The BioProcess Systems Engineering group (BioPSEg) @ The Institute for Biotechnology and Bioengineering

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BioPSEG is part of the Institute for Biotechnology and Bioengineering a R&D unit ("Laboratório Associado"), founded in October 2006 aiming to be a strategic infrastructure for the development of the Portuguese R&D and innovation policies in the areas of Biotechnology, Bioengineering, Biomaterials and Life, Biomedical and Agricultural Sciences.

IBB is a nation-wide Institution and a partnership of 5 research units based in university campuses located in the North (Braga and Vila Real), Centre (Lisboa) and South (Faro) of Portugal:

- Instituto de Biotecnologia e Química Fina at Instituto Superior Técnico, Lisbon
- Centro de Engenharia Biológica (CEB), Universidade do Minho, Braga
- Grupo de Investigação 3B´s-Biomateriais, Biodegradáveis e Biomiméticos, Universidade do Minho, Braga
- Centro de Genética e Biotecnologia (CGB), Universidade de Trás-os-Montes e Alto Douro, Vila Real
- Centro de Biomedicina Molecular e Estrutural (CBME), Universidade do Algarve, Faro
• The IBB contribution to the development of these cutting-edge and fast growing/moving topics relies on the integration of different scientific and technological subjects and competences of excellence, through 6 interdisciplinary Research Thrust Areas:
  
  – Biomolecular Science and Engineering
  – Genetics, Molecular and Cell Biology
  – Functional, Comparative and Evolution Genomics
  – Bioprocess and Biosystems Engineering
  – Biomaterials for Tissue Engineering and Regenerative Medicine
  – Catalysis and Reaction Engineering

• These research areas support the IBB activities focused on 4 Thematic Areas:
  
  – Industrial Biotechnology
  – Health Biotechnology
  – Agricultural Biotechnology
  – Environmental Biotechnology and Chemistry
BioPSEg is part of the Centre of Biological Engineering at the University of Minho. CEB is awarded as “Excellent” by FCT.

The BioPSE group carries out research in Computer-Aided Process Engineering applied to Biotechnological, Chemical, Biopharmaceutical & Environmental processes with particular emphasis on the following areas of activity:

- Systems Biology, Bioinformatics, and Metabolic Engineering
- Modelling, Monitoring, and Control of Bioprocesses
- Image Analysis and Chemometrics in Wastewater Treatment and Biotechnology
- Knowledge-Based Expert Systems in Supervision & Control
- Process Integration and Design for Pollution Prevention: Synthesis, Analysis and Optimization
- **Systems Biology of recombinant microorganisms**
  - The main purpose is to gain fundamental insight into the molecular mechanisms governing the main metabolic bottlenecks observed during the production of heterologous protein with *E. coli* and use this information to identify strategies for how these processes can be eliminated.
  - This approach involves the use of genome-scale analysis of the transcriptome, proteome, and fluxome.

- **In Silico Metabolic Engineering Platforms**
  - New algorithms are being developed by using genome-scale metabolic models that enable identification of gene knockout strategies for obtaining improved phenotypes.
  - As the problem of finding optimal gene deletion strategy is combinatorial, new faster algorithms are being developed to accomplish this task.

- **Mathematical and Computational Tools for Large-Scale Microbial Modelling**
  - New representation schemes are being used for the generation of simulated high-throughput data that is then systematically compared with experimental results on different types of “omics” for model optimization.
• Software-Sensors for on-line estimation of kinetic parameters and state variables
  – Algorithms are designed for estimating on-line kinetic parameters, like specific growth rates, in bioprocesses. The tuning problem of observer-based estimators is one of the main issues

• Adaptive Control of Fermentation Processes
  – Model-based adaptive linearizing control laws are derived for the regulation of substrates/products during the fed-batch fermentations
  – Applications: recombinant proteins production in high cell density culture of *E. coli* growing on glucose; baker's yeast production

• Experiment design for bioprocess modelling
  – Optimal experimental design for yield coefficients estimation in an unstructured growth model of fed-batch fermentation of *E. coli* is being pursued
  – Feed profiles are designed by optimisation of a scalar function based on the Fischer Information Matrix
• Activated Sludge in Wastewater Treatment Processes:
  – Monitoring of Activated Sludge using IA (correlation with settleability, SVI). Data from morphological sludge characterization using image processing is treated using PLS

• Protozoa in Wastewater Treatment Processes:
  – IA is being used in automatic recognition of protozoa and metazoa populations in conjunction with multivariate statistical techniques as Discriminant Analyses and PCA

• Anaerobic Digestion:
  – IA to characterize granular anaerobic sludge from EGSB Reactors fed with oleic acid. IA allows for automatic detection of granules disintegration constituting a tool to recognize anaerobic granulation time
Other Applications in Biotechnology and Food Technology:

- Classification of *Saccharomyces cerevisiae* morphology using image analysis
- Morphological Analysis of *Yarrowia lipolytica* under Stress Conditions through Image Processing
- Automatic counting of viable/non-viable yeasts by epifluorescence microscopy with acridine orange as dying agent
- Characterization of bubbles in a bubble column by image analysis
- Simultaneous monitoring of lactic acid bacteria and yeast during Vinho Verde fermentation using phase contrast microscopy coupled to image analysis
Expert systems for wastewater treatment plants:

- Supervisory expert system based on fuzzy logic rules are under development for the diagnosis and the control of a high rate lab-scale wastewater treatment plant used for organic matter and nitrogen removal.

- Artificial Neural Network and Neural Fuzzy models (Adaptive Neural Fuzzy Inference System - ANFIS) are being used for monitoring and prediction of biological wastewater treatment systems.
• Educational tools for pollution prevention through process design and process integration:
  – The Solver feature of the Excel® spreadsheet is being used for the optimization of several chemical engineering systems, ranging from pollution prevention problems to mass-exchange networks.

• Semi-Infinite Programming in Air Pollution Control problems:
  – Keeping pollution level in a given region below a given threshold; computing the maximum pollution level in a given region; and air pollution abatement are the kind of problems being solved with SIP approaches.

• Strategies for Waste Minimization in Process Synthesis:
  – Evaluation of different optimization methods in solving pollution prevention and control problems
Team

- 15 people: 6 PhD, 6 PhD students, 3 research assistants
Main Equipment – Fementation Lab

- 2 Fermenters full equipped with instrumentation and computer control
- *Flow-Injection Analysis* (acetate and glucose)
- Mass spectrometer (residual gas analysis)
- NIR spectrophotometer
- 2D Electrophorese
- GC-MS
- HPLC, ...
Wastewater Treatment Lab – Main Equipment

• Aerobic and Anaerobic reactors full equipped with instrumentation and computer control
• Sequential Injection Analyser (NH$_4^+$, NO$_3^-$)
• Multiparameter UV & NIR probes
• YSI Respirometer
Image Analysis Lab – Main Equipment

- 1 vertical confocal microscope OLYMPUS FLUOVIEW1000
- 3 epifluorescent microscope OLYMPUS BX51w/ OLYMPUS DP 71 camara, Zeiss Axiscop, Leitz.
- 1 stereosce microscope OLYMPUS SZ 4045TR-CTV
- 1 inverted microscope Nikon Diaphot 300
- Video camaras: SONY 3CCD DXC-9100P; SONY CCD AVC D5CE,
- Digital camaras: ZEISS AxioCam HRc, OLYMPUS DP 71
- Frame Grabbers: DT3155 (Data Translation, Inc.), DT2851 (Data Translation, Inc.), Matrox Meteror
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