# Systems Biology: What is it? And why apply it to microbial systems?

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**Application of systems approaches to the microbial world.** We are convinced that the world of biomedical and biological research undergone a revolutionary change in recent years due to the development of 'genomic science". Therefore, our lab is taking a bold step in applying the global approaches of "discovery science" and "systems biology" to explore the world of microbial pathogenesis. These global approaches employ contemporary genomics and proteomics technologies to dissect the molecular mechanisms of the biology and pathogenesis of the host-parasite interaction. Our work requires bioinformatics to plumb the depths or mine the vast new data sets we are generating. Specific projects ongoing in the lab include:

- Genome sequencing and analysis of the protozoan *Cryptosporidium parvum*, a Category B agent of biological terrorism.
- Genome sequencing and analysis of *Streptococcus sanguis*, an important bacterial cause of dental caries and bacterial endocarditis.
- Functional genomics of differentiation of the protozoan parasite *Trypanosoma cruzi*, cauasative agent of Chagas' Cardiomyopathy, scourge of Latin America.
- The *T. cruzi* Interactome, a project with the goal of mapping the interactions of all of the macromolecules (proteins and RNAs) in this important parasite.
- The *T. cruzi* Proteome, a project in its initial stages has the goal of studying the proteins expressed by *T. cruzi* during all stages of its development and differentiation.

Technologies that we apply in these projects invoke use of the Genomics and Transcriptomics capabilities of the Nucleic Acids Research Facilities, the Proteomics capabilities of the Mass Spectrometry Resource for Biocomplexity, and the Bioinformatics capabilities of the Bioinformatics Computational Core Laboratories. Thus, we are performing high throughput sequence analysis coupled with bioinformatics to sequence, analyze and annotate the genomes of *C. parvum* and *S. sanguis*. High throughput sequencing is also allowing us to generate the *T. cruzi* UNIGENE library, with the goal of containing a single unique and full length copy of the messenger RNAs derived from all of this parasite's genes. The UNIGENE library feeds into our development of the *T. cruzi* Biochip. In collaboration with Brazilian colleagues, we are establishing a chip containing at least one probe for every *T. cruzi* gene. The *T. cruzi* Biochip will be used to study the gene expression profiles, or the functional genomics, of the development and differentiation of this complex and interesting parasite. In the *T. cruzi* Interactome Project, we are using yeast and bacterial one-, two- and three- hybrid systems to characterize all of the protein-protein and protein-RNA interactions in *T. cruzi*. As the Proteome Project gears up, we will be comparing and combining the results of the expression profiling that measures gene-specific RNA levels, with the results from the proteomics analysis that provide the gene-specific protein levels, at every stage fo the parasites life cycle. Finally, we are working with bioinformaticists and applied mathematicians with the goal of developing 'in silico' models of a Virtual Parasite.

In this laboratory, students, technicians, postdoctoral fellows, information technologists and programmers, and faculty work side-by-side to achieve our goals. The deeply integrative nature of the research dictates such a team effort if the effort is to be successful. Students are therefore exposed to a very broad basis of biological and biomedical science, and are cross-trained in several disciplines upon completion of their degrees. It is generally recognized that such broad-based and interdisciplinary training will be essential for the future successful independent scientists.