FINAL TECHNICAL REPORT
for Cooperative Agreement NCC 2–974

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"Theoretical Modeling and Computer Simulations for the Origins and Evolution of Reproducing Molecular Systems and Complex Systems with Many Interactive Parts"

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Our research effort has produced nine publications in peer-reviewed journals listed at the end of this report. The work reported here are in the following areas: genetic network modeling (publication [1, 2, 7]); autocatalytic model of pre-biotic evolution [3]; theoretical and computational studies of strongly correlated electron systems [4,5]; reducing thermal oscillations in atomic force microscope [6]; transcription termination mechanism in prokaryotic cells [8]; the low glutamine usage in thermophiles obtained by studying completely sequenced genomes [9]. In the following, we discuss the main accomplishments of these publications.

Theoretical modeling of genetic network is made possible by recent advances in biotechnology such as gene chips capable of taking a snapshot of the state of a cell at the genomic level. We discussed common practices in analyzing gene expression data [7] and explored the way in which a genetic network can be inferred from the expression data from gene chips[1]. We have developed a reverse engineering algorithm based on mutual information inference[1]. We have also discussed the difficulties with the current models of genetic networks [2].

In [3], we discussed a cellular automata model of prebiotic evolution. We have paid special attention to the spatial dynamics of the autocatalytic networks first studied by Eigen and Kauffman.

In [4,5], we continue our work on the two-chain Hubbard model, which is a theoretical model of high transition temperature superconductors (the so-called ladder compound). Using the density matrix renormalization group method, we computed the phase diagram of the two-chain Hubbard model [4] and studied its spin and charge dynamics [5]. We found satisfactory agreement of our calculations with the weak coupling renomalization group treatment of the same model by Balents and Fisher.

In [6], we show that the thermal fluctuations of very soft mechanical oscillators, such as the cantilever in an atomic force microscope (AFM), can be reduced without changing the stiffness of the spring or having to lower the environment temperature. We derived a theoretical relationship between the thermal fluctuations of an oscillator and an actively controlled external dissipative force. This relationship is verified by experiments with an AFM cantilever where the external active force is coupled through a magnetic field. This active noise reduction approach can significantly improve the accuracy of static positions or static force measurements in a number of practical applications.

In collaboration with Professors R. Laughlin and K. Harrington of Stanford University, we put forward [8] a hypothesis that polymerase processes an internal memory capable of being reprogrammed by the DNA sequences it reads, based on our reading of the existing literature on intrinsic transcription terminators in prokaryotes. Large molecular weights of polymerase suggest that it should behave similarly to the non-crystalline materials in having slow relaxation times and meta-stable configurations. We have found strong evidence that challenges the conventional theory of the ρ-independent transcription termination in *E. coli*. Our proposal, if verified by the experiments, could revolutionize the current paradigm of transcription regulation. We found that the temperature-dependent termination efficiency previously interpreted as support for the chemical kinetic model can be equally explained by ionization of a component of polymerase required for its termination function. A theory developed fits the data nicely. The ionizing component is likely to be Mg^{+2} ion. We found in the literature a description of the anti-termination sequences that render the polymerase to read through terminators, which provide support for polymerase memory. We also found tandem terminator experiments which are consistent with termination being deterministic. We have also proposed experiments which will test our proposal.

In [9], amino acid usage of proteins in thermophiles was calculated using the quantile method. Comparison of thermophiles with bacteria reveals that the most striking difference between thermophiles and mesophiles is the much-lowered usage of glutamine. Asparagine and glutamine are two most unstable amino acids which are subjected to deamination.

Publications supported by NCC 2-974

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3. D. Stassinopoulos, S. P. Colombano, J. D. Lohn, G. L. Haith, J. Scargle, **S. Liang**, "Spatial Autocatalytic Dynamics: An Approach to Modeling Prebiotic Evolution", *InterJournal Complex Systems*, (1999) 252. (http://www.interjournal.org/)
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9. **S. Liang**, G. Cooper, J. Trent, A. Weber, "Deamination of Glutamine in Thermophiles", in preparation.