# ITR-(NHS)-(sim): Computational Models for Gene Silencing: Elucidating a Pervasive Biological Defensive Response

(A joint collaboration of Virginia Tech and New York University)

## PROJECT SUMMARY


In recent years, an exciting new phenomenon has been discovered in biology, known variously as RNA interference (RNAi), post-transcriptional gene silencing (PTGS), or gene silencing. From the realization that RNAi is a naturally occurring cellular defense mechanism, biologists and pharmaceutical scientists have been quick to explore its potential for transgenic research, therapeutic intervention, drug discovery, and development of novel biological agents. RNAi technologies are rapidly evolving to achieve higher value and to fit new uses. A current trend is the development of high-throughput RNAi screening technologies and commercial enterprises built around such capabilities. The scientific study of RNAi is not only worthy of intrinsic scientific merit, but also important for its myriad applications in defense, public health, and national priorities facing our country.

This project is a multi-institutional, multi-disciplinary research effort to advance our understanding of RNAi mechanisms and to provide a resource for rapid analysis of RNAi effectiveness. Researchers from Virginia Tech and New York University are developing an integrated systems biology framework — CMGS (Computational Models for Gene Silencing) — that models RNAi function at both the molecular and cellular levels. CMGS will integrate molecular modeling and simulation techniques, physical annotation capabilities, curation of data from literature and experiments, as well as inferencing technologies to model and infer the effects that an RNAi intervention might have. The computational investigators leverage considerable expertise in building software tools useful to life science collaborators and in building scientific problem solving environments; the integration of enhanced tools into the CMGS system will provide a computationally powerful approach to pose questions about RNAi, analyze data from interference experiments, and reason about RNAi processes.

**Intellectual Merits:** The CMGS system is a powerful, explanatory environment that is greater than the sum of its parts and that, by blending molecular modeling, sequence analysis, data representation, and inferencing algorithms into a coherent methodology, serves as a template for understanding how complex systems biology frameworks can be designed. CMGS will hence not only aid in its particular domain of application but also systems biology software projects with similarly broad scope.

**Broader Impacts:** This research involves a collaborative team of computer scientists and life scientists who are committed to increasing the number of scientists trained to bridge the gap between biology and computation and also to enhancing the participation of under-represented groups. Students from under-represented groups have spent, and will spend, the summer in research labs at VT, monitored by the PIs, and their students; funding is provided from VT by the Multicultural Academic Opportunities Program and through the Fralin Biotechnology Center. The five VT researchers are participants in the interdisciplinary doctoral program in Genetics, Bioinformatics, and Computational Biology (GBCB). Every GBCB student is educated both in biology and in computation, and hence the program contributes to the immediate national need for young life scientists to be trained in the nature and value of bioinformatics tools and approaches. In addition, the GBCB program may attract more women into advanced computational science research than traditional computer science.

CMGS will be delivered as a web-based system for use by the broader biological systems modeling community to support interactive prediction and inferencing scenarios. We will use CMGS in courses offered under Virginia Tech's GBCB program, providing a powerful environment that demonstrates the utility of multiple modes of investigation. By integrating computational and biological expertise, CMGS will also serve as a tool that exposes life sciences students to computational fields.