

A Biological Computing Framework for Living Systems

Providing a foundation for programmable medicine

This platform is designed to enable programming of a biological computer for autonomous drug dosage and disease treatment by sensing any of the approximately 250 extracellular proteases encoded in the human genome while remaining bio-orthogonal and biocompatible. Georgia Tech's platform utilizes protease-based biological circuits in order to leverage for diagnosis the abnormal signaling characteristic of specific diseases and disorders, including certain cancers, autoimmune diseases, and dangerous bacterial infections that cause sepsis.

With the potential to extend rapid advances in biological computing to practical applications in programmable medicine, Georgia Tech's first-of-its-kind technology concept applies biological enzymes (in this case, protease activity acting on target substrates) as bits that can be used as computable elements within living systems. The technology provides a framework that combines classical bitwise operations of enzyme cascades with biological bits that can also process analog information, which is crucial for use in medical applications.

Summary Bullets

- **Innovative:** Builds on probabilistic computing principles to construct analog biological bits, enabling an entirely new set of logic gates and algorithms and potentially allowing users to solve previously intractable problems
- **Robust:** Can sense every extracellular protease encoded in the human genome, for which there is a known peptide substrate, enabling a simple plug-and-play framework for communicating with a variety of biological activities and offering performance competitive with DNA-based computers but with increased processing speed
- **Relevant:** Provides a framework based on biological activity and constructed from biological materials, which enables a direct interface with and understanding of living materials and systems

Solution Advantages

- **Innovative:** Builds on probabilistic computing principles to construct analog biological bits, enabling an entirely new set of logic gates and algorithms and potentially allowing users to solve previously intractable problems
- **Robust:** Can sense every extracellular protease encoded in the human genome, for which there is a known peptide substrate, enabling a simple plug-and-play framework for communicating with a variety of

biological activities and offering performance competitive with DNA-based computers but with increased processing speed

- **Relevant:** Provides a framework based on biological activity and constructed from biological materials, which enables a direct interface with and understanding of living materials and systems
- **Convenient:** Does not require rewiring of cells or gene circuits but rather simple rewiring of molecular materials that can then be combined with living systems
- **Scalable:** Features universal inputs and outputs, enabling a large library for addressing individual bits for large-scale integration

Potential Commercial Applications

- Georgia Tech's technology framework is designed to allow scientists to write biological software for diagnosis and treatment of diseases and conditions associated with aberrant protease signaling. Specific applications may include:
 - Programmable medicine
 - Autonomous therapeutic dosing
 - Diagnosis and treatment of disease and infection
 - Cancer
 - Autoimmune disease
 - Bacterial infections, sepsis

Background and More Information

Rapid advances in engineered biological circuits are motivating the design of new treatment and detection platforms for practical applications in programmable medicine. The development of foundational components, such as molecular logic gates and genetic clocks, has enabled the design of bio-circuits with increasing complexity. However, current approaches to interfacing computers with living systems and to develop biological computers are limited in terms of scaling and long-term applicability. Bioelectronics approaches currently suffer from limited theoretical understanding of bio-interfaces and large quantities of data that require human processing. They rely on careful rewiring of genetic circuits or sensing of proteins and enzymes in low abundance. Georgia Tech's innovation addresses these shortcomings with an unprecedented approach that applies biological enzymes as bits of protease activity, thereby building the foundation for probabilistic, scalable, widely applicable programmable medicine.

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IP Status

The following patent application has published: WO2020061257A9

Publications

[Protease Circuits for Processing Biological Information](#), Nature - October 6, 2020

Images

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