From Social Networks to Therapeutics and Connectomics

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"There is a rhythm and a pattern between the phenomena of nature which is not apparent to the eye, but only to the eye of [mathematical] analysis".

(Richard Feynman, physicist)

Abstract

Social networks and related analysis methods are becoming novel and powerful information processing techniques in therapeutics, drug discovery and systems biology. At the same time, they are permeating into neuroimaging and defined the novel area of "imaging connectomics" allowing the complete mapping of inter-regional interactions to capture the brain connectivity and its topology [4]. The application of the initial social networks to medical sciences is enabled based on mathematical graph theory.

Social Networks

- Social networks: novel paradigm in social sciences to represent a perspective different from individuals, social groups, or social categories.
- Social network analysis: novel computational tool aimed at large data analysis and visualization, combining structural theories of social interaction with corresponding methods for its analysis.
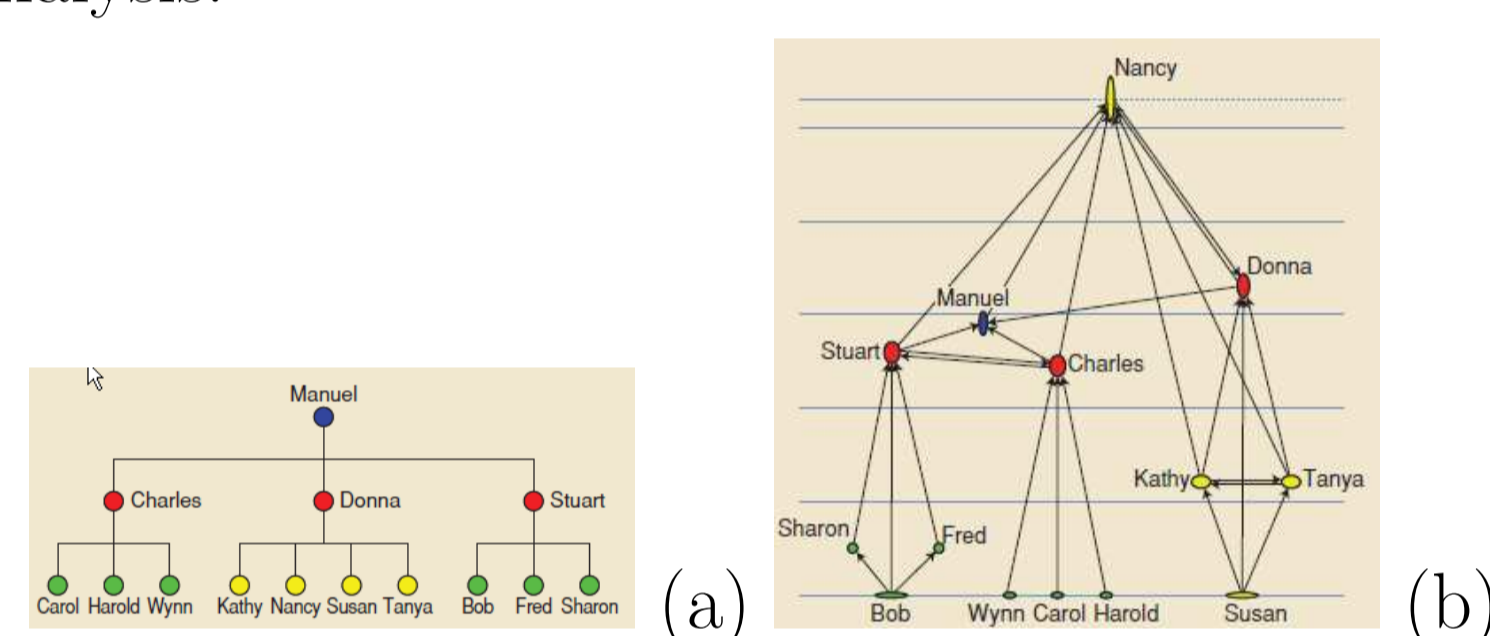

FIGURE 1: Social network [1]. (a) Formal organizational hierarchy and (b) informal advice network.

In computational science, social networks are defined as relations among a bounded set of actors with the the typical data model being a graph $G = (V, E)$ with vertices V representing actors, edges E representing relations, and potentially many attributes for both. In addition to graph theory, the empirical nature of the field imposes statistical approaches as a complementary tool.

Static and Dynamic Graph Theory

- New models are needed to "connect the dots" $\rightarrow$ graph networks: make occult connections between datasets obvious.
- Static graph: snapshot of a single representation, dynamical graph: time evolution of relations among actors.
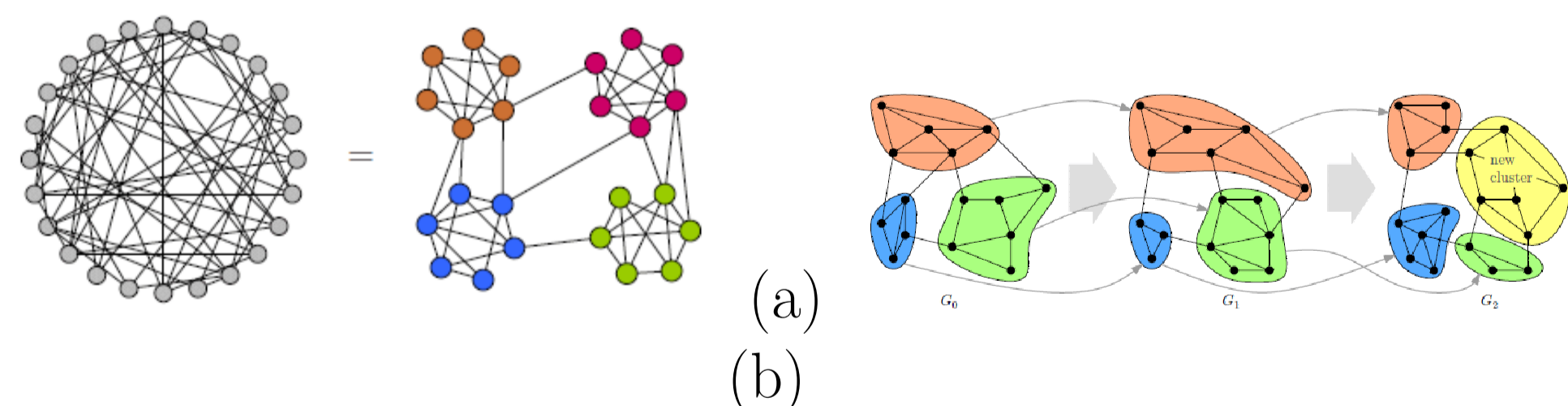

FIGURE 2: Graph structures. (a) Graphs excel at hiding their structure. Graph clustering aims at revealing their structure. (b) Time-dependent graph clustering. Three time steps of a dynamic graph: smooth dynamic clustering and cluster tracking over time (gray arrows).

Therapeutics

- Analysis of transcriptomic, proteomic and metabolomic datasets with existing knowledge-based tools: reveals only interconnected pathways that are already represented in the scientific literature.

- Novel technique to replace standard correlation networks to better reveal the topological properties reflecting the response to therapeutically interventions.
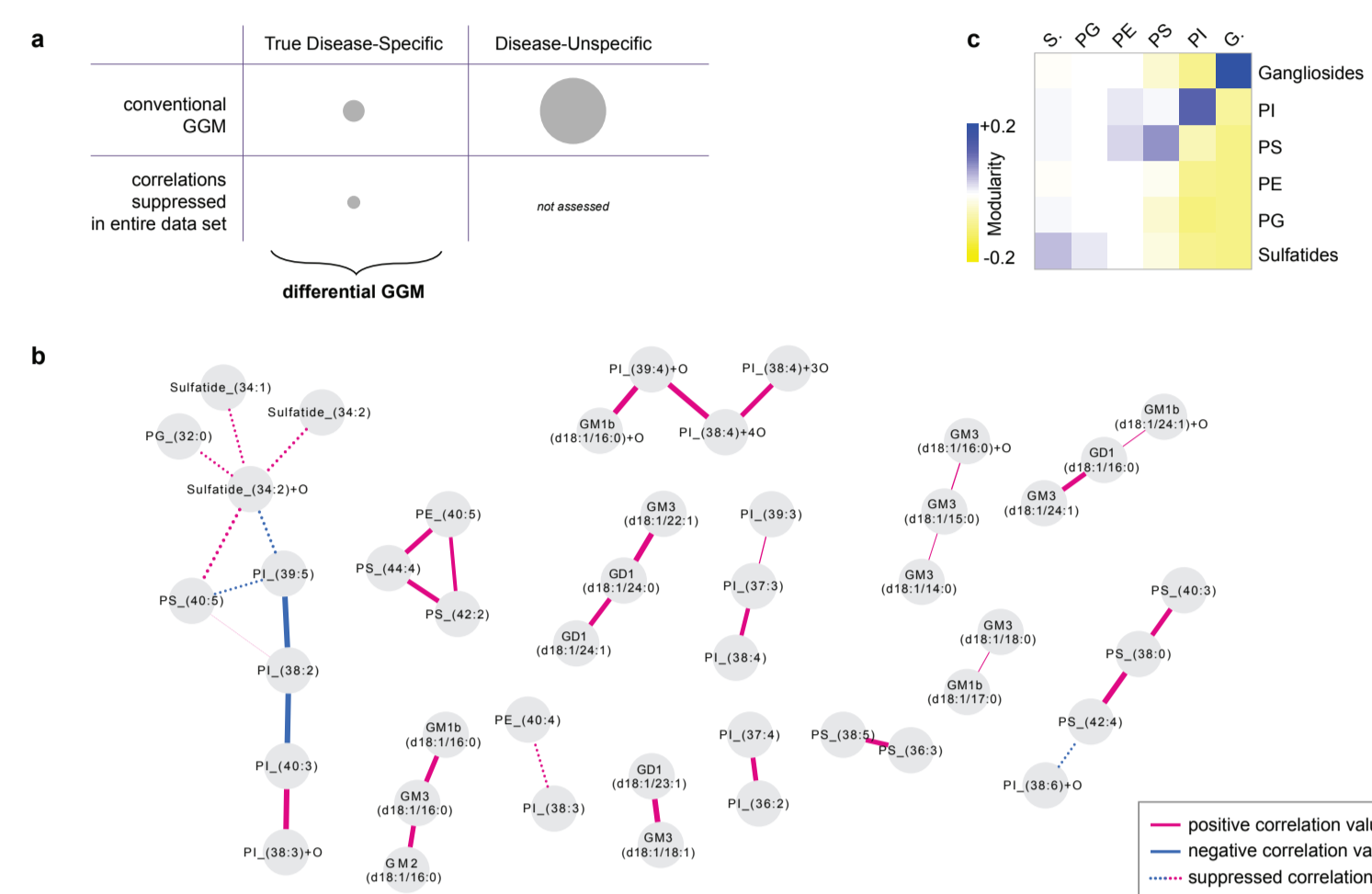

FIGURE 3: Lipids specifically regulated when glioblastoma (GGM) cell lines were effectively perturbed. a. Relative number of disease specific and unspecific lipid-lipid partial correlations in the GGM. b. Disease relevant GGM which is associated with the combined perturbation of p53 adenoviral transfection prior to SN38 chemotherapy in U87 Glioblastoma cell lines. c. Modularity matrix was calculated by using the lipid specie as class label for the GGM in b. The abbreviations are: phosphatidylglycerols (PG), phosphoinositol (PI), phosphoserine (PS) and phosphotidylglycerol (PG) [6].

Connectomics

- Drug discovery for neurodegenerative brain diseases (schizophrenia, substance abuse and mood disorders) has stagnated.
- Need for new biomarkers and validated therapeutic targets in the field of neuropsychopharmacology.
- Improved methods to approach brain studies by understanding functional networks: social networks applied to cognitive neuroscience.
- Goal: representation of small-world networks found in the brain and elucidate how pro-cognitive drug effects modulate functional brain network organization, can predict relapse in patients recovering from substance abuse and determine the early onset of childhood schizophrenia.
- "Imaging connectomics": complete mapping of inter-regional interactions to capture the brain connectivity and its topology [5].
- Processing synergy: neuroimaging generating these maps, graph theoretical techniques modeling brain as a complex network of interconnected processing nodes.
- Graph theoretical measures: quantify if treatment induced changes in topology or network organization enable or inhibit information processing and whether theory-driven biomarkers of pro-cognitive drug effects can be used in relapse prediction.
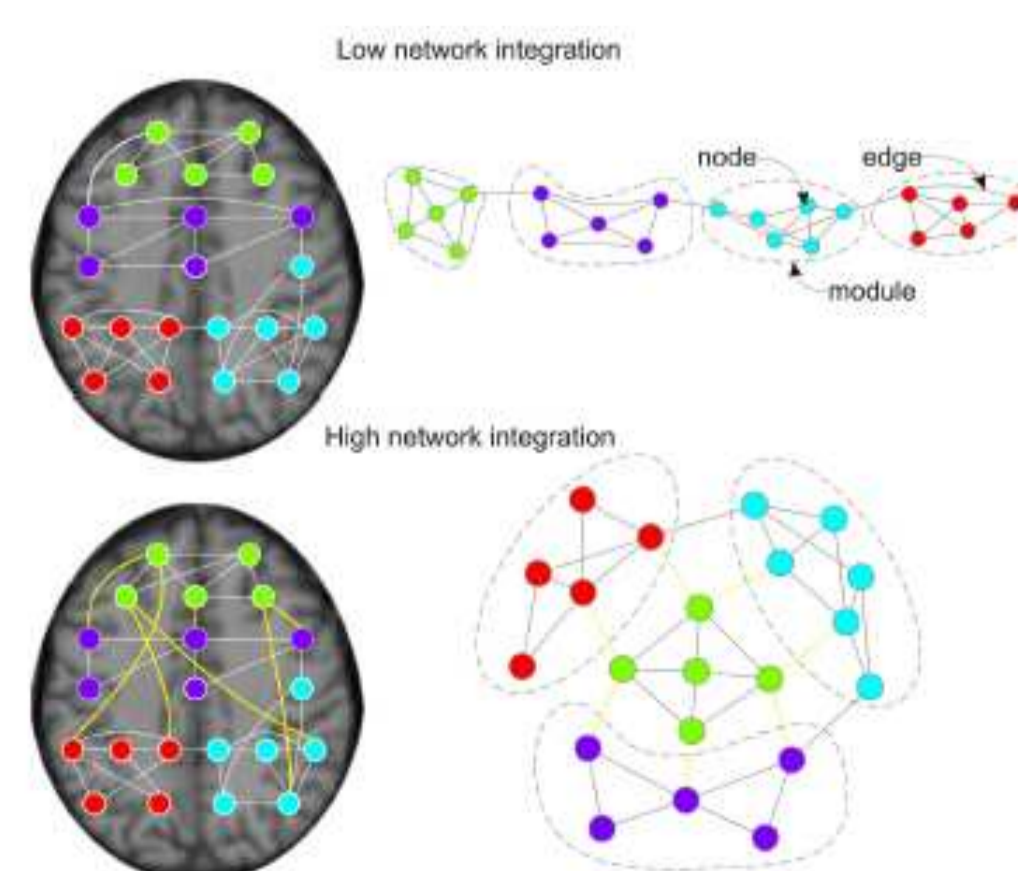

FIGURE 4: Types of network integration. Pro-cognitive drug effects increase integration of functional brain graphs and have a higher capability for information transfer [5].
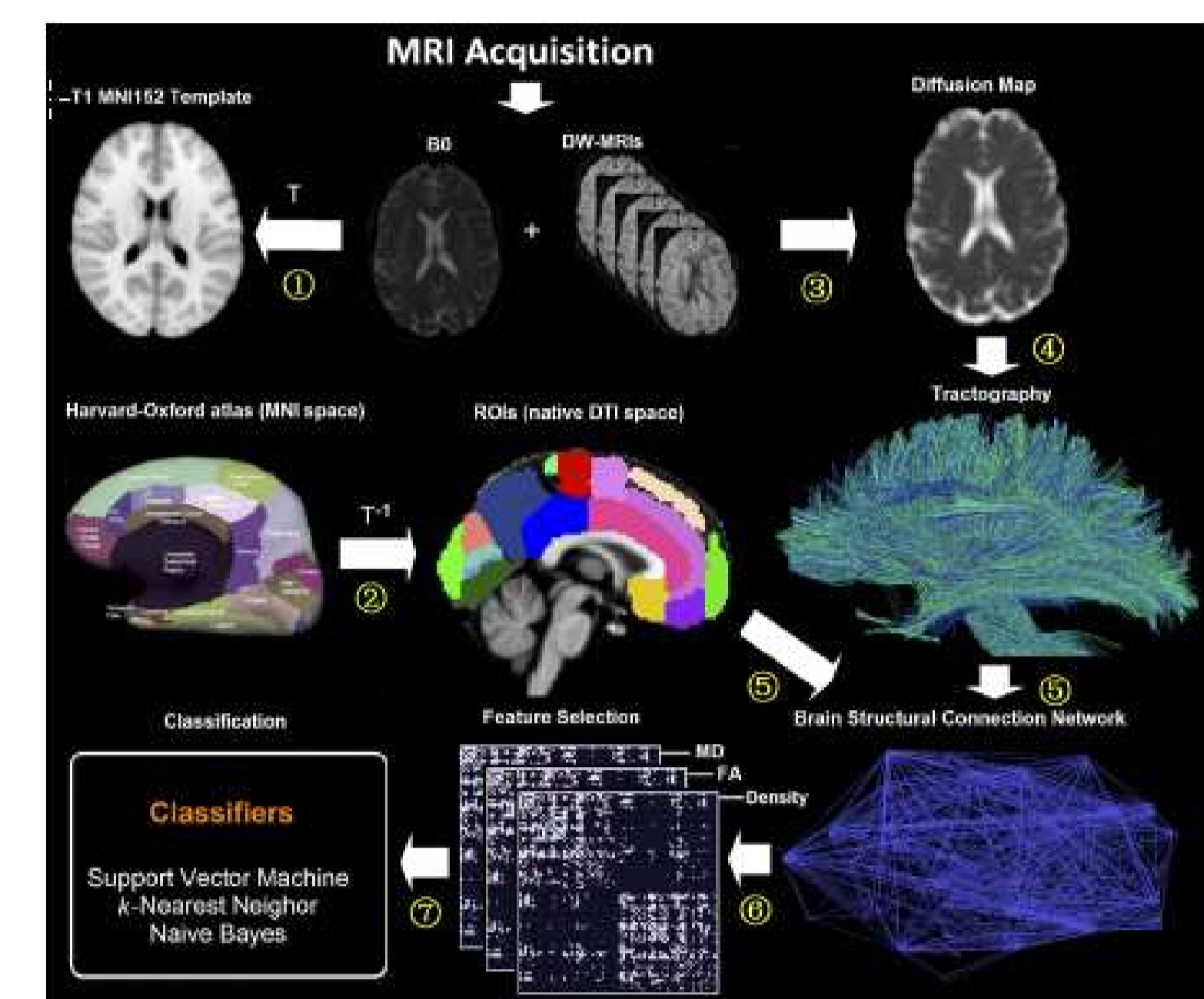

FIGURE 5: Computerized diffusion-weighted magnetic resonance imaging (DWI) to determine individual structural connectivity networks [2].

Dynamics of Neurodegenerative Diseases

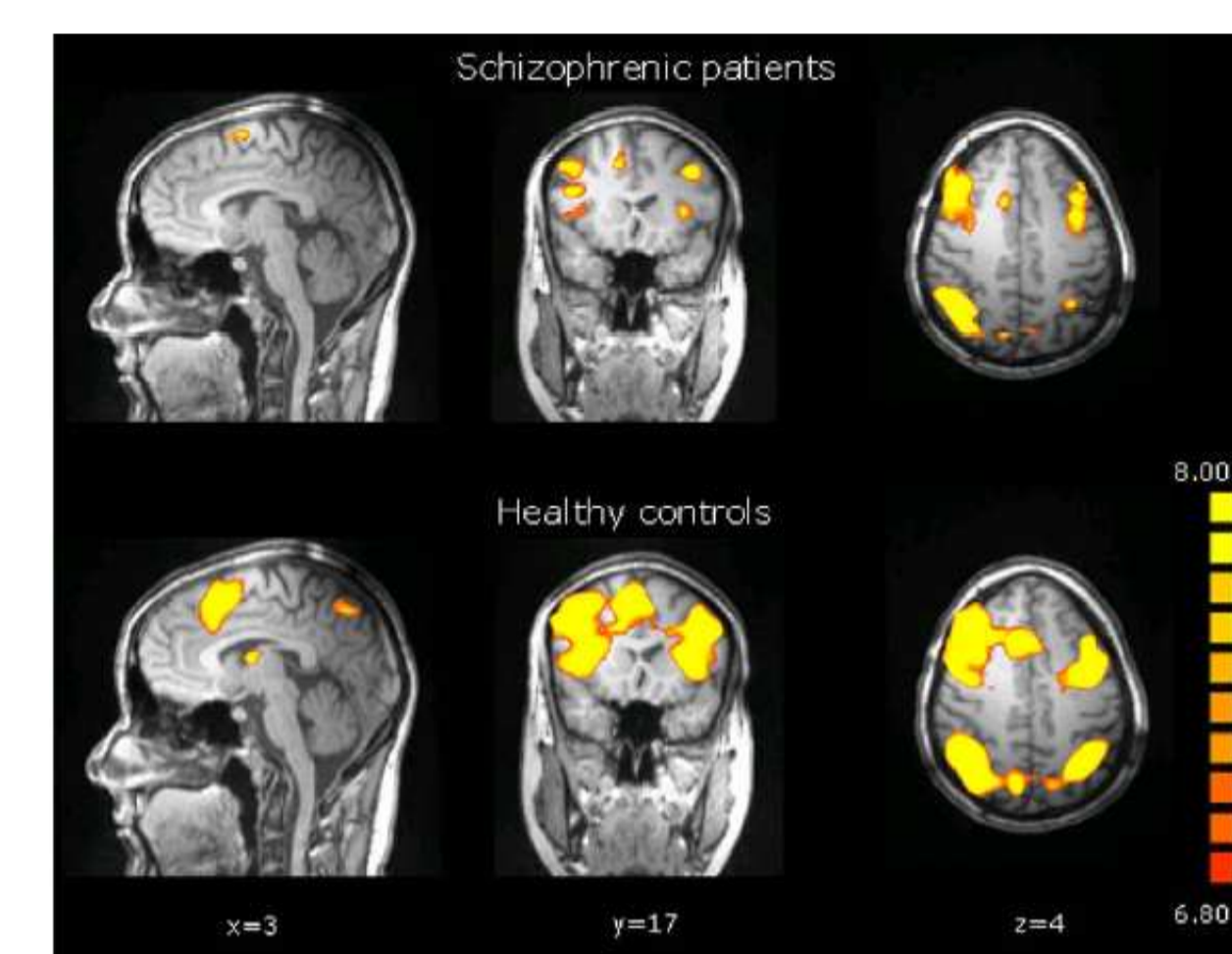Study of dynamical graphs in connection with disease prediction and relapse:

FIGURE 6: Evolution over time of schizophrenia [3].

Conclusions

We implemented and evaluated novel graph model techniques to extract relevant measures serving as biomarkers from between- and within-network to show the differences between drug effects in both systems biology and imaging connectomics. Future studies that yield insights based on integrated analyses promise to deliver new therapeutic targets and biomarkers for personalized medicine.

References

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