

MAGNet Center Summary

The Center for Multiscale Analysis of Genetic Networks (MAGNet) was established in 2005, with the mission of providing the research community with novel, Structural and Systems Biology methods and tools for the **dissection of molecular interactions in the cell** and for the **interaction-based elucidation of cellular phenotypes**. A key component of this mission was the validation of these tools through collaborative projects with experimental biologists, whose scientific goals could not have been accomplished without them. These goals were largely exceeded and MAGNet has developed into a major center in Computational Structural and Systems Biology, producing both high-impact science and valuable software tools for the research community. Objective criteria supporting this statement include: number and quality of scientific publications, funded collaborations supported by MAGNet tools, software downloads, utilization criteria, and impact on the Systems Biology community via MAGNet organized activities. MAGNet has also had a profound impact on the academic environment at Columbia University, providing the impetus for the creation of a *new Department of Systems Biology*, under the leadership of Drs. Califano and Honig. Briefly, some key accomplishments of our Center include:

RESEARCH IMPACT: Since 2005, MAGNet supported research produced 261 papers, including 86 in journals with Impact Factor (IF) ≥ 9.38 (PNAS). Of these, 27 were published in journals with IF ≥ 22.97 (Nat. Biotech.). The results presented in these publications were often of a seminal nature, including for instance (a) the elucidation of the role of DNA shape in protein-DNA binding specificity (1-3), the identification of the Master Regulators of the mesenchymal subtype of Glioblastoma (4), and the discovery of an extensive microRNA-mediated regulatory network of RNA-RNA interactions in brain tumors (5). These findings were driven by the Center's Driving Biological Projects (DBPs, <http://magnet.c2b2.columbia.edu/?q=node/6>) and were the result of close collaboration between experimental and computational biologists. In all cases, the computational methods and software tools developed by MAGNet investigators were instrumental in enabling the scientific discovery.

COMMUNITY RESOURCES/SOFTWARE/COLLABORATIONS: MAGNet algorithms and tools have been broadly adopted by the community. We have designed new (often first-of-a-kind) methods for the dissection of transcriptional (2, 6-11), post-translational (12-15), genotype-phenotype (16, 17), and cell-cell interactions (18-21), as well as for regulatory-network based analysis of cell phenotypes (13, 22, 23). In addition to being independently available from the originating investigator labs, these algorithms have been implemented in the *geWorkbench* platform (24), which has been downloaded more than 10000 times by more than 800 unique users. Attesting to its community impact, *geWorkbench* has been supported by one of NCI's Knowledge Centers, independent of MAGNet support (25), allowing comments, bug fixes, and new functionality requests to be continuously tracked via user discussion groups. Individual tools, such as ARACNe (6), have also been downloaded thousands of times and have been incorporated in other platforms, such as the Minet Bioconductor package (26) and GenePattern (27). Furthermore, MAGNet methods and tools have been used in numerous biological projects, including the 10 Center DBPs and 73 collaborative projects, of which 39 have resulted in NIH funded activities. These have been instrumental in validating the computational methods and in demonstrating their value to address important biomedical problems, especially in oncology.

TRAINING & DISSEMINATION: MAGNet Education and Dissemination Cores have achieved significant impact on the training of computationally-savvy structural and systems biologists and in fostering dialogue at the interface between computational and experimental sciences. Over 100 pre-doctoral students and post-doctoral fellows currently work in MAGNet investigator labs (61 have received MAGNet funding), and they benefit from the interdisciplinary environment that has been created. Additionally, we have organized and developed important conferences and meetings that attract hundreds of scientists each year, including (a) the DREAM conference, to establish objective, community-based benchmarks to test reverse-engineering algorithms, (b) the RECOMB Systems Biology conference, which brings together a community of close to 500 researchers, (c) the NY Academy of Science Systems Biology Interest Group, and (d) the Keystone meeting on Biomolecular Interaction Networks: Function and Disease. Finally, MAGNet provides key informatics support to Columbia's Clinical and Translational Science Award program and to the Herbert Irving Comprehensive Cancer Center. As a result of the impact that MAGNet has had to biomedical research both at Columbia University and at the national level, in 2010 the University approved the creation of a new department of Systems Biology to consolidate and streamline the Center's research and education activities. This has enabled us to hire several talented faculty members (Dr. Saeed Tavazoie from Princeton, Drs. Sagi Shapira and Peter Sims from Harvard, Dr. Yufeng Shen from Columbia, and Dr. Chaolin Zhang from Rockefeller) whose arrival is further increasing the capacity of our center and extending our research interest to exciting new fields, including single cell studies, neurobiology, and infectious diseases.