**E. coli Automatic Directed Evolution Machine**

**A Universal Framework for Evolutionary Approaches in Synthetic Biology**

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**Background**

Evolutionary approaches are an alternate of approaches based on design, especially when there is no enough information for design.

Directed evolution is widely used in bioengineering to get desired molecules or biological systems, but the process takes a lot of time to optimize conditions manually. Evolutionary algorithm is a set of well developed theory to control the evolution process in engineering. Our project focuses on automating directed evolution with evolutionary algorithm, or program E. coli to evolve in the direction we want.

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**Design**

**The Goal of E. coli Automatic Directed Evolution Machine (E.ADEM) Project**

E.ADEM Framework

Possible Design of Scoring Function

Our Prototype Machine

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**Assembly & Measurement**

To verify our parts and get the necessary parameters in our system, we did many measurements. Most of designed parts work very well according to our data.

**Constitutive promoters:** We measured the strength of the promoters using GFP(BBa_I3504) as the reporter and utilized the flu/o/d to indicate the promoter strength.

**Hybrid promoter:** We designed a hybrid promoter Plux-tet. It could be measured with the presence of luxR and tetR. We applied AHL and aTc as stimulus signals and measured the fluorescence output.

**Quorum sensing parts:** We also measured the response of the hybrid promoter to endogenous Lux.

**ccdB parts:** We used ccdB to control the population density and work as the Selection Function. But all the 8 versions of ccdB we constructed, with and without lacZa, LVA, and with 2 different RBS, do not work well. The growth curves cannot be repeated measured.

**Modeling**

We described the dynamics of biochemical reactions in our 11 systems in term of ODE and simplified them properly. Take the system of AHL receiver as an example, we successfully established a method to estimate the parameters, using our experimental data, under the help of USTC_Software Team.

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**Abstract**

Evolution is powerful enough to create everything, from biomolecules to ecosystems. The ultimate goal of E. coli Automatic Directed Evolution Machine (E.ADEM) project is to manage the power of evolution, by engineering a robust system framework that can automatically create anything we want in synthetic biology, from various types of parts to complex systems. Each demand can be converted into designing a scoring function to give the evolution process a direction. E.ADEM is designed by implementing evolutionary algorithm back into biology. The core of E.ADEM is a self-adaptive controller that can adjust variation rate and selection pressure, based on fitness score, population size and average fitness score calculated by a quorum sensing device. After comprehensive measurement using constitutive promoter family stimulus signals and modeling of the components, a prototype machine is built. Modular design and PoPS device boundary standard will ensure the extensibility and universality of the machine.

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**Other Work**

**Software tool:** We developed a software to pick PCR primers from random sequence (not from given sequence). It will be very useful in synthetic biology. The software is based on primer3.

**Human practice:** We considered many possible issues and solutions on safety, security, ethics, ownership, sharing, and innovation in detail.

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**Conclusions**

**Achievements:** For the first time, evolutionary algorithm will be run in E. coli. Our framework will enable a lot of evolutionary approaches in synthetic biology. This year we have submitted over 170 parts to the registry, many of these parts are characterized, the data can be easily found on the pages of the parts.

**Beyond iGEM:** E.ADEM project will continue on the OpenWetWare. Based on our work started from iGEM 2009, the project should continue with the inspiration and perspiration from students and researchers around the world with the similar interests. We are anticipating your participation!  
http://openwetware.org/wiki/E._coli_Automatic_Directed_Evolution_Machine_project