Emergent Models in Complex System Simulations of Genetic and Biochemical Networks

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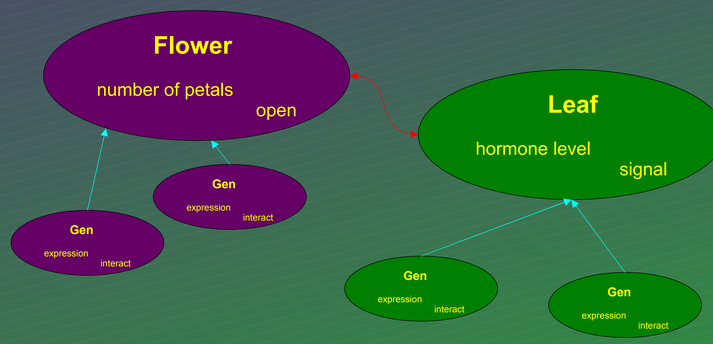
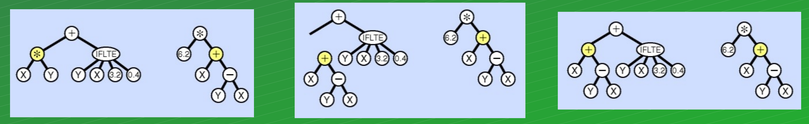
We are exploring simulation methods for complex systems consisting of many interacting entities. A high level architecture for a software environment to simulate complex systems is proposed[3]. The simulation environment mimics a complex system's processes and structure by modeling it as interacting and concurrently executing software agents and processes. These agents and processes exist at various hierarchical levels. Properties and behavior of agents at each level depend on those on a lower level, and mechanisms modeling the emergence of higher level properties and behavior from lower level properties and behavior are studied. As an example of such mechanisms, genetic programming algorithms can discover macro-level emergent models from micro-level properties and behavior. These algorithms can also be applied to the inverse problem of deriving micro-level models from known macro-level behavior. Applications in computational molecular biology include on the one hand discovering macro-level gene expression patterns and behavior from micro-level genetic and biochemical networks, and on the other hand reverse engineering micro-level interactions in these networks from macro-level observed gene expression and phenotype data.



A plant is a complex system composed of organs, in turn determined by genes

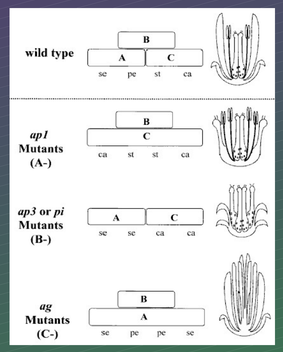


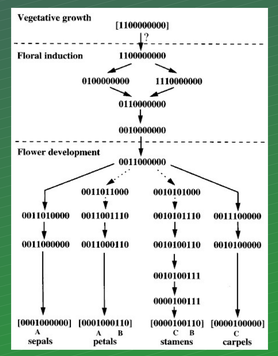
Genetic programming looks for an optimal function, for example using the crossover operation[4]

Macro-level properties and behavior

Observe

Derive: genetic programming with functions describing chemical reactions[5]

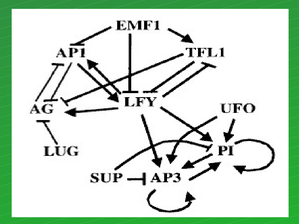




Phenotype and gene expression in wild-type and mutant flowering of Arabidopsis thaliana according to the ABC model[6]

Derive: genetic programming with functions describing macro-level patterns[3]

Simulate



Micro-level properties and behavior

Biochemical or genetic network[6]

Interactions between micro- and macro-levels[3]

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[3] Stolk H., Gates K., Hanan J. 2003. *Discovery of Emergent Natural Laws by Hierarchical Multi-Agent Systems*. The 2003 IEEE/WIC International Conference on Intelligent Agent Technology, Halifax, Canada.
[4] Luke, S. 2003. *ECJ 9: A Java-based Evolutionary Computation and Genetic Programming Research System.* http://www.cs.umd.edu/projects/plus/ec/ecj/, Internet.
[5] Koza J.R., Mydlowec W., Lanza G., Yu J., Keane M.A. 2000. *Reverse Engineering and Automatic Synthesis of Metabolic Pathways from Observed Data using Genetic Programming*. Stanford Medical Informatics Technical Report SMI-2000-0851.
[6] Mendoza L., Thieffry D., Alvarez-Buylla E.R. 1999. *Genetic Control of Flower Morphogenesis in Arabidopsis Thaliana: A Logical Analysis*. Bioinformatics, vol. 15, p. 593-606.