

SYSTEMS BIOLOGY – Prof. Pasquale Palumbo
Laurea Magistralis Degree in Mathematical Engineering (6 CFU)
University of Aquila – Academic Year 2010/2011

Systems biology is an emerging research area, which aims to provide mathematical models helping to understand the dynamic interactions occurring within and between cells. This course gives the mathematical tools to model, analyze and identify gene transcription networks dealing with most important network motifs. The case study of the cell cycle is also investigated in details.

Detailed program.

- **Transcription networks [1].** *The rules of transcription:* promoters and transcriptor factors, activators and repressors. *Graph properties of a transcription network:* in/out degree distribution, clustering coefficients and modularity, scale-free distributions and hubs. *ODE approach:* modeling the clearance and production rate, Hill functions and logic input functions, dynamics of gene regulation. *Network motifs* emerging by comparison to randomized networks: negative/positive autoregulation, coherent/incoherent Feed-Forward Loops (FFL), Single-Input-Modules (SIM), Multi-Output Feed-Forward Loops (MO-FFL), bi-fan, diamonds, Dense-Overlapping-Regulons (DOR). *Possible functions of network motifs in transcription networks:* speed up of the response time, increase robustness, produce oscillations, introduce sign-sensitive delays, generate pulses or temporal programs of expression. *Biological examples from the E. Coli:* the arabinose system, the lactose system, the galactose system; temporal programs and assembly steps of the flagella motor.
- **Mathematical tools to identify gene networks [2,3,4].** *State observers* for linear and nonlinear systems. The Ackerman formula. Asymptotic observers: the Luenberger observer. Applications to gene transcription networks: a case study on the FFL.
- **Growth and cell cycle models [5,6,7,8].** *Models of the cell growth:* the case of eukaryotic cells. Cell cycle models: balanced exponential growth. Modelling the cell cycle of the budding yeast *Saccharomyces cerevisiae*: asymmetrical division. Age and protein distribution functions for daughter and parent cells.

References:

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- [3] F. Cacace, A. Germani, P. Palumbo, “Observer-based identification of a Multi-Output Feedforward Loop from gene expression data”, *Proc. 48th IEEE Conference on Decision and Control (CDC09)*, pp.3507–3512, Shanghai, China, 2009
- [4] L. Farina, A. Germani, G. Mavelli, P. Palumbo, “Identification of regulatory network motifs from gene expression data”, *J. Math. Model. Algor.*, Vol.9, pp.233–245, 2010.
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- [6] L.H. Hartwell, M.W. Unger, “Unequal division in *Saccharomyces cerevisiae* and its implications for the control of cell division”, *The Journal of Cell Biology*, Vol.75, pp.422–435, 1977.
- [7] M. Vanoni, M. Vai, L. Popolo, L. Alberghina, “Structural heterogeneity in populations of the budding yeast *Saccharomyces cerevisiae*”, *J. Bacteriol.*, Vol.156, No.3, pp.1282–1291, 1983.
- [8] L. Mariani, E. Martegani, L. Alberghina, “Yeast population models for monitoring and control of biotechnical processes”, *IEE Proceedings*, Vol.133, No.5, pp.210–216, 1986.