SPECIAL ISSUE

SYSTEMS AND SYNTHETIC BIOLOGY
Edited by M. H. Kamnash and J. Stelling

523 The Hallmarks of Mathematical Oncology
By J. A. Bull and H. M. Byrne

| INVITED PAPER | This article reviews classes of mathematical models used to understand and treat cancer, with the perspective of upcoming validated and clinically applicable cancer models.

541 Metabolic Networks, Microbial Consortia, and Analogies to Smart Grids
By A. Theorell and J. Stelling

| INVITED PAPER | This tutorial article introduces approaches to predict fluxes in chemical reaction networks inside living cells, with an emphasis on similarities to (smart) electrical grids.

557 Machine Learning Approaches to Single-Cell Data Integration and Translation
By C. Uhler and G. V. Shivashankar

| INVITED PAPER | This article describes how problems arising in the analysis of individual biological cells and of cell-to-cell variability have inspired foundational developments in machine learning.

577 Spiking Control Systems
By R. Sepulchre

| INVITED PAPER | From control and circuit theory perspectives, this article reviews efforts toward developing a control theory of natural and engineered spiking (mixed discrete and continuous) systems.

590 Learning Outside the Brain: Integrating Cognitive Science and Systems Biology
By J. Gunawardena

| INVITED PAPER | This article uses concepts ranging from cognitive science to control theory to discuss how learning in biological systems is possible outside of, or even without, a brain.

613 Synthetic Gene Circuits: Design, Implement, and Apply
By A. Lezia, A. Miano, and J. Hasty

| INVITED PAPER | This article gives a broad overview of the field of synthetic biology, focusing on the engineering of genetic circuits.

511 POINT OF VIEW
Are the Ethics of Synthetic Biology Fit for Purpose?
A Case Study of Artemisinin
By J. Dalziell and W. Rogers

518 SCANNING THE ISSUE
Systems and Synthetic Biology
M. H. Kammash and J. Stelling

708 FUTURE SPECIAL ISSUE/SPECIAL SECTIONS

On the Cover:
This month’s cover is an artist’s depiction of the role DNA plays as the design template for all living organisms and its importance in synthetic biology.

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SPECIAL ISSUE: Systems and Synthetic Biology

631  **Cybergenetics: Theory and Applications of Genetic Control Systems**  
By M. H. Khammash  
| INVITED PAPER | This expository article presents an introduction to the exciting field of genetic control systems (cybergenetics). It covers the basic theory, implementation, and applications of this nascent field.

659  **Advances in the Computational Design of Small-Molecule-Controlled Protein-Based Circuits for Synthetic Biology**  
By S. Kretschmer and T. Kortemme  
| INVITED PAPER | This article reviews the field of computational protein design, focusing on the advances in the engineering of synthetic small-molecule-binding protein sensors as well as sensor–actuator proteins.

675  **Bayesian and Algebraic Strategies to Design in Synthetic Biology**  
By R. P. Araujo, S. T. Vittadello, and M. P. H. Stumpf  
| INVITED PAPER | This article provides an overview of two complementary approaches (algebraic and Bayesian) for rational design in synthetic biology.

688  **Synthetic Morphogenesis: Introducing IEEE Journal Readers to Programming Living Mammalian Cells to Make Structures**  
By J. A. Davies  
| INVITED PAPER | This article shows how complex tissues can develop from a small number of elementary behaviors and proposes ways in which they can be manipulated to yield synthetically designed shapes.