How to Develop Students' Creativity? —A Case of Student Competition of Biomolecular Design

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Educational effect of STEM education especially a design competition for students in the field of nanotechnology is discussed in this paper. Molecular design competition BIOMOD is founded in 2011, now becomes an influential competition attracting many young generations to DNA nanotechnology. The background of the competition, its structure and an example of awarded project is introduced to demonstrate educational effects of the competition.

Key words: STEM Education, Molecular Design, BIOMOD

1. Introduction

Education through competition is getting more and more popularity not only in robotics (various types of ROBOCON is popular in Japan) but other fields of science and technology. In this paper, we focus on the biomolecular design competition (BIOMOD) to discuss educational effect of such design competitions (Fig. 1).

Thanks to rapid progress in biology, chemistry and information sciences, we are now able to design biomolecules with desired shape and functionality. Amongst them DNA is known to the most useful material available at this moment. DNA nanotechnology or DNA nanoengineering have been rapidly developing in this decade, providing various possibilities of nanodevices and nanostructures made of synthesized DNA. The field is now expanding to molecular robotics by combining DNA nanostructure, DNA computer and DNA devices into an integrated system (i.e. a molecular robot).

Designing objects in molecular size is somewhat different from designing ordinary visible size objects like architectural structures. To characterize the properties of designed molecules, we need to adopt various indirect methods such as electrophoresis and spectroscopy. Direct imaging of the molecules by using high resolution microscopy (i.e. single molecule imaging by an atomic force microscope (AFM) or a transparent electron microscope (TEM)) is possible but usually these are time consuming and cost a lot. Molecular design requires broad range of knowledge, from chemistry, physics, biology, computer science to mechanical engineering in both design and characterization of the molecule.

In order to master this kind of intrinsically inter- and multi-disciplinary subject, ordinary education system for sciences and technologies do not work very well. Students may lose their motivation after years of learning process of fundamental knowledge in these subjects. This is the main reason why we need so-called "STEM" education in molecular design. STEM is a way of education based on the idea of educating students in Science, Technology, Engineering and Mathematics in an interdisciplinary and applied approach. Rather than teaching these four disciplines as separate and discrete subjects, STEM integrates them into a cohesive learning program based on real applications.

In applied biology area, the first attempt to educate students by STEM approach is iGEM (International Genetically Engineered Machine Competition)[4]. This is an intercollegiate competition of undergraduate students competing in unique design of genetic network. No specific goal is given in this competition, instead, teams have to develop their own concept of novel genetic network, and show its feasibility through some experiments by using a genetic modules provided by the convention. The first iGEM congress held at MIT in 2003, and it now grows into a huge world-scale congress in which more than 200 teams from all over the world join every year.

BIOMOD was founded on the similar concept in different technology area (DNA Nanotechnology) in 2011 at Harvard Unversity. In BIOMOD, similar to iGEM, no specific goal is determined, participants can develop projects on their own ideas. Whereas, the number of participating team is limited to 30 to keep its friendly atmosphere and time for intensive discussion. No material (such as genetic modules in iGEM) is not provided by congress, however, instructions to use design tools of DNA nanosturcutre (CaDNAno, CanDo etc.) are provided. In Japan, molecular research group organized in SICE (Society of Instrument and Control Engineers) supports students' activities in BIMOD to promote molecular robotics for younger generations. The domestic workshop called BIOMOD Japan is organized by the group provides an opportunity to rehearse presentations in English. Also the group published a text book for BIOMOD students (BIOMODers) (Fig. 2).

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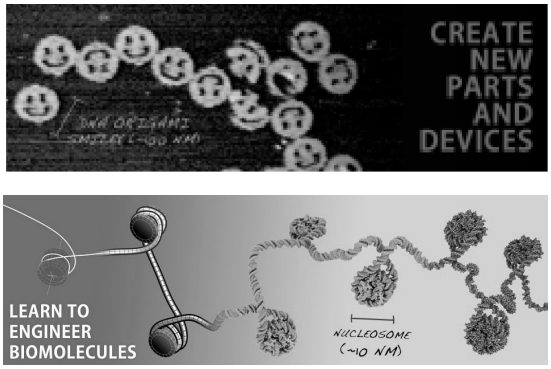

Fig. 1. BIOMOD website [1].

Fig. 2. Text book entitled "Introduction to DNA molecular Design" written by Molecular Robotics Research Group, SICE (in Japanese). Open textbook for BIOMOD students, released in April, 2016 [2]. A handy text book (the first text book of this kind in any language) is very helpful for beginners who want to learn necessary basics of DNA nanotechnology.

Fig. 3. Team Sendai of Tohoku University awarded Grand Prize at BIOMOD 2015.

2. BIOMOD

BIOMOD is an open-ended competition. Competition of open-ended design is beneficial because participants can have experience of the whole research process from the brain storming to get the project idea to the final presentation to show the results, and it eventually provides an effective on-the-job training to develop the qualities and skills to become a scientist and engineer.

Definition of BIOMOD is given in its web site: "BIOMOD" is a design competition in which undergraduate teams compete to master control of biomolecules on the nanometer scale. Focus areas may include—but are not limited to—biomolecular robotics, biomolecular logic and computing, and structural bionanotechnology, Students conceive and execute projects during the summer and then gather in congress in Novermber to present their work and win awards.

This competition is organized by Dr. Shawn Douglas at Wyss Institute, Harvard University (later he moved to UCSF). The first notice was delivered through E-mail around January 2011 announcing the concept of the competition for student level. We (Research group in Molecular Robotics, SICE, Japan) decided to join the competition through supporting student teams and sent Dr. Shogo Hamada (assistant professor of author's lab at that time) to Boston to discuss about the rules and judging system for the competition. Many of our proposals about them have been reflected in the structure of the competition.

For the BIOMOD participants, it is required to report their activities by three different forms (Table 1). First and most important report is Wiki pages that expected to provide every details of the project. Second is a YouTube video that summarizes the outline of the project. Third is an oral presentation at the conference in Boston. Those items are evaluated by judges at the conference. The judges are volunteered from mentors from all the teams. Evaluations are given by a certain numerical rating system (this is a part of our proposal to give transparency to the competition), without a subjective evaluation such as comments and impressions.

An example of project timeline is given as follows (BIOMOD site [1]).

• January–March: Team organizers should recruit team members: post flyers and email announcements, interview interested students, and send notifications early while everyone is still finalizing their summer plans (in Japan, we have to start from April because of our academic term).

• April–May: Register your team. Students should begin independent background reading to start learning about topics that may interest them. Organize brainstorming meetings to determine project topic.

• June–August: Do the project! Also, start planning the YouTube video as early as possible. Book travel arrangements and apply for Visas if necessary.

• September–October: Complete project wiki, video, and presentation. Register for Jamboree (as mentioned above, we have domestic congress in September in Japan).

3. Project Example

In this section, as an example of BIOMOD project, we take Team Sendai's project of 2015 [3] (Fig. 3). In this project, students of Tohoku University tried to design and fabricate DNA nanostructure module capable of controlling their stacking number. This work is later published as a journal paper [5].

3.1 Project motivation

In nature, various biological functions are realized by multimeric proteins (the same molecule binds together to form a cluster). Those proteins have intrinsic curvature

Table 1. Evaluation system of BIOMOD.

Online evaluation		Onsite evaluation
Wiki (50 points)	Video (25 points)	Presentation (25 points)
Detailed description of project	Digest of the project (promotion video)	Oral presentation and discussion
Idea, feasibility	Impact	Clarity
Reproducibility	Simplicity	Production
Achievements	Quality of contents	Impact

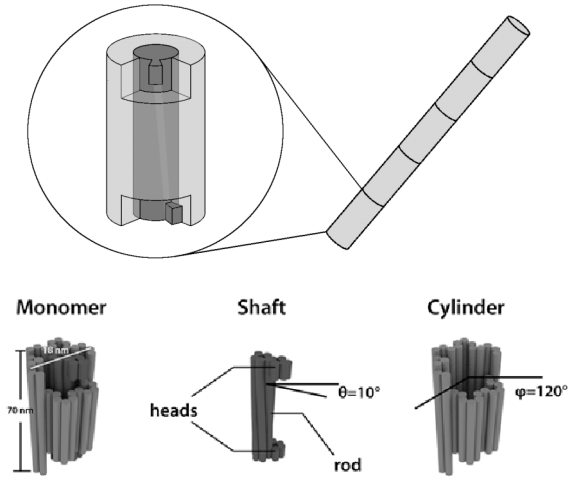

Fig. 4. Design of homomultimer [3]. Top: A Monomer: rotatable shaft (dark grey) is embedded in a cylinder (light grey). Bottom: Detail of DNA origami design. Twisted shaft counts the number of stacking by accumulating angular distortion.

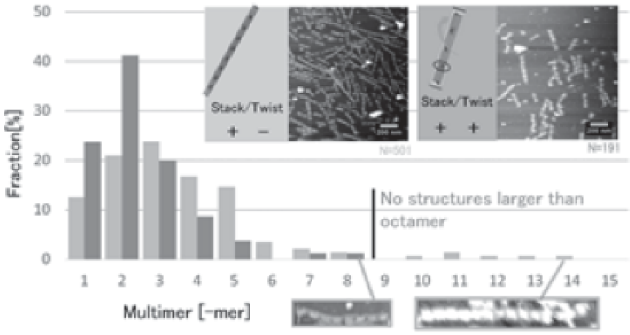

Fig. 5. Experimental result [3]. Number of stacking is quantized by AFM images. Comparison between twisted shaft and non-twisted shaft shows that no cluster larger than octamer was formed for twisted ones.

and the number of monomers in a cluster is determined by their circular assembly (i.e. once they form a circle no more monomer can bind to the cluster). In linear assembly there always exists both ends, thus, it is difficult to control the number of proteins without additional capping mechanisms. In order to solve this problem, the student team proposed a novel mechanism to control the number of monomers by employing a mechanism inspired by "Vernier". They designed a nanoscale DNA origami monomer that can count the number of stacking using the mechanism. It consists of a hollow cylinder and a twisted shaft, where the shaft can rotate inside the cylinder. Since the shaft is slightly twisted, there is a phase shift between stacking angles at the ends. When the monomers stack, the phase shift accumulates on the shaft. The monomers are capable of stacking until the accumulated twist reaches the limit defined on the cylinder. The elaborate design enables us to make size-controllable DNA origami complexes, which provide a novel possibility for structural nanotechnology.

3.2 Design

To achieve the goal, we propose a novel mechanism capable of controlling the assembling process of nanoscale linear homomultimer. We have designed a DNA origami monomer consisting of a cylinder and a twisted shaft, where the shaft can rotate inside the cylinder (Fig. 4). The shaft works as a vernier to count the number of stacked monomers while the grooves on the cylinder limit both the movement of the shaft and the number of stacking. Furthermore, the number of stacking can be tuned by adjusting the twist angle of the shaft and the groove width of the cylinder.

3.3 Result of experiments

The formation of the structure was confirmed by cryo-TEM observation. The size of observed structure was in good agreement with the design of DNA origami monomer. In order to evaluate the concept of size-controllable linear homomultimer, we observed the DNA origami structures by AFM. From the images of AFM, we statistically analyzed the stacking number of monomers with and without twist by making histograms (Fig. 5). The data shows that distributions of stacking number between two monomers were essentially different. In the case of monomer with twist, most of them formed dimers, where the largest multimer consisted of 8 monomers. In contrast, some of the multimers made of untwisted monomers were larger than octamer. This clearly indicates that the stacking number of monomer was limited by a twisted shaft.

4. Conclusions

Through the activities of BIOMOD, we have noticed there are many advantages to participate to this kind of student competition. Students feel varieties of difficulties, and learn a lot of things through experiencing project. Achievements are not only experimental skills but ways of thinking and perspective to broad possibilities surrounding them. (It is nice to see that some of the students seem to start thinking as if he/she were a real scientist.) The following are students' impressions extracted from inquiry.

Faced difficulties

Endless trials and errors

Difficulties in presentation

Difficulties in getting original idea for the project
Difficulties in English

Achievements

Learning international perspective (level of other teams/students)
Learning experimental skills, learning from mistakes
Feeling of accomplishment/team work
Getting used to speaking in English/presentation skills

As a conclusion, the educational effects of the competition could be summarized as follows:

1) Getting self-motivation is the most important influence of the competition. Mind of students have been clearly changed from "waiting for information" style to "thinking by themselves as a researcher" type of attitude.

2) Giving presentation in English in front of peers from over the world provides an opportunity (and certain pressure) to open their eyes to the importance of English communication and the level of global standard.

3) Understanding concrete problems need to be solved and thinking ways to solve them is quite effective to learn many different types of methodologies of biochemistry, simulation on the job. Team work ability is developed through the activities.

It is not only fun but advantageous to grow young researchers in emerging field like molecular robotics.

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