

Modular Modeling of an Artificial Organ System

By John LaRocco

Summary

Current synthetic biology research is focused on the molecular level, but viable artificial organs require a systematic framework for integration, sustenance, and coordination [1] [2]. While synthetic microbiology and tissue engineering are fundamental components, a higher level view of integration is often non-existent in the literature [2] [3].

A relevant research field is the development of closed-loop combinations of neural tissue and robotics, such as animats and hybrotts [4]. As such, a proposed framework for a simple, modular synthetic organism will be evaluated. A closed-loop circulatory system would be used to sustain a “brain” via homeostatic maintenance of a balance of essential nutrients and waste removal. The modular “brains” used would include a cultured neural network [5], a simulated neural network [6], and a hybrid system using a sealed neuronal culture [4]. Research would be initially conducted by simulation and then experimentally.

The implications of the system may be applicable to a number of fields, including hybrotts [4], artificial organ design [2], synthetic biology [7], artificial life [8], and automated control systems [9]. While similar simulations have been previously performed [10] [4], none have examined an entire synthetic organ system in the context of modular nodes.

Goals

The initial goals of this research would be to design a mathematical model, a simulation based upon the model, and then a physical system based upon the simulation. The end product should be a model and system with ease of assembly and use, as well as the potential to regulate the desired characteristics of an artificial organ attached to it. The development of an API for such a system and supporting documentation would be a longer term goal.

Methods

The proposed model would be based upon a simple isolated brain scenario, with a set of artificial organs in series along a closed-loop artificial circulatory system [11] [12]. Different parameters for the number of modules may be included, but minimally a “brain,” a source of nutrition, and a filtration system for removing metabolic waste products in series around a closed loop should be included [13]. The theoretical model would be based upon metabolically-inspired control systems [5][14] [15] [16] [17] [18]. In addition, although other software can be used for the initial implementation of the system, the development of an Arduino-based implementation and supporting documentation would be a longer term goal.

Intellectual Merit

An important gap within the literature would be closed regarding the development of a modular synthetic organism. The system would be designed to test methods for integrating and controlling artificial organs. At the very least, the system would propose an adaptive facsimile of the circulatory system and the regulation of flow rates. The modular design would enable other types of artificial organs to be added, allowing more complex artificial organ systems, and potentially even a synthetic organism, to be developed [1] [19] [20].

Broader Implications

While artificial organ systems would be the primary field to benefit from this project, the modular

approach and system could be adapted for a number of other processes, from educational toys to industrial processes. Complex industrial processes could be regulated in a manner approximating metabolism, allowing for more efficient autonomous control of bioreactors and other systems [14] [15] [16] [17] [18]. By having open documentation and making use of available hardware such as an Arduino, the barriers to entry and adoption would be greatly lowered.

Future Funding

Immediate potential for commercialization exists for research, industry, education, and even recreation. Kits could be used to test the capabilities of artificial organs or regulation of industrial processes. Educational and scientific toys including sets of “starter modules” could be sold to schools and universities. For example, the development of simulated models on Arduino could be a starting point. The ability to make simple organic systems modular could greatly accelerate development by lowering the barriers to entry. Furthermore, the resources required from this research are readily available in many existing labs, potentially lowering the initial cost.

Bibliography

- [1] K. Eng, A. Babler, U. Bernardet, M. Blanchard, A. Briska, J. Conradt, M. Costa, T. Delbruck, R. Douglas, K. Hepp, D. Klein, J. Manzolli, M. Mintz, T. Netter, F. Roth, U. Rutishauser, K. Wassermann, A. Whatley, A. Wittmann and R. Wyss, "Ada: constructing a synthetic organism," *Proceedings from the IEEE/RSJ International Conference on Intelligent Robots and Systems*, vol. 2, pp. 1808-1813, 2002.
- [2] G. Catapano, "Artificial organs design: Towards the integration of disciplines," *Proceedings from the Middle East Conference on Biomedical Engineering*, pp. 185-187, 2011.
- [3] K. Iniewski, "Building Interfaces to Developing Cells and Organisms: From Cyborg Beetles to Synthetic Biology," in *CMOS Biomicrosystems: Where Electronics Meet Biology*, Wiley-IEEE Press, 2011, p. 325–354.
- [4] S. Potter, A. El Hady and E. Fetz, "Closed-loop neuroscience and neuroengineering," *Front Neural Circuits*, vol. 8, p. 115, 2014.
- [5] N. Sharkey and T. Ziemke, "A Consideration of the Biological and Psychological Foundations of Autonomous Robotics," *Connection Science*, vol. 10, no. 3-4, pp. 361-391, 1998.
- [6] C. Insaurralde, "Artificial Homeostasis for Engineering Systems: Involuntary Reflexes in Physiologically-Inspired Control Applications," *Proceedings from the Annual IEEE International Conference on Systems, Man, and Cybernetics*, pp. 4831-4836, 2013.
- [7] D. Ackley, "Bespoke Physics for Living Technology," *Artificial Life*, vol. 19, no. 3-4, pp. 347-364, 2013.
- [8] T. Demarse, D. Wagenaar, A. Blau and S. Potter, "Neurally controlled computer-simulated animals: a new tool for studying learning and memory in vitro," *Society for Neuroscience Annual Meeting*, 2000.
- [9] R. Humza, O. Scholz, M. Mokhtar, J. Timmis and A. Tyrrell, "Towards Energy Homeostasis in an Autonomous Self-Reconfigurable Modular Robotic Organism," *Proceedings from Computation World: Future Computing, Service Computation, Cognitive, Adaptive, Content, Patterns*, pp. 21-26, 2009.
- [10] S. Potter and T. DeMarse, "A new approach to neural cell culture for long-term studies," *Journal of Neuroscience Methods*, vol. 110, no. 1-2, 2001.

- [11] R. White, M. Albin, J. Verdura and G. Locke, "The isolated monkey brain: operative preparation and design of support systems.," *J Neurosurg*, pp. 27:216-225, 1967.
- [12] R. White, M. Albin, D. Yashon, J. Verdura, J. Austin, P. J. Austin and Y. Demian, "Autoregulation in the isolated brain during profound hypothermia and hypercarbia.," *Brain and Blood Flow*, p. 209, 1970.
- [13] R. White, L. Wolin, L. Massopust, N. Taslitz and J. Verdura, "Primate cephalic transplantation: neurogenic separation, vascular association.," *Transplantation Proceedings* , pp. 3:602-604, 1971.
- [14] C. Gunay and A. Prinz, "Finding sensors for homeostasis of biological neuronal networks using artificial neural networks," *Proceedings from the International Joint Conference on Neural Networks*, pp. 1025-1032, 2009.
- [15] J. Kodjabachian and J. A. Meyer, " Evolution and Development of Modular Control Architectures for 1D Locomotion in Six-legged Animats," *Connection Science*, vol. 10, no. 3-4, pp. 211-237, 1998.
- [16] R. Muioli, P. Vargas and P. Husbands, "A multiple hormone approach to the homeostatic control of conflicting behaviours in an autonomous mobile robot," *Proceedings from the Annual IEEE Congress on Evolutionary Computation*, pp. 47-54, 2009.
- [17] M. Mokhtar, J. Timmis, A. Tyrrell and R. Bi, "An Artificial Lymph Node Architecture for Homeostasis in Collective Robotic Systems," *Proceedings from the Annual IEEE International Conference on Self-Adaptive and Self-Organizing Systems Workshops*, pp. 126-131, 2008.
- [18] S. Nolfi, "Evolutionary Robotics: Exploiting the Full Power of Self-organization," *Connection Science*, vol. 10, no. 3-4, pp. 167-184, 1998.
- [19] I. Harvey, E. Paolo, R. Wood, M. Quinn and E. Tuci, "Evolutionary Robotics: A New Scientific Tool for Studying Cognition," *Artificial Life* , vol. 11, no. 1-2, pp. 79-98, 2005.
- [20] E. Ruppin, "Evolutionary autonomous agents: A neuroscience perspective," *Nature Reviews Neuroscience*, vol. 3, pp. 132-141, 2002.