



Poster and slides

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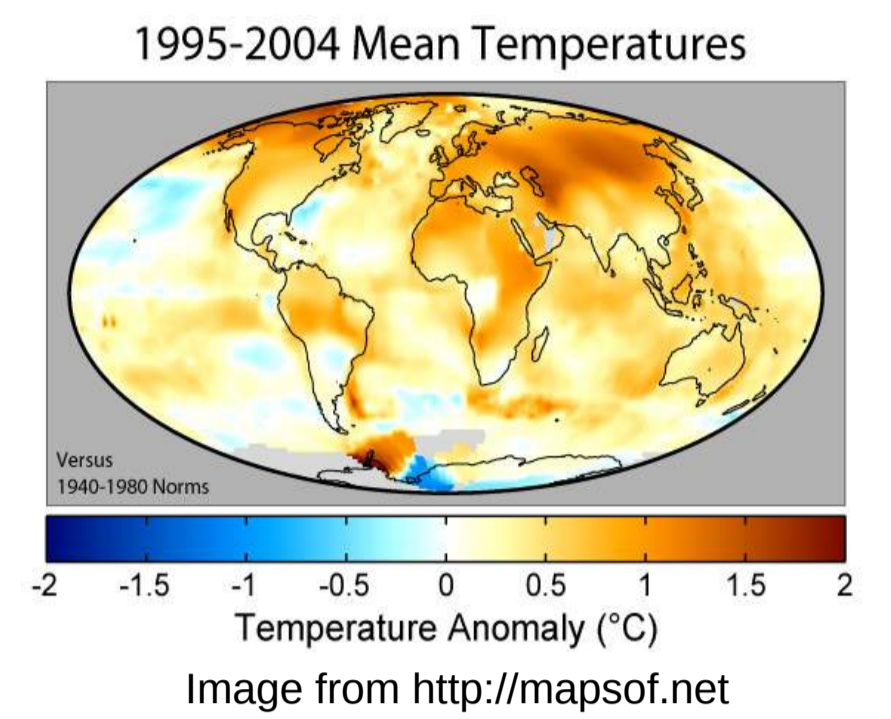
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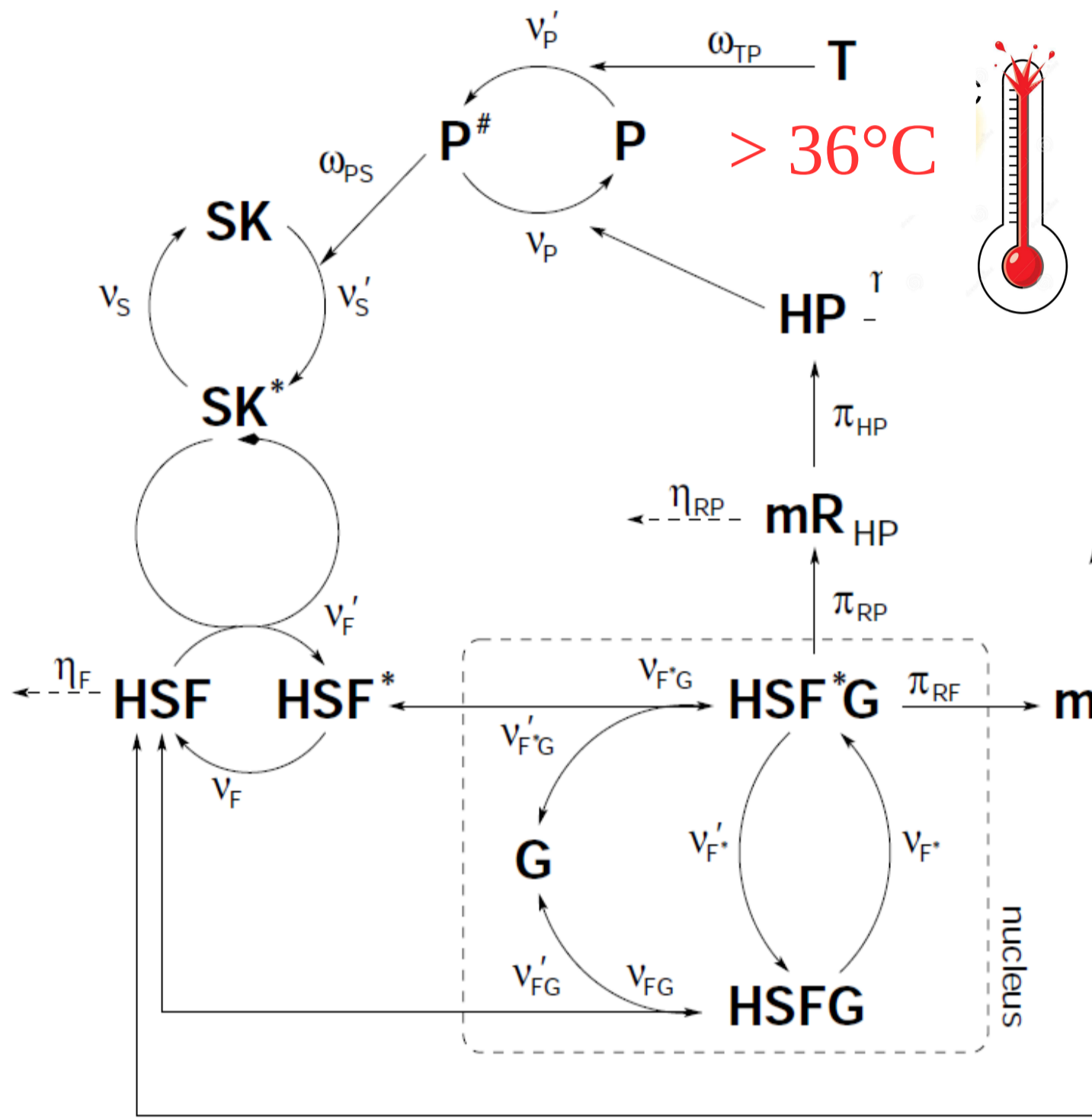


Introduction

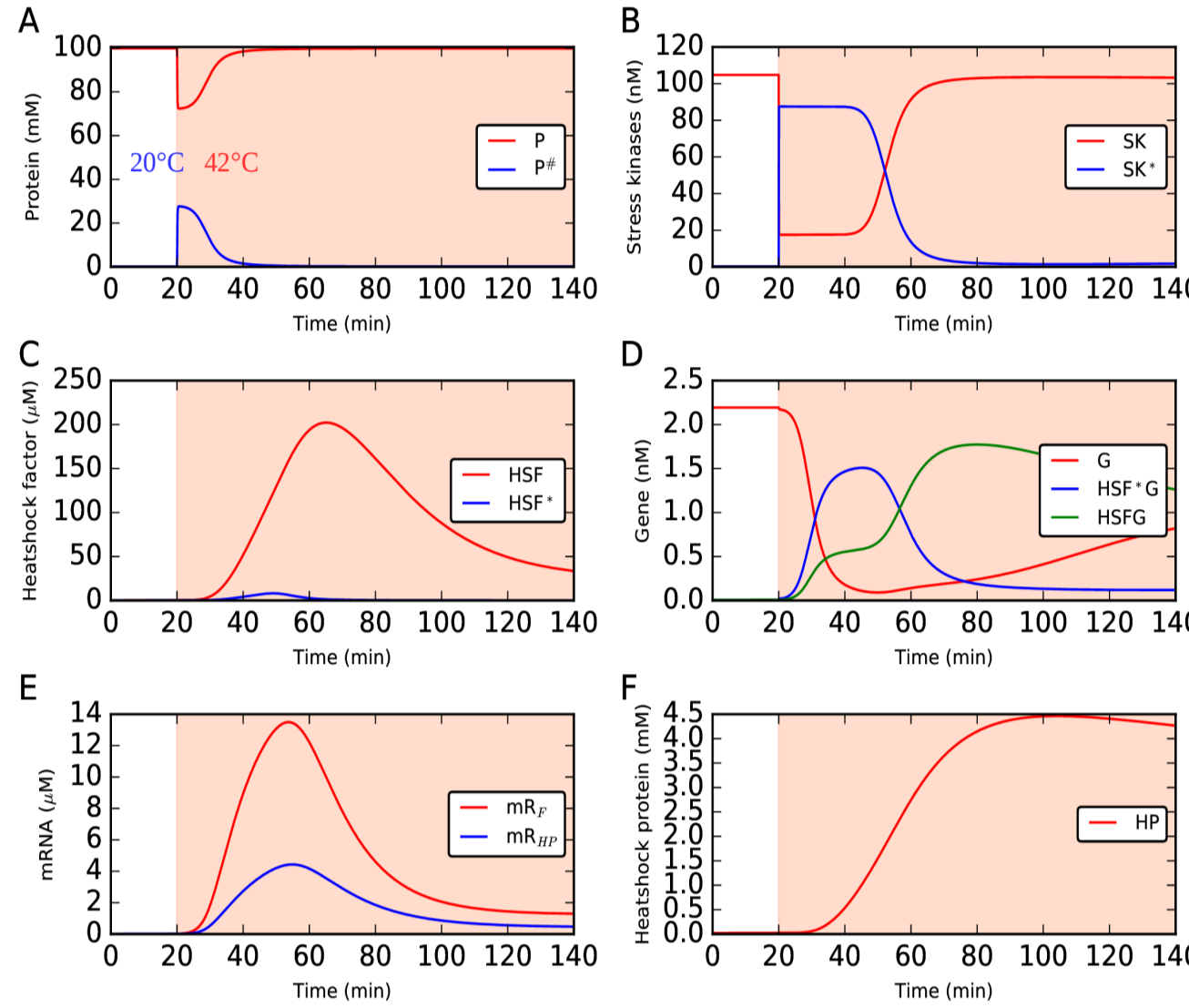
Organisms exposed to temperatures higher than usual can activate a heat shock response (HSR) allowing them to react to the new conditions. Due to global warming, crop plants will encounter more frequent heat waves which might reduce their crop yield [1]. We focus on *Chlamydomonas reinhardtii*, a well known model organism for green algae. Processes involved in the HSR are highly conserved among species, thus similar mechanisms might be at work in crop plants. Here we present the implementation of a data driven mathematical model for the HSR in *C. reinhardtii*, originally proposed by Ebenhöf and Skupin. The signalling network structure is based on the experimental results of [2], also used in addition to those of [3] for validation of the model. The model aims at capturing general features of the mechanism and allows to reproduce the qualitative behaviour of the above mentioned data. In *C. reinhardtii* the HSR can be elicited also by light, via a regulatory pathway independent from the one activated by temperature. We thus propose an extension of our model to include the description of this activation mechanism.



The dynamical model of the heat shock response (HSR)



Typical response to heat shock



Temperature increase unfolds proteins P. Degenerated proteins P[#] (concentrations in panel A) trigger the HSR. The stress kinase SK are activated, SK* (B), and in turn phosphorilate the heat shock factor HSF into HSF* (C). This binds to free gene loci G (D), activating the production of mRNA_F and mRNA_{HP} (E), which are translated into HSF and heat shock protein HP (F). The chaperone HP helps refolding P[#], switching off the response. ODEs are used to describe the time-evolution of concentrations. The reactions are modelled using mass action kinetics, a part from SK activation (Michaelis-Menten), HSF activation and the action of Temperature (Hill kinetics).

ODEs, mainly mass action kinetics

e.g.:

$$\frac{d[P^{\#}]}{dt} = -\nu_P + \nu'_P$$

$$\nu_P = k_P \cdot [P^{\#}] \cdot [HP] \quad \nu'_P = k'_P \cdot [P] \cdot \frac{T^n}{T_0^n + T^n}$$

Hill kinetics

$$P^{\#} + HP \rightarrow P + HP$$

$$P \rightarrow P^{\#}$$

$$\frac{d[SK^*]}{dt} = -\nu_S + \nu'_S$$

$$\nu_S = k_S \cdot [SK^*] \quad \nu'_S = k'_S \cdot [SK] \cdot \frac{[P^{\#}]^m}{K_D + [P^{\#}]^m}$$

Hill kinetics

$$SK^* \rightarrow SK$$

$$S + P^{\#} \rightarrow SK^* + P^{\#}$$

$$\frac{d[HSF^*]}{dt} = -\nu_F + \nu'_F + \nu'_{F*G} - \nu_{F*G}$$

$$\nu'_F = k'_{HSF} \cdot [HSF] \cdot \frac{[SK^*]}{1 + [SK^*]}$$

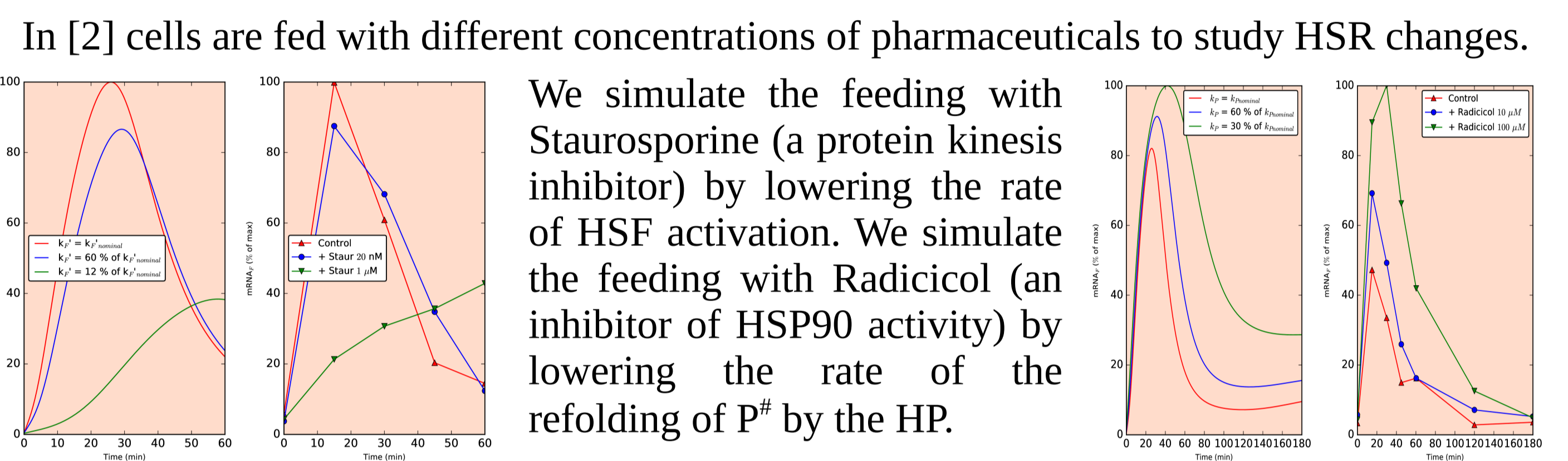
Michaelis-Menten

$$HSF + SK^* \rightarrow HSF^* + SK^* + \dots$$

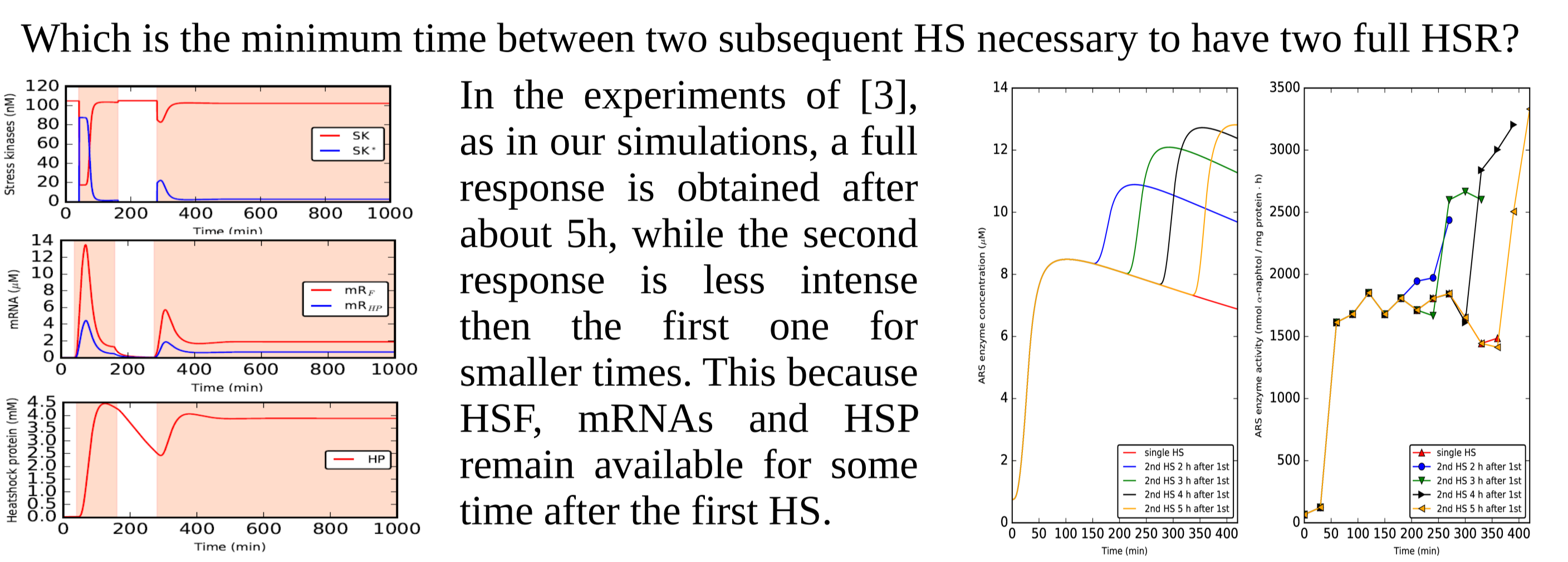
Comparison with experimental data: determination of the parameters' values and validation of the model

With a biologically reasonable, rough estimate of the parameters, the model is able to reproduce the qualitative behaviour of the heat shock responses observed in experiments. We next would like to split the data in two subsets, use one to obtain the parameters set which minimizes the least square distance from the data, and the other to validate the model.

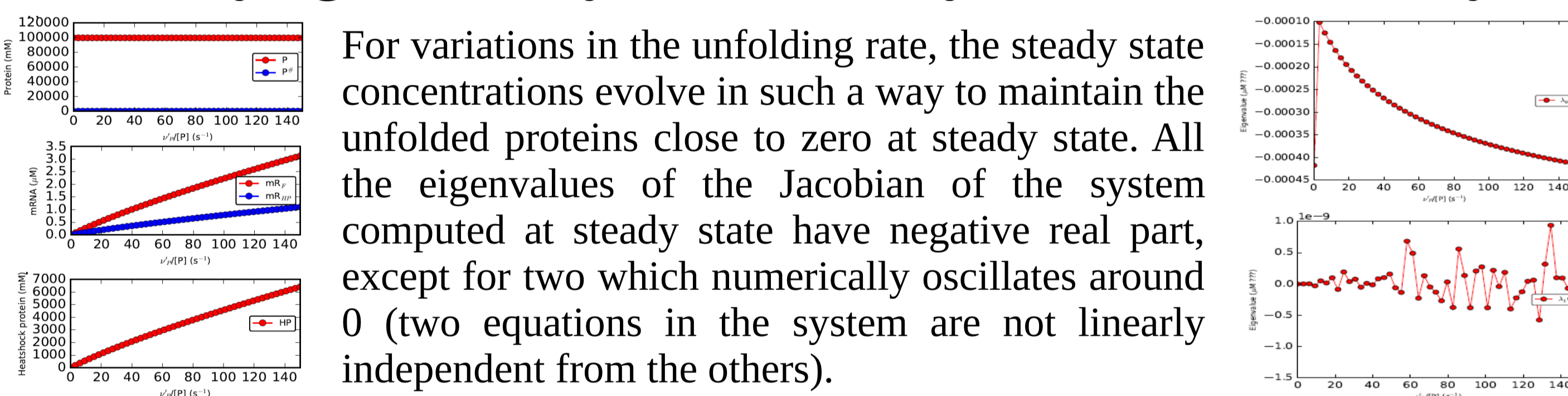
Experiments on feeding with pharmaceuticals (data from [2])



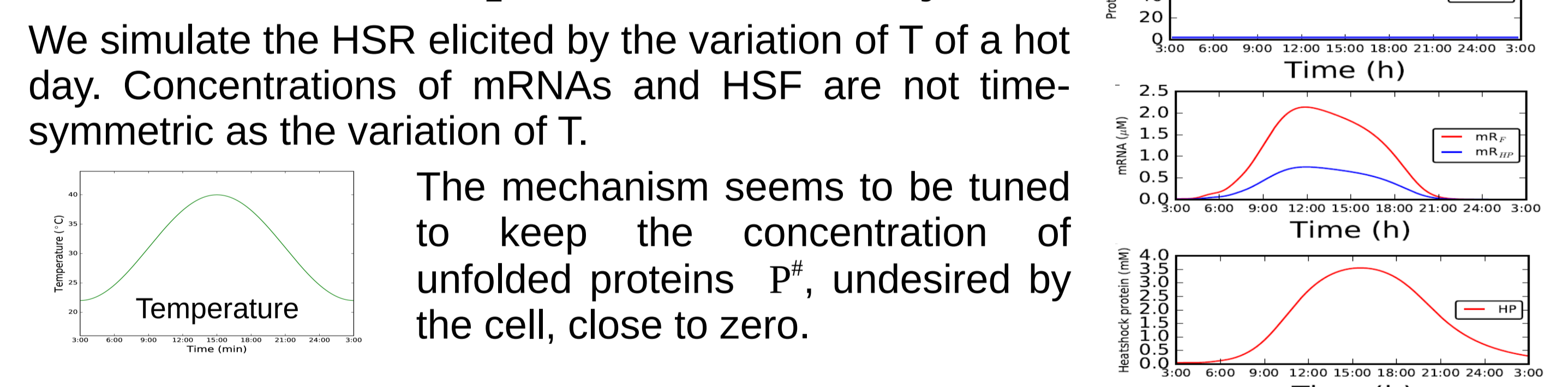
Experiments on double heat shock (data from [3])



Studying the steady state of the system and its stability



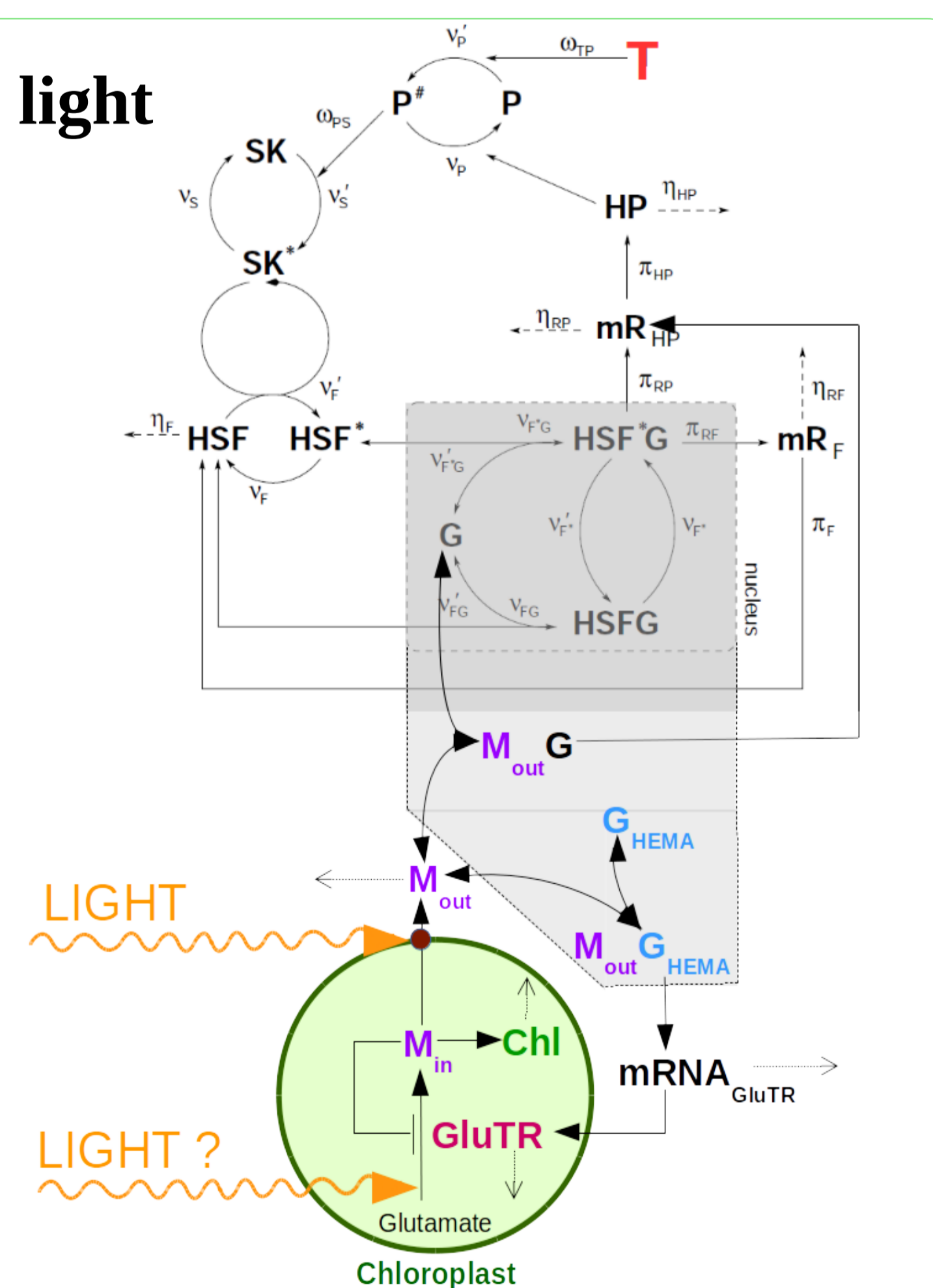
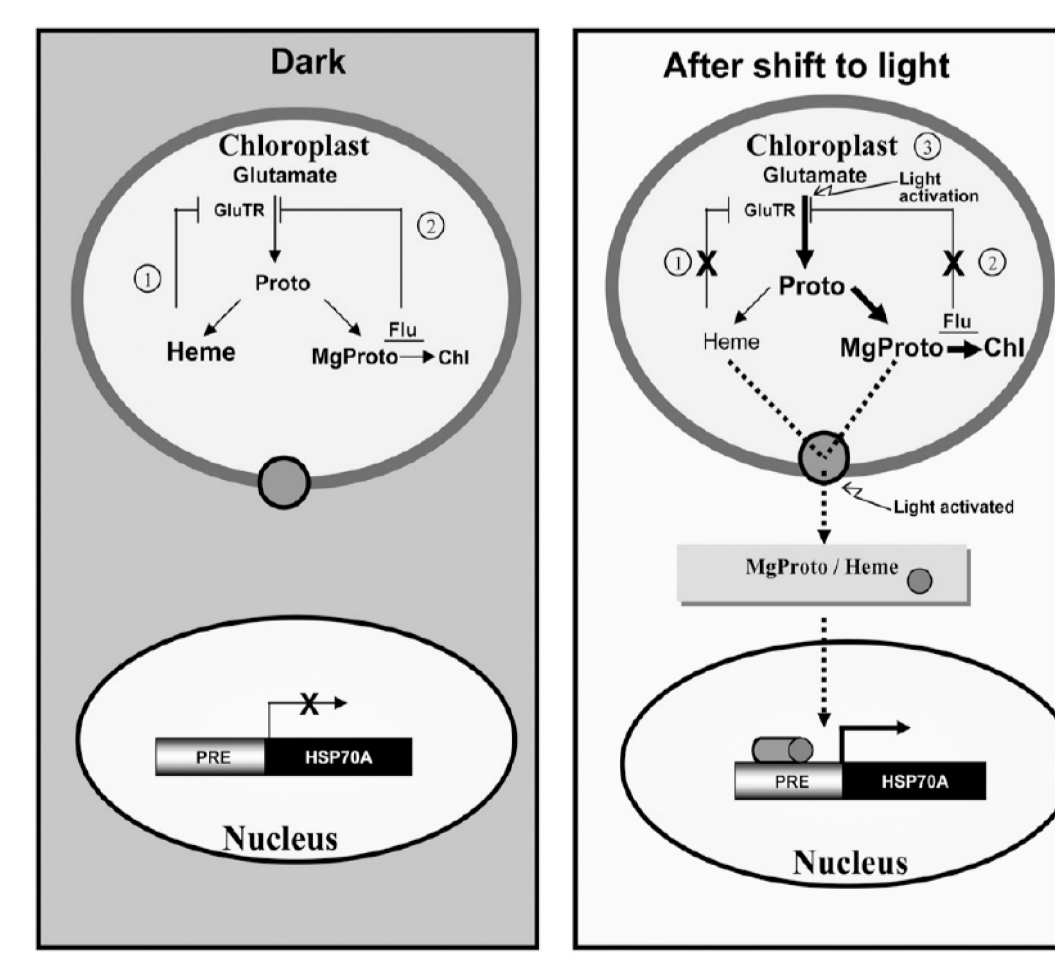
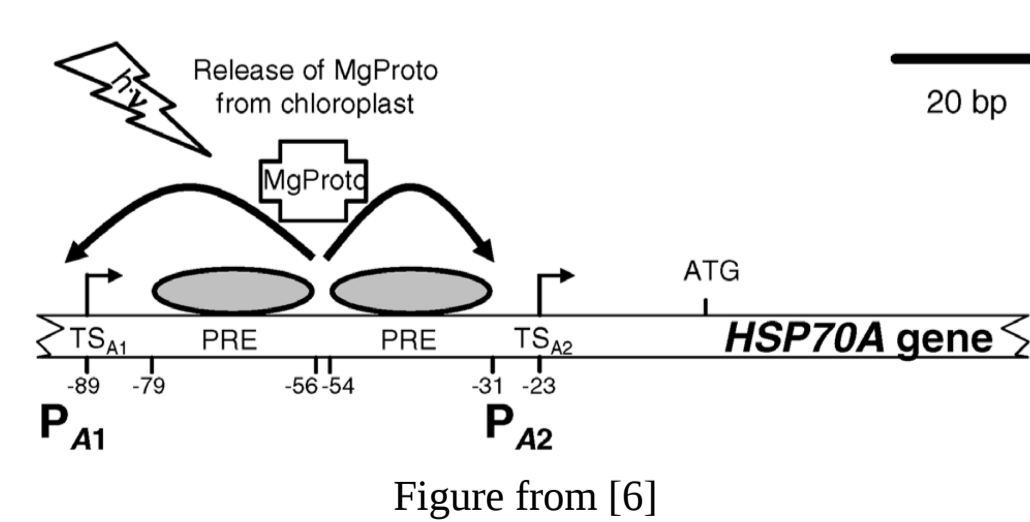
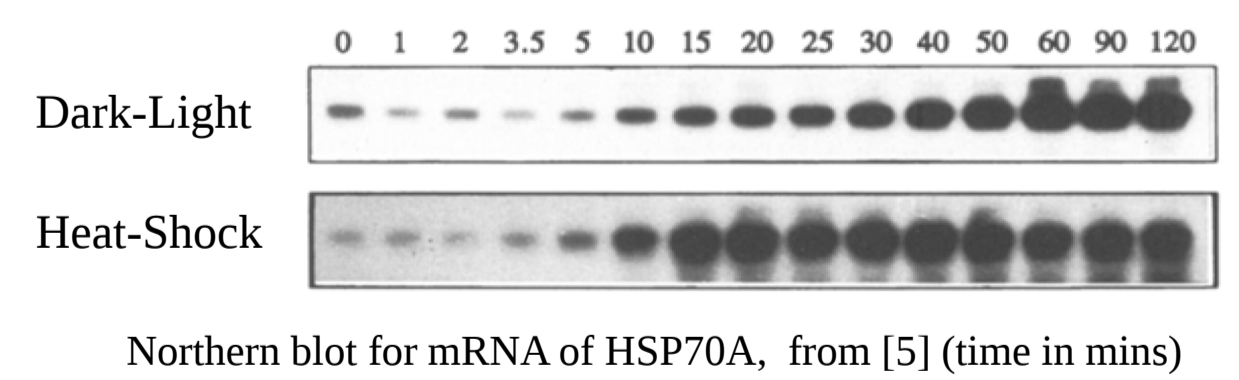
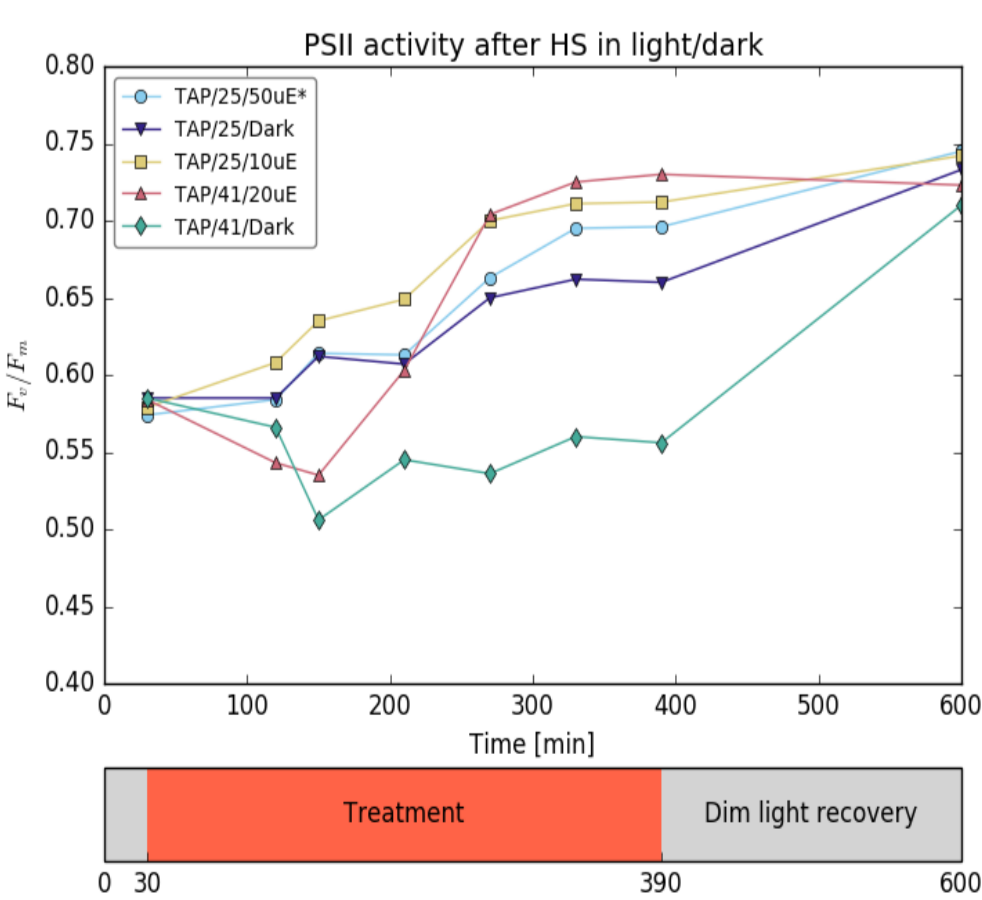
The heat shock response in a hot day



Proposing to extend the model to include activation of a heat shock response by shift from dark to light

Question: how does light control the activation of the HSP genes in *Chlamydomonas reinhardtii*?

- Preliminary Experiments: recovery from photo inhibition after different treatments.[§]
- Observation I: shift from dark to light can induce the expression of certain HSP genes [4].
- Observation II: the pathways regulating T induction and light induction of HSP70A gene are independent [5].
- Observation III: the HSP70A promoter region has transcription sites activated by HSF and MgProto [6].
- Observation IV: MgProto mediates the activation by light of the gene HSP70A [7].
- Observation V: MgProto is an intermediate in the biosynthesis of Chlorophyll.
- Observation VI: also the HEMA gene, necessary for the synthesis of Chlorophyll is activated by MgProto [8].



Bibliography

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Acknowledgements

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