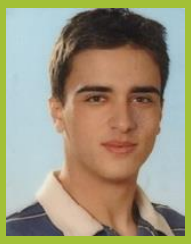
SCIENCESPRINGDAY

FACULDADE DE CIÊNCIAS E TECNOLOGIA
UNIVERSIDADE NOVA DE LISBOA

Chemistry Department

A Hybrid Systems Framework to Design Standard Biological Parts for Synthetic Biology: Application to *Pichia pastoris*

Systems Biology and Engineering Group



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2006 – 2009 – Bachelor in Molecular and Cell Biology
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Objectives

We aim to develop novel computational methodologies for synthetic biology based on hybrid systems theory and to apply these methodologies to improve the expression of heterologous proteins by *P. pastoris*. This general objective encompasses two other:

1 Development of efficient computational methods for the selection and design of target biological parts.
2 Apply the developed models in the optimization of the standard biological parts (SBP) sequence aiming at the maximization of a target biological function, validating experimentally the model, in *Pichia pastoris*.

Methodology

The computational tools that were used in this work are based on hybrid parametric-nonparametric models that join booth mechanistic and statistical models (Fig. 1). The chosen approach is to use DNA descriptors that accurately quantify specific features of each biologic part, and use them to predict their strength (either protein/mRNA production rate or regulatory influence). We used a multilinear and machine learning framework which was applied to a previously developed thermodynamic model (Salis *et al.*). In this case, we used a parallel hybrid modeling framework wherein a mechanistic models runs in tandem with a statistical model to improve the prediction accuracy of the protein synthesis rate from the respective RBS DNA sequence.

Expected Results

We aim to develop models that establish new approaches to design SBP or that improve the current methods capabilities. The starting point is a free Gibbs energy based model for the *E. coli* RBS design (Salis *et al.* – Fig. 2). So far we have implemented this model, and applied an hybrid model (Fig. 1) and we achieved the following preliminary results (Fig. 3).

In the future we expect to expand this model for the *P. pastoris* translation initiation case-study. Afterwards we will develop other SBP models, and validate them experimentally in *P. pastoris*.

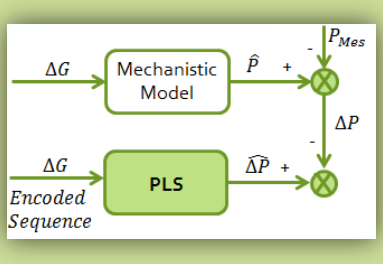

Fig. 1 – Parallel hybrid model used to improve the mechanistic model

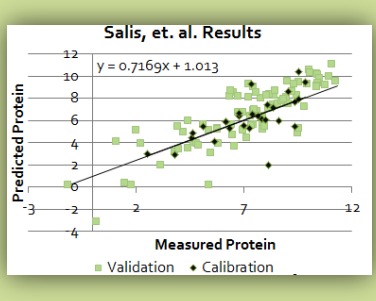

Fig. 2 - Protein measured and predicted by the mechanistic model (Salis *et al.*)

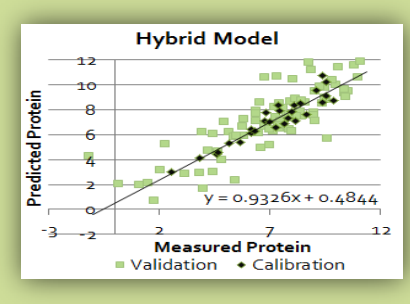

Fig. 3 – Protein measured and predicted by the hybrid model

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References: Salis, H.M. *et al.* Nat. Biotec., 2009. 27(10):946-950.