



CORE

ALBERTA INFORMATICS CIRCLE OF RESEARCH EXCELLENCE

2005 Research Report

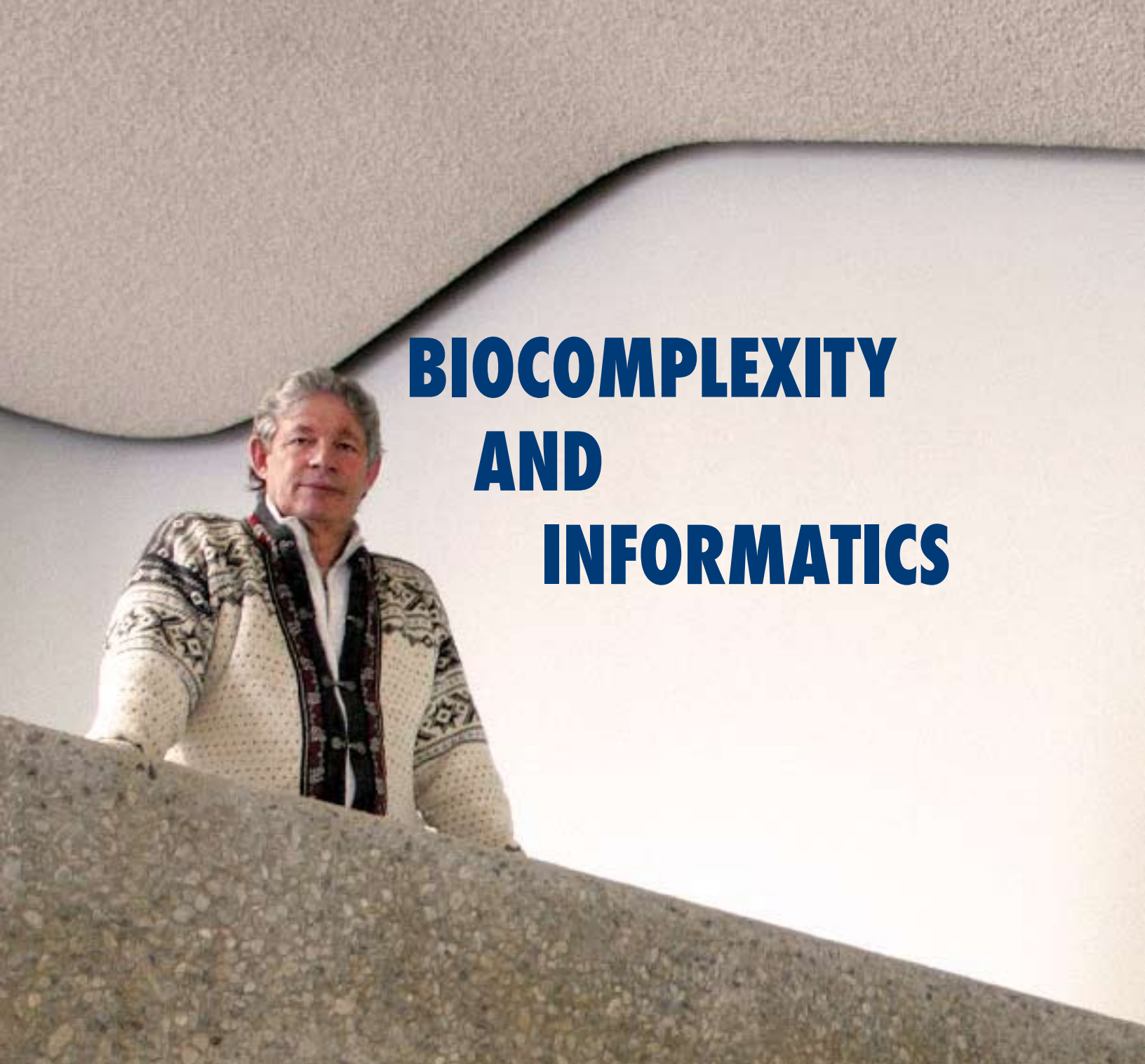
STUART KAUFFMAN

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This document is an excerpt from the 2005 iCORE Annual Research Report. For information or copies, please contact iCORE.

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BIOCOMPLEXITY AND INFORMATICS

The Institute for Biocomplexity and Informatics was established for the exploration and understanding of the logic, structure and dynamics of genetic regulatory networks.

EXECUTIVE SUMMARY

The Institute for Biocomplexity and Informatics (IBI) was proposed during the summer of 2004, and approved in the late Fall of 2004. This report therefore covers the first three months of actual operation of the IBI – January, February, and March of 2005.

During these first three months of operation, a full range of normal startup activities were accomplished.

- Deputy Director Bob Este was hired effective January 1st 2005
- Initial connection and potential collaboration networks were established both on campus at the University of Calgary and elsewhere (other universities, private enterprise; government)
- Director Dr Stuart Kauffman was hired effective February 1st 2005
- Physical offices were established at the University of Calgary, February 15th 2005
- Postdoctoral fellow Dr André Ribeiro and contract research assistant Chris Davis were retained
- Junior faculty, postdoctoral fellows, and graduate students positions were advertised
- Formal relations was established with the Alberta Innovation Center for Machine Learning (AICML) at the University of Alberta for the purposes of exploratory research collaboration and the hire of a postdoctoral student to work in connection with the IBI
- IBI was established as an official “institute” at the University of Calgary, in accordance with University of Calgary policy
- Strategic plans and meetings with key players (were put in place) to pursue additional funding for the IBI

Strategic plans were begun for other aspects of IBI development and activities including:

- Plans to establish wet lab space for the IBI at the University of Calgary and acquire appropriate laboratory research equipment and the placement of computer networks
- Establishing the setup for the inaugural annual IBI conference at the Banff Centre
- Establishing ongoing collaboration with virtual institute members, and especially, ongoing collaboration among the University of Calgary departments that are an integral part of the IBI (Biological Sciences, Physics and Astronomy, Computer Science, Electrical and Computer Engineering, and Biochemistry and Molecular Biology [Faculty of Medicine])

In addition, extensive initial planning has taken place for expansion of the IBI’s interrelated theoretical and experimental research capacities. Theoretical work has moved ahead strongly in the first three months, extending the original research strands of the IBI to now include extensive examination of cancer and stem cell differentiation research, mechanisms, technologies, and outcomes. In addition, focused exploration of screening approaches and techniques to identify small molecules that control stem cell and cancer cell differentiation is underway. Substantial efforts have begun in the preparation of patents stemming from this exploration.

RESEARCH PROGRAM OVERVIEW

The IBI was established for the exploration and understanding of the logic, structure and dynamics of genetic regulatory networks, and identified the following three research strands in the proposed research program to achieve this understanding:

- 1) The generation of models of small known networks
- 2) Solving of the “inverse problem” using machine learning
- 3) Using the ensemble approach to construct model genetic networks

In the first three months of operation, the IBI has commenced early-stage investigative programs in all three of these areas. Logically, with the IBI wet lab still to be built, during the first three months of operation much of this work has been restricted to extensive literature review and theoretical investigation; however, this work has not only been very fruitful in its own right, but is essential for the design and activation of the laboratory experimental program which is now in the early stages of development.

RESEARCH PROJECTS

Based on the original set of research program goals, and with the addition of new work that has been undertaken since the IBI commenced operations to augment these initial goals, work of the IBI during the first three months of operation has yielded the following:

- 1) Examination of the effects of noise on ergodic sets among attractors in Boolean networks

- 2) Development and extension of “Califano” inverse engineering algorithm to time series gene expression data

- 3) Literature review with respect to cancer, stem cells, transdifferentiation and differentiation therapy in preparation for experimental work

- 4) Project with AICML has been laid out to extend “Califano” algorithm

This work has created the foundation for:

- 1) Extension of “Califano” algorithm to realistic molecular simulations of genetic regulatory networks (in collaboration with AICML)

- 2) Extension of literature review into a patent application regarding a new approach to cancer therapy

- 3) Clarification of experimental procedures for cell- and molecular-based assays concerning stem cell differentiation and cancer stem cell differentiation

OBJECTIVES FOR NEXT YEAR

The research plan for the next twelve months includes extensive work in the strongly interrelated theoretical, experimental, invention, and fund-raising realms.

With regard to theory, we first expect to explore and develop a suite of theoretical approaches having to do with noise in ergodic sets related to theories of cell types and cell differentiation. This work has already begun and will be extensively developed. We are actively laying the foundation to work closely with AICML at the University of Alberta, especially in the areas of collection, analysis, and synthesis of data collected from novel experiments to be carried out at the University of Calgary wet lab and elsewhere. Initial collaboration in this area has already begun and will be extensively developed as the IBI’s own wet lab is operational.

With regard to experiments carried out at the University of Calgary wet lab and in other venues, we expect to carry out novel work on cancer and stem cell differentiation experimental design, techniques and procedures, and data collection. This will include extensive collaborative work having to do with the screening of small molecules that control stem cell and cancer cell differentiation. As a result (and especially in collaboration with the AICML), this wet lab experimentation and collaboration will lead to ongoing



Randy Goebel, Stuart Kauffman, Bob Este and Brian Unger at the 2005 IBI Launch

ing exploration and implementation of novel machine learning approaches and strategies.

With regard to invention, we expect that the collaborative theoretical and experimental work now beginning and being extensively planned as briefly described above will follow initial and very promising work that has already been undertaken to do with the generation of new patentable ideas and inventions.

All of this indicates that the work of the IBI will be of first rank importance in the general arena of systems biology and biomedicine.

Inventions stemming directly from this first rank theoretical and experimental work of the IBI have very strong potential for commercialization; therefore, aggressive exploration and development of additional funding sources is now being strategized.

RESEARCH TEAM MEMBERS AND CONTRIBUTIONS

NAME	ROLE/TOPIC
Dr Stuart Kauffman	IBI Director Associate member of the Southern Alberta Cancer Research Institute awarded the Trotter Prize in March 2005 Co-authored seven publications
Bob Este	IBI Deputy Director Presented or had papers accepted for presentation and publication with the 2005 IEEE International Conference on Systems, Man, and Cybernetics ('Intelligent Information Infrastructures for Distributed Systems') in Hawaii, and with UNESCO Heritage of Technology 2005 in Gdansk, Poland.
Dr André Ribeiro	Postdoctoral Fellow
Chris Davis	Contracted Research Assistant

Stuart Kauffman with some IBI research team members and collaborators, Banff 2005



COLLABORATIONS

DR KAUFFMAN HAS CO-AUTHORED AND SUBMITTED FOR PUBLICATION PAPERS WITH:	
Ilya Shmulevich MD	Anderson Cancer Center
Philip Clayton	Claremont School of Theology
Richard Melmon	Founder, NetService Ventures Group
Wim Hordjik	Santa Fe Institute
Sheldon Dealy	University of New Mexico
Josh Socolar	Duke University
John Grefenstette	George Mason University

INTELLECTUAL PROPERTY

In the first three months of operation, the following developments have taken place in the realm of intellectual property: extensive review of the literature having to do with cancer and stem cell differentiation has commenced, extensive discussions have taken place with legal counsel for the University of Calgary and advisory personnel of University Technologies Inc. of the University of Calgary, addressing the policies, processes and procedures that relate to the researching, development, and filing of patents based on the work of the IBI, and original patent documents have been drafted in preparation for filing.

The implications of these developments include the following: the knowledge base of the IBI regarding intellectual property is becoming robust and substantial, the present theoretical work of the IBI is demonstrating a strong capacity for creative problem solving, invention, and new systems biology knowledge generation, and the theoretical knowledge base of the IBI is becoming extremely robust in preparation for the extensive experimental work that will follow shortly.

FUNDING

Stuart Kauffman, as one of our newest iCORE Chairs, is busy ramping up his team and equipping his research lab with funds from his iCORE Chair (\$910K) and the University of Calgary (~\$372K).



PUBLICATIONS

REFEREED JOURNAL PUBLICATIONS

"Noise in a Small Genetic Circuit" - Ilya Shmulevich, Trent Tolouse, Stuart Kauffman - accepted pending minor revisions, *Complexity*, 2005

"Pathways of Differentiation" - with Josh Socolar, Sheldon Dealy, Stuart Kauffman - accepted pending minor revisions, *Complexity*, 2005

"Analysis of Coevolutionary Landscapes" - Wim Hordjik, Stuart Kauffman - accepted pending minor revisions, *Complexity*, 2005

"Are Eukaryotic Cells in the Ordered Regime?" -- Max Aldana, Ilya Shmulevich, Stuart Kauffman - submitted, *Proceedings of the National Academy of Science*, USA

"Distributed Robustness in Genetic Nets" - Max Aldana, Stuart Kauffman - submitted, *Proceedings of the National Academy of Science*, USA

"The Rise of Animalia" - Richard Melmon, Stuart Kauffman - submitted, *BioEssays*, 2005

"Agency, Emergence and Organization" - Philip Clayton, Stuart Kauffman - submitted, *Biology and Philosophy*, 2005

REFEREED CONFERENCE PROCEEDINGS

Este, Robert A., "New Minds for New Times: A Study of Andragogical Instruction for Engineers," *Proc. 4th Int'l Conf. Heritage of Technology*, 2005: 87-94; Gdansk, Poland

Este, Robert A., and Stuart A. Kauffman, "Some Thoughts on Unprecedented Conceptual Challenges Presented by Holonic Multi-Agent Systems," *IEEE International Conference on Systems, Man, and Cybernetics* ('Intelligent Information Infrastructures for Distributed Systems'); accepted for conference presentation, October 2005

SPECIAL / INVITED PRESENTATIONS

Kauffman, Stuart A., "Toward a Physical Definition of Life", *Endowed Lecture Series, at the ceremony awarding the Trotter Prize, College of Science* (in collaboration with The Dwight Look College of Engineering), Texas A&M University, March 2005

AWARDS

Kauffman, Stuart A., The Trotter Prize, College of Science (in collaboration with The Dwight Look College of Engineering), Texas A&M University, March 2005

