**Team name: Systematic Trio**

**Your name: Yunyoung Choi, Haeun Kang, Soonjun Kwon**

**Team project topic: Modeling a metabolic or electrochemical pathway (i.e. citric acid cycle, photosynthesis, etc)**

| **Paper title** | **Jornal name** (impact factor; number of citations) |
| --- | --- |
| A Hybrid Flux Balance Analysis and Machine Learning Pipeline Elucidates Metabolic Adaptation in Cyanobacteria | iScience (5.08; 79) |
| **Paper URL** (to a pdf file in your team’s cloud folder) | **Data URL** (to data stored in the team folder) |
| [A Hybrid Flux Balance Analysis and Machine Learning Pipeline Elucidates Metabolic Adaptation in Cyanobacteria.pdf](https://drive.google.com/file/d/1y1DI_dDCyxZT3EPIHl-ZFEUEBQ44nXgF/view?usp=sharing) | https://drive.google.com/drive/folders/1e\_3jLWQ7YI1iuN9\_qe68Wjm4h3rDPfkS?usp=sharing |
| **Goal, key hypothesis, main methods, and importance of this paper** | |
| **Goal of this paper:** The goal of this paper is to understand the metabolic adaptation of cyanobacteria by using hybrid Flux Balance Analysis and Machine Learning.  **Key hypothesis:** The key hypothesis of this paper is combining metabolic modeling with machine learning techniques will help to provide a better understanding of cyanobacteria such as important genes or reactions for adaptation of cyanobacteria.  **Main methods:**  The main method of this paper is a hybrid approach of combining machine learning with genome-scale metabolic models (GSMMs). This method can help to provide new information that can not be found through only transcriptomics.  **Model type:**  Machine learning models and GSMM were used. GSMM (genome-scale metabolic model) to simulate the metabolism. Specifically, GSMM of Synechococcus sp. PCC 7002 were used. Also, Flux Balance Analysis was used to understand adaptation mechanisms. Specifically, regularized flux balance analysis was used to observe flux response between conditions across photosynthesis and energy metabolism. Also, machine learning techniques are used such as PCA, k-means clustering, and LASSO regression. This was used to find some important genes and reactions in cyanobacteria. This helps with integrating multi-omic data with the GSMM to refine phenotypic predictions.  **Importance of this paper:**  The importance of this paper lies in the implications of machine learning to understand metabolic adaptation in cyanobacteria. Cyanobacteria are photosynthetic microorganisms that can be used to produce renewable biofuels. So, understanding about cyanobacteria can be very useful. However, unfortunately, their metabolic pathways are very complex and not yet fully understood. It was hard to find and understand metabolic pathways of cyanobacteria with only transcriptomics. However, by combining machine learning models, this can help to find some important genes or reactions that are related with cyanobacteria adaptation.  Therefore, the topic that are dealing with this paper has a potential for developing more efficient methods for understanding metabolic pathways of cyanobacteria and on producing biofuels and other bioproducts using cyanobacteria. | |

| **Paper title** | **Jornal name** (impact factor; number of citations) |
| --- | --- |
| Reconstruction and analysis of genome-scale metabolic model of a photosynthetic bacterium | Biomed central (7.25; 90) |
| **Paper URL** (to a pdf file in your team’s cloud folder) | **Data URL** (to data stored in the team folder) |
| [Reconstruction and analysis of genome-scale metabolic model of a photosynthetic bacterium.pdf](https://drive.google.com/file/d/13l7TdWTSRCowfqDhhEE7l3a-EUJBA88x/view?usp=sharing) | https://drive.google.com/drive/folders/1BrShN-C2B6Q9Or8IoqeEMLxs6uU6jnvp?usp=sharing |
| **Goal, key hypothesis, main methods, and importance of this paper** | |
| **Goal of this paper:**  Developing tools to uncover stoichiometric and regulatory principles in the *Synechocystis* metabolic network is crucial for effectively utilizing its metabolic potential.  **Key hypothesis:**  The hypothesis of the article is that the manually curated metabolic reconstruction of *Synechocystis* sp. PCC6803, a cyanobacterium, can be used to simulate environmental and genetic perturbations in the metabolic network, allowing for the assessment of projects for the production and optimization of an added value metabolite. The reconstruction is expected to be a valuable tool towards the development of a photo-biological production platform.  **Main methods:**   * **metabolic network reconstruction** to construct a *Synechocystis*-specific database of genes, proteins, enzymes, and metabolites. * **Flux balance analysis (FBA)** was used to solve the steady-state stoichiometric model, where linear programming was employed to find a feasible solution for intracellular fluxes. * **The minimization of metabolic adjustment (MOMA) algorithm** was also used to search for the point in the feasible space of the solutions space of the knock-out that has the smallest distance to the original wild-type flux state.   **Model type:**  The model(*i* Syn669) described in the paper is a genome-scale metabolic network model for *Synechocystis* sp. PCC6803, which simulates the metabolic processes of an organism at a genome-scale level. It includes 882 metabolic reactions, 790 metabolites, and information from 669 genes related to metabolic reactions.  **Importance of this paper:**  The paper describes the development of a genome-scale metabolic model for Synechocystis sp. PCC6803, a cyanobacterium that is a model organism for studying photosynthesis. This model is comprehensive and includes all the known information about the metabolism of the organism. The model can be used to simulate the production of all the metabolic precursors of the organism under different growth conditions. This can help researchers understand the metabolism of the organism and also aid in the development of biofuels and other useful products. The model can also be used to identify essential genes for survival, study the organism's potential to produce hydrogen, and perform *in silico* metabolic engineering analysis. This model will be a valuable tool for the applied and fundamental research of *Synechocystis* sp. PCC6803, as well as for the broad field of metabolic systems biology. | |

| **Paper title** | **Jornal name** (impact factor; number of citations) |
| --- | --- |
| Unique attributes of cyanobacterial metabolism revealed by improved genome-scale metabolic modeling and essential gene analysis | PNAS (9.661; 99) |
| **Paper URL** (to a pdf file in your team’s cloud folder) | **Data URL** (to data stored in the team folder) |
| [Unique attributes of cyanobacterial metabolism revealed by improved genome-scale metabolic modeling and essential gene analysis](https://drive.google.com/file/d/1EnHOAw3G_yWUTmHiuDGXA2tuwCgghpU1/view?usp=share_link) | <https://zhanggroup.org/Ecoli/>  <https://drive.google.com/drive/folders/1QqE5Mw_UWtkKzs5DyrF_Ek3iaYeLd1Ph?usp=share_link> |
| **Goal, key hypothesis, main methods, and importance of this paper** | |
| **Goal of this paper:** Developing a Genome-scale models (GEMs) of metabolism in *S. elongatus* using random barcode transposon site sequencing (RB-TnSeq) essential gene and physiological data specific to photoautotrophic metabolism.  **Key hypothesis:** The essential gene, and loss of function mutants are that an abridged TCA pathway, focused on generation of precursor metabolites is the physiologically relevant TCA process for *S. elongatus.*  **Main methods:** Mechanistic modeling of photon absorption and self-shading addresses modeling light as a metabolite. apply to any phototrophic GEM.  **Model type:** Coupling of strong experimental support and photoautotrophic modeling methods by making improvements to the accuracy of the model through GEM predictions of gene essentiality. resulted in a highly accurate model of S. elongatus metabolism that highlights previously unknown areas of S. elongatus biology. Of 2,723 genes in the *S. elongatus* genome, 785 (29%) were included in the final version of the model, and 118 of these genes (15%) had updated functional annotations.  **Importance of this paper:**  Importance of this paper develop a GEM of metabolism in *S. elongatus* using random barcode transposon site sequencing (RB-TnSeq) essential gene and physiological data specific to photoautotrophic metabolism. The model A metabolic model of cyanobacterium, Synechococcus elongatus PCC 7942, was created, and the accuracy of the model is very high. This mean model of S. elongatus metabolism that highlights previously unknown areas. The model explicitly describes photon absorption and accounts for shading, resulting in the characteristic linear growth curve of photoautotrophs. In method part, the metabolic reconstruction was assembled using an established protocol, and biomass-normalized photon absorption rate for a given wavelength range was calculated from the combination of irradiance, optical absorption cross-section, and the chlorophyll a component of the biomass equation. The future addition of omic datasets to the model will both greatly improve in silico representation of S. elongatus metabolism and identify additional biological unknowns. | |