

# SYSTEMS BIOLOGY OF OXYGENIC PHOTOSYNTHESIS

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## a. Background:

Natural photosynthesis will play a key role in the future supply of feed, food and energy for mankind. This is not only because this process is a source of inspiration in the development of photocatalytic nanodevices, but also because growth of phototrophic organisms directly yields a variety of feed-, food- and energy products. Particularly because of the latter, it is important that oxygenic photosynthesis proceeds with maximal efficiency. However, whereas its intrinsic maximal efficiency is already rather low [1], the oscillatory nature (with 24 hr and shorter rhythms) at which sunlight is available, further lowers the actual efficiency, often to well below 1 % of the incoming amount of radiation energy, even for the best food and energy crops.

The low actual efficiency is due to various mechanisms of energy dissipation, many of which, however, have their origin in the thylakoid membrane, like the photochemical and non-photochemical quenching of incoming excitons. Significantly, the methodology of synthetic biology offers exciting prospects to increase photosynthetic efficiency to values close to the theoretical maximum.

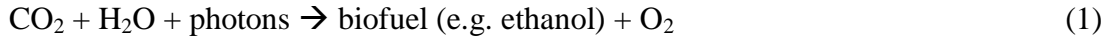
## b. Objective:

Multi-scale modeling of structural-, energetic-, metabolic-, regulatory- and gene-expression aspects of the integrated network that catalyzes conversion of CO<sub>2</sub> and light into bioenergy. The most suitable system to tackle first for this modeling is a cyanobacterium which functions as a catalyst in the direct production of biofuel [2]. Nevertheless, the majority of the knowledge to be generated will be applicable broadly in the entire domain of oxygenic photosynthesis, including the major food crops.

## c. Approach:

The first goal is to set up a physics- and chemistry-based systems biology description of photosynthetic energy transduction in the thylakoid membranes of *Synechocystis sp.* PCC6803 that next will be combined with an overall metabolic network model of the organism. As a starting point related models from anoxygenic photosynthesis can be used [3, 4]. The evolving model will form the basis of a general engineering platform for solar energy to biofuel conversion. For this it will be necessary to integrate (i) the gene-regulatory and physiological networks, which will be resolved in more detail with “omics” analyses, and (ii) the morphogenetic regulation, to be derived by dynamic structure-spectroscopy of the thylakoid system based on functional imaging analysis, into an overall model of cell function. A significant amount of the required data is already available in the literature; more data will become available through the FES-supported program on 'Towards BioSolar Cells'.

Application of the methods of synthetic biology has already produced several variants of *Synechocystis* PCC6803 that accumulate significant quantities of bio-fuel. Nevertheless, to maximize such a production rate to the extent that the cyanobacterial cell can be considered a catalyst for the reaction:



will require more work that can only be carried out successfully in parallel with systems understanding of the engineered organism. Nevertheless, this approach is crucial because it will rationalize and simplify all basic considerations concerning photosynthetic efficiency. In addition, it will allow reliable prediction of scale-up conditions.

In conclusion, it will be important to focus on multi-scale modeling of the direct metabolic conversion of solar energy into biofuel, based on the dynamic structure/spectroscopy of the thylakoid system, and its regulation by environmental factors and on high-throughput assays of the omics characteristics of the organism. This “physical systems biology model” will be constrained by dynamic boundary conditions, both during primary growth for the realization of maximum photosynthetic capacity for biomass formation, and during the production phase, when the organism is converting solar energy directly into biofuel.

For this we will develop methodologies to integrate multiple kinds of omics data with the help of quantitative mechanistic models with biologically meaningful parameters. This approach will be partially based on the global- and target analysis methods, developed to identify and characterize the dynamics of pigment-protein complexes. For aspects of the networks in which stochastic fluctuations make a significant impact on the outcome of the modelling, Green's Function Reaction Dynamics will be used to describe the relevant subsystem(s). Length of the elementary time steps for the multi-scale modelling is dictated by the circadian regime imposed upon central metabolism.

d. Expected results:

- Mathematical simulation of the integration of an energy-dissipation/conservation network and the underlying morphogenetic processes of the thylakoid
- Functional integration of genomics data on the photosynthesis process, from the complexity level of a living organism to that of an (industrial) ecosystem
- Development of innovative methods for multi-scale modeling at all relevant length- and time-scales for cellular systems biology
- Functional integration of genomics photosynthesis data at the complexity level of an (industrial) ecosystem, including circadian oscillations
- A systems-biology model to guide further optimization of photo-fermentative chimeras for biofuel production

e. Proposed team:

Van Grondelle/Dekker/Van Stokkum: quantumphysics and bioenergetics

Hellingwerf/Teixeira de Mattos: molecular physiology and growth

Bruggeman/Teusink/Westerhoff: kinetic modeling and metabolic control analysis

Ten Wolde: Green's function reaction dynamics and biochemical network modeling and more...

f. References:

- 1] Zhu XG, Long SP and Ort DR (2008) *Curr Opin Biotech* **19**, 153-159
- 2] Hellingwerf KJ and Teixeira de Mattos MJ (2009) *J Biotechnol* **142**, 87-90
- 3] Sener MK, Olsen JD, Hunter CN and Schulten K (2007) *PNAS* **104**: 15723-15728
- 4] Klamt S, Grammel H, Straube R, Ghosh R, Gilles ED (2008) *Mol Syst Biol* **4**: 156