On Tuesday 25/11/2008, from 14:00 to 17:30, **Rof. Isabel Rocha** (Department of BioEngineering, University of Minho, Portugal) will give two seminars titled:

Modelling and Optimization of fed-batch fermentation processes

and

Metabolic Engineering strategies aided by Systems Biology

This two-part seminar (with a coffee break in between) will take place in the Seminar room of the Department of Electronics (Boulevard Dolez 31, 7000 Mons)

Abtract 1 : Modelling and Optimization of fed-batch fermentation processes

In addition to the considerable number of valuable products that have long been produced using fermentation techniques, such as recombinant proteins and antibiotics, biotechnology has been replacing traditional manufacturing processes in many areas that were until recently dominated by the chemical industry. When compared with conventional production methods, biotechnological processes have relatively low energy requirements and environmental costs, as well as decreased waste generation associated with the possibility of generating biodegradable products and of using renewable raw materials.
This new field of biotechnology, called Industrial or White Biotechnology can be therefore defined as the use of cells or enzymes for the production of commodity and specialty chemicals. The share of biotechnological processes in the production of various chemical processes is expected to raise from the current 5% to 20% already by 2010 [1]
In this new reality, rational fermentation optimization approaches gain a novel fundamental importance since, when compared with biopharmaceutical processes, the margins in industrial biotechnological processes are much lower and competitiveness depends more on product price than on patent protection. In fact, for such processes, an increase in productivity or efficiency can have a direct and strong impact in profitability.
However, those processes are typically very complex, involving different transport phenomena, microbial components and biochemical reactions. Furthermore, the nonlinear behavior and time-varying properties make bioreactors difficult to control with traditional techniques[2]. For these reasons, the application of model-based control and optimization strategies to biotechnological processes, as opposed to most of the remaining engineering fields is still not widely implemented.
For that purpose there is the need to consider reliable quantitative mathematical models, capable of describing the process dynamics and the interrelation among relevant variables. Additionally, robust optimization techniques must deal with the model's complexity, the environment constraints and the inherent noise of the experimental process.
The optimization of these processes is traditionally handled by analytical and numerical methods, whose results degrade when the complexity of the problem increases. A different approach comes from the use of general purpose optimization algorithms taken from the field of Evolutionary Computation (EC). Evolutionary Algorithms (EAs) are suitable to the optimization of a number of the fermentation process parameters,

namely the initial values of relevant state variables, the trajectory of controlled variables over time and even the duration of the process[3,4].

In this talk, the optimization of bioprocesses will be covered, focusing on the construction of mathematical models of fed-batch fermentation processes and on the application of evolutionary algorithms to determine the best feeding policy for the maximization of a desired product.

1 Hatti-Kaul,R. *et al.* (2007) Industrial biotechnology for the production of bio-based chemicals - a cradle-to-grave perspective. *Trends in Biotechnology* 25, 119-124

2 Bastin,G. and Dochain,D. (1990) *On-line estimation and adaptive control of bioreactors*, Elsevier Science Publishers

3 Rocha, I. Model-based strategies for computer-aided operation of recombinant *E. coli* fermentation. 2003. Universidade do Minho.
Ref Type: Thesis/Dissertation

4 Rocha,M. *et al.* (2004) Evolutionary algorithms for optimal control in fed-batch fermentation processes. *Applications of Evolutionary Computing* 3005, 84-93

Abstract 2: Metabolic Engineering strategies aided by Systems Biology

The Systems Biology approach has been replacing the reductionist view that dominated biology research in the last decades. The ultimate aim of such an approach is to develop computational models so that the response of biological complex systems to any kind of perturbation can be predicted, aiding efforts related with drug discovery, biotechnological process optimization and metabolic engineering.

In metabolic engineering problems, due to the complexity of metabolic networks, it is often difficult to identify *a priori* which genetic manipulations will originate a given desired phenotype. Genome-scale metabolic models [1,2], available for several microorganisms, can be used to simulate the metabolic phenotype and therefore help the tasks of metabolic engineering. This simulation can be performed by calculating the fluxes through all metabolic reactions using techniques like the Flux Balance Analysis (FBA) [3] or the MOMA [4] approaches, among others.

Several approaches have been developed that use metabolic models to enable the identification of gene knockout strategies for obtaining improved phenotypes [5-7].

In this talk, the main efforts and difficulties in designing efficient cell factories will be covered, emphasizing on the process of re-constructing metabolic models from genomic information.

1 Patil,K.R. *et al.* (2004) Use of genome-scale microbial models for metabolic engineering. *Current Opinion in Biotechnology* 15, 1-6

2 Rocha,I. *et al.* (2008) Design and application of genome-scale reconstructed metabolic models. *Methods Mol. Biol.* 416, 409-431

3 Edwards,J.S. *et al.* (2002) Metabolic modelling of microbes: the flux-balance approach. *Environmental Microbiology* 4, 133-140

4 Segre,D. *et al.* (2002) Analysis of optimality in natural and perturbed metabolic networks. *Proceedings of the National Academy of Sciences of the United States of America* 99, 15112-15117

5 Burgard,A.P. *et al.* (2003) OptKnock: A bilevel programming framework for identifying gene knockout strategies for microbial strain optimization. *Biotechnology and Bioengineering* 84, 647-657

6 Patil,K.R. *et al.* (2005) Evolutionary programming as a platform for in silico metabolic engineering. *BMC Bioinformatics* 6

7 Rocha,M. *et al.* (2007) Evaluating simulated annealing algorithms in the optimization of bacterial strains. *Lecture Notes in Artificial Intelligence* 4874, 473-484

Prof. Isabel Rocha is an active researcher in the field of Systems Biology, Bioinformatics and Metabolic Engineering. She is Associate Professor in the Department of BioEngineering of the University of Minho (Braga) and takes an active part in the MIT Portugal teaching program on Computational Biosystems Sciences & Engineering, Leadership, BioTeams