



## Networks of Biological Processes

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### Introduction

Biological processes in the soil and associated properties are highly variable at different spatial scales. The sources of spatial variability in soils include both natural and anthropogenic processes that may act at microscopic, aggregate, field, landscape, or regional scale. Together these factors create complex mosaics of environments affecting biological processes at different scales. Identifying the sources of spatial heterogeneity and quantifying the heterogeneity of biological processes in soils are challenging. However, once understood, spatial heterogeneity may offer management options that affect ecosystem productivity, biodiversity, and soil and environmental quality.

A fast growing subject of computational biology is the study of biological systems at various levels of organisation. The majority of this field's research has been on dividing genes into biological pathways or processes. The next step in achieving the goal of a systems-level understanding of the cell is to figure out how these partitioned cellular activities interact to fulfil the cell's goals [1]. With the aim of helping to decipher this higher order connectivity we propose a new methodology for gleaning patterns of interaction between biological processes, manifested by a significantly enriched web of protein-protein interactions, transcriptional coordination or genetic interactions.

The notion of Linked Processes and the resulting new network of biological processes, the Process Linkage Network (PLN), whose nodes match to biological process terms in the Gene Ontology (GO) database, are at the heart of the methodology presented in the study [2]. We can find diverse interactive and cooperative linkages between processes using this methodology and a variety of experimental data and annotations. Many of these connected terms are far apart in the GO-hierarchy, implying that the idea of organising biological data as a single taxonomy may need to be reconsidered.

Physical protein-protein interactions (PPI-PLN), transcriptional co-expression (expression-PLN), and genetic connections are all used to build and study PLNs (GI-PLN). An examination of the various PLNs reveals some intriguing results: Many of the processes shown to be linked in the various networks are congruent with biological understanding, while others signal that more research is needed to fully understand their existence and significance [3]. For example, the process "protein ubiquitination" (GO:0016567) is anticipated to be PPI-linked to protein catabolism processes, expression-linked to rRNA processing activities, and GI-linked mostly to cell cycle related processes. The Results section provides a biological explanation for these connections. More broadly, many linkages connect processes that look unrelated when only the GO hierarchy is taken into account, despite the fact that the connection is strongly supported by current biological understanding [4]. This may be due in part to the fact that the proposed links are created for a specific organism, although the Gene Ontology is intended to be universal. As a result, these links enrich and supplement the GO hierarchy's inherent relationships between processes [5].

Another area where the knowledge gained from our new methodology could be useful is in the prediction of functional annotation for proteins. The functional prediction methods use the relationships between GO-processes derived from the ontology,

therefore it's only reasonable to use the links between processes discovered by our method as well [6]. We show that carefully integrating links into functional prediction algorithms improves the methods' coverage as well as their accuracy.

We show that once it is known that two *S. cerevisiae* genes participate in PPI-linked processes or expression-linked processes, the chance of the two genes genetically interacting is dramatically increased. This multi-scale perspective on biological networks, examining relationships between the elementary parts as well as "modules" in the form of biological processes suggests a promising new direction for developing a deeper insight into biological function [7].

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