**PROJECT SUMMARY**

1. **Senior Personnel PI**: Gloria Coruzzi (NYU Biology)

**CoPIs**: Dennis Shasha (NYU Computer Science), Alessia Para (NYU Biology).

**Senior Personnel:** Manpreet Katari (multinetworks)?

**Collaborators?**: Ulises Rosas (morphometrics), Gabriel Krouk (physiology?)

**2. Intellectual merit of proposed project (Project Summary)**

In now classic experiments on the interactions of primary macronutrient signals - N (nitrate), P (phosphate) and K (potassium) - Murashige and Skoog showed that specific combinations of N with P and K could lead to an increase in biomass under low N ([Murashige and Skoog, 1962](#_ENREF_1)). We aim to identify the regulatory networks underlying this “NPK interaction effect” on biomass, by combining genomic, phenomic, and network inference approaches. Specifically we seek to elucidate the genes and regulatory networks responsible for the integration of nutrient signals that control biomass. We seek to discover: 1. The conditions that optimize biomass. 2. The morphological traits in the roots that are markers for high biomass. 3. The genes that are markers for high biomass. 4. The genetic circuits that control those genes. 5. Genes whose over-expression or repression can increase biomass. Our experimental and analytical strategy is the result of a highly successful collaboration between biologists and computer scientists, and involves an iterative cycle of experimentation and computation, as follows:

**Aim 1. Generation of an NPK nutrient-to-phenotype matrix**. We will determine the effects of a matrix of NPK combinations on plant growth using morphometric analysis of seedlings (shoot and root) and biomass (of older plants). We will correlate these datasets to: i) identify early morphometric markers of biomass, and ii) to select three NPK:phenotype states for comparative analysis: 1) High-N:High biomass, 2) Low-N:Low biomass, and 3) LowN:High biomass.

**Aim 2*.* Identification of nutriome-responsive pathways and predictors of biomass**. Using transient treatments and a developmental series, we will generate transcriptomes (“nutriomes”) from the matrix of NPK treatments from Aim 1. Parametric and non-parametric analysis will allow us to uncover early molecular markers for biomass, and to identify the metabolic pathways (e.g. N, C-metabolism, photosynthesis, etc.) whose regulation is correlated with biomass production.

**Aim 3. The dynamic nutriome and predictive regulatory nextworks.** We will generate fine-scale, time-series transcriptome data from the three NPK:phenotype states determined in Aim 1, and use machine-learning approaches (e.g. state-space modeling) to derive causal TF regulatory networks controlling the metabolic pathways identified in Aim 2. While we have successfully used time-series data to derive causal networks (Krouk et al 2010) the novel aspect of this proposal will be to integrate/compare such networks across multiple nutriome states, and to generate predictive regulatory networks that identify central integrators of the NPK effect on biomass.

 **Aim 4. Validation of candidate regulatory nodes**. We will validate candidate regulators *in silico* (using cross-validation) and *in vivo* using mutants and transgenics – in which we will monitor molecular, trancriptome and phenotypic changes. The results of these validations will generate new hypotheses, which will iterate the systems biology cycle of experimentation and computation.

**Justification for NSF Network and Regulation goals**

This research addresses a number of the goals of the Networks and Regulation cluster:

1. Fundamental research about how cells integrate environmental signals (e.g. nutrients NPK) with their internal genetic & metabolic programs to regulate physiology & development. (Aim 1 & 2)
2. Uncovering mechanisms of signal transduction, metabolic pathways and networks. (Aim 2 & 3)
3. Development of quantitative, predictive theories of cellular function through iterative cycles of theory and experiment. (Aim 3 & 4)

**3. Broader impacts of proposed research**

A. **Applications to Agriculture**: Modification N-use efficiency in plants.

B. **Development of informatic tools**: Development of regulatory network inference approaches.

C. **Training in Systems Biology**: Postdocs & students are trained in Systems Biology by co-mentorship

between biologists (Coruzzi) and Math/Computer scientists (Shasha) from The Courant Institute .

D. **Collaborations:** This project collaborations related to computational phenotyping (Ulises Rosas), and high-throughput technology (McCombie, CSHL).