as the formation of new compounds through addition and or subtraction of proteins. All changes discussed were emulating logical gates that are present in computational systems (integrated circuitry). The current experiments are being conducted using DNA and enzymes, however it was pointed out that the substrate could be RNA or any other number of protein structures. The only

reason that DNA is being used currently is because of the prohibitive cost of RNA enzymes and the relatively short lifespan of the enzymes and proteins involved in the RNA process.

One of the main hopes for this technology is in the delivery of medications. If brought to fruition, this technique could allow for a substance to be injected into a patient - and the substance would correctly diagnose the patient's problem and administer the appropriate drugs. This technology is also being offered up for a potential means of computation, however I feel that the underlying methods will prohibit this. For example, it was pointed out that although you do get a binary response from the system, it requires a buildup over time. This time is on the scale of minutes, not nanoseconds. If you stack several of these processes end-to-end then you only amplify the problem. This was evidenced by the simple communication gates that were shown during the presentation. The simple two-step process was taking twice as long as the other processes shown, so differentiation did not look feasible until 15-30 minutes had gone by.

3 Process

The process is fairly simple; a given amount of genetic material is present in a test tube. This genetic material has been fabricated using enzymes in such a way that the molecule has a very specific shape and structure. By exploiting different enzymes the experimenters can inhibit or promote structure change. As mentioned above, structure change can occur in several different ways. Some changes simply involve a slight unraveling of the protein while others result in subtraction or addition to the molecule. In the discussed experiments all the changes resulted in a change in fluorescence. This was not a functional necessity, just a means of validating the results of the experiment. To facilitate the reaction excess enzyme is added to the solution. This guarantees that the solution will show the maximal change in fluorescence.

4 Gates

As mentioned above, the experimenters have been able to emulate logical gates through their experiments. This is quite useful towards their eventual goal of a drug delivery system. It is with these gates that they hope to build up more complex systems of inhibition and stimulus, eventually resulting in diagnosis and drug administration. During the lecture the following gates were mentioned: yes gates, not gates, and gates, XOR gates, multiple and gates, A and not B gates, and the list goes on. This is exciting because they are able to create any logical expression through the conjugation of these gates. As mentioned above - there is an inherent problem with time, but only if you perform the operations in serial. Several of the experiments discussed were actually able to carry out much of the computation in parallel by having two different molecules reacting to the same enzyme.

It was unclear to me through the presentation how the molecules were being made, but it sounded as though the experimenters were purchasing them from supply houses. They did discuss very briefly that they use various Ligase enzymes (enzymes capable of creation and concatenation of proteins) to complete their gates, so it does sound as though the gates are actually made in house.

5 Florescence as a means of Validation and Verification

Florescence turned out to be a convenient and simple test for the results of the experiment. Florescence would either be suppressed or induced according to the enzymes and reagents present. The method is simple and cheap in comparison to the other methods available to verify molecular shape. A base line reading is taken of the substance before reaction occurs, then a continuous measurement is made through the course of the reaction. By measuring the change in fluorescence, the experimenters can verify that the reaction did proceed as expected.

The change in fluorescence is accomplished by the creation, destruction, hiding, and exposing of the florescent protein sequences. The basic idea is that if you place a florescent protein at a point on this molecule and the molecule changes shape - the fluorescence of the molecule will change. The experiments have even gotten as complex as to utilize two different fluorescing compounds, allowing for a 2 output system. The problem with adding more outputs is that these systems experience "bleeding" of the results. That is, If one output is 1 and one 0, the two results may experience a kind of mean averaging effect - the outputs will be more like .75 and .25 instead of 1 and 0.

6 Conclusion

Overall I found this to be the most interesting lectures I heard this semester, hence my choice of topic. I felt the most common misconception was that a decision making network was a computational device, which I do not believe to be the case. The kinds of interactions possible are too simplistic and slow to provide computational ability in the modern sense of the word "computation", however this technology is perfectly suited towards its medical applications. I truly hope to see much more research in this area as I feel it will yield interesting results and benefits.