

Global robustness and identifiability of random, scale-free and small-world networks

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Introduction

Scale-free topology has been found in many biological networks and is suggested to contribute to the network robustness, i.e. rendering low sensitivity to perturbations. As we rely on data extracted from perturbation experiments for reverse engineering, a practical question arises, i.e., does robustness affect network identifiability? The intuitive answer is yes, however no study has been conducted to investigate it. In this work, we assess the identifiability and its possible structural basis in random, scale-free or small-world networks by conducting *in silico* simulations.

Models and Analysis

We systematically simulated knock-down perturbations on SBML models of artificial gene networks at a homogenous pre-steady state^[1] with SOSlib^[2]. Dynamic reachabilities are assigned with a threshold of ratio in activity change of the target and compared with structural reachability (Fig 1A). Networks are reverse engineered with an alternative pathway approach^[3] where the priors are searched via heuristic method^[4] (Fig 1B,1C). For each node pair, three subnets (*pathnets*) are derived and their complexities are calculated (Fig 2A). The shortest pathway and node connections are also examined. These structural features are compared between topologies and between TP and FN, and TN and FP within a topology (e.g. Fig 2B; see Fig 1 for abbreviations).

Conclusions and Discussions

In general, all networks are highly robust (Fig 1A), and their identifiability is low (Fig 1B). Scale-free networks show the highest robustness and the lowest identifiability (Fig 1C). Relationships between edge identifiability and structural features are very different in different network topologies (Fig 2C). Identifiability is sensitive to more of these features in scale-free networks than in others. In particular, tail complexities are negatively related to TP, in agreement with that node could be stabilized by feedback loops (Gong and Zhang, submitted to ICSB-2007). Together with comparison of structure measures between the networks, it is established that higher tail connections and lower head complexities can explain the lower TP, while lower complexities of head/tail self-pathnets and between-pathnet, but not shortest pathway lengths, explain the higher TN in scale-free networks.

In conclusion, node connections do not directly reflect identifiability, rather, more complex structural features underlie the distinct reverse engineering performances between the topologies. The lessons learned from these networks underscore the importance to design sophisticated algorithms in order to identify the edges hidden in the simple perturbation experiments and to design cost-efficient multi-perturbation experiments.

References

- [1] Mendes et al, 2003, Bioinformatics, 19: ii122.
- [2] Machne et al, 2006, Bioinformatics, 22: 11.
- [3] Gong and Zhang, 2007, Ann NY Acad Sci, (in press)
- [4] Ruths et al, 2006, J Comput Biol, 13: 9.

Figure 1: Robustness and identifiability of the networks. Each point represents the average in a network of a topology (50 networks for each topology). (A) Network reachability; (B) and (C) Reverse engineering performance.

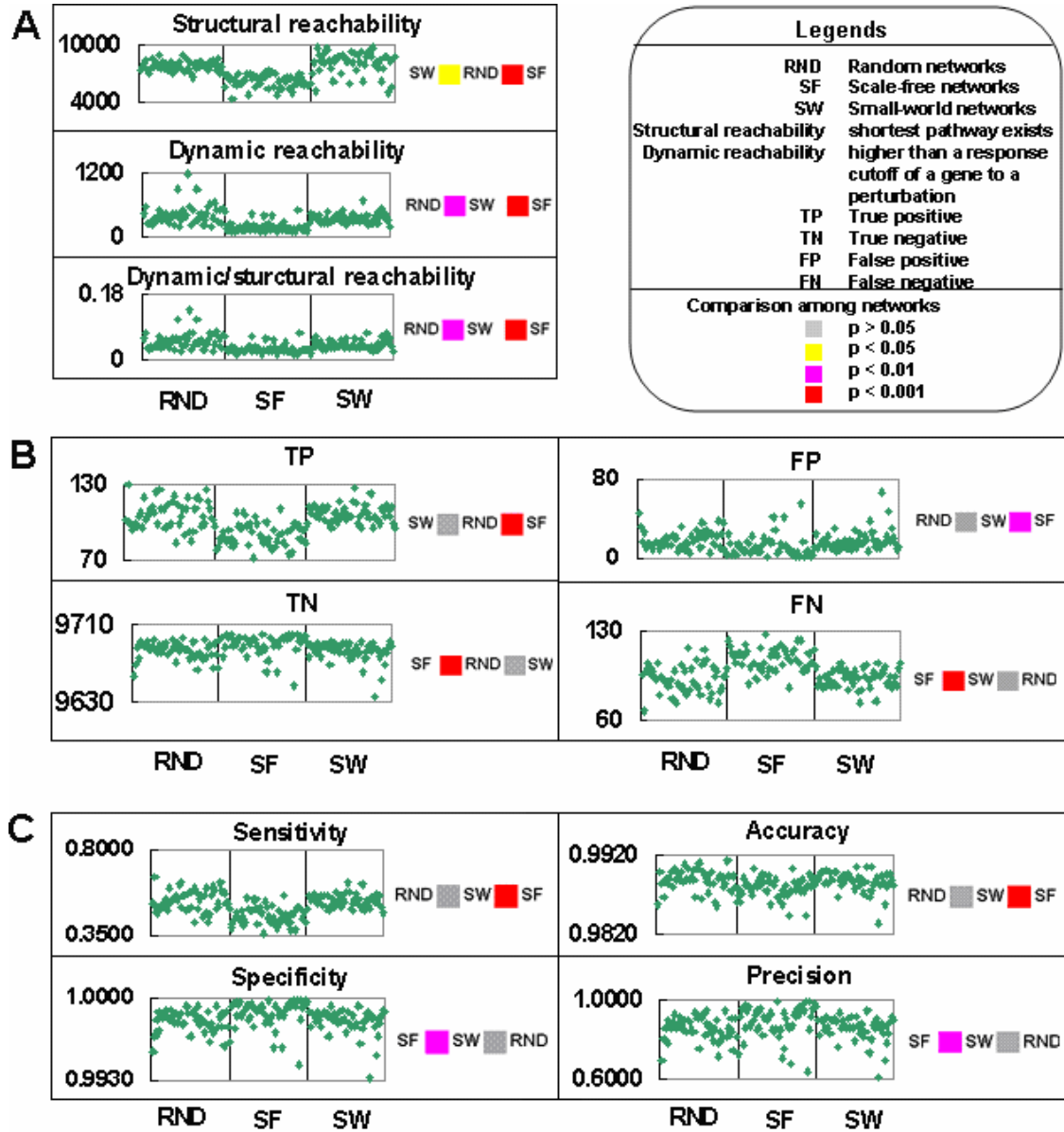
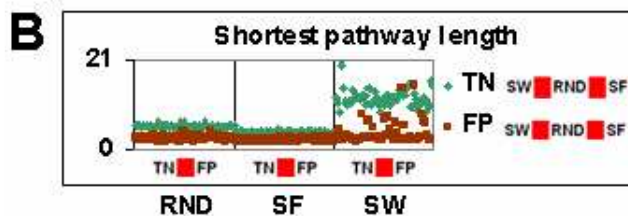
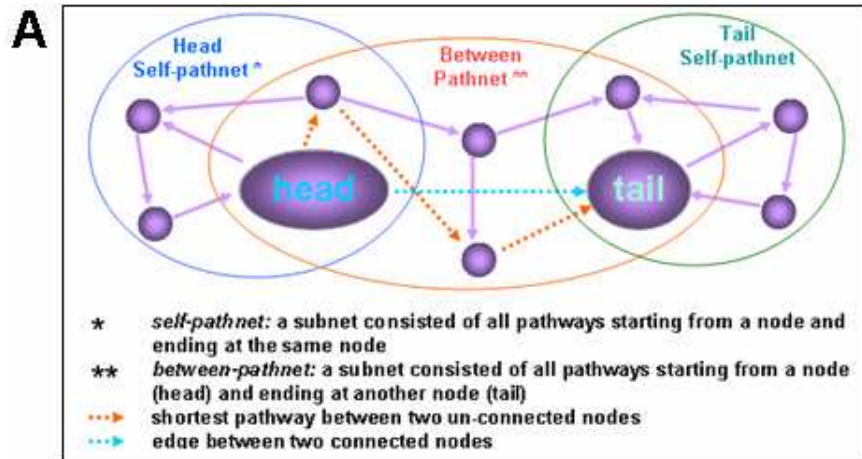


Figure 2: Structural features related to distinct network identifiability. (A) Pathnets relevant to a node pair; (B) Shortest pathway length comparison; (C) Summary of the effects of structural features on edge identifiability, highlighting the distinct behaviours in scale-free networks.



C

Structural features			SF vs RND & SW		RND		SF		SW	
			TP+FN	TN+FP	TP	TN	TP	TN	TP	TN
Node connection	head	input								
		output								
	tail	input								
		output								
Node self pathnet complexity	head	downstream								
		interaction								
		connection								
	tail	downstream								
		interaction								
		connection								
Between-pathnet complexity	downstream									
	interaction									
	connection									
Shortest pathway length			x		x		x		x	

downstream number of nodes in a pathnet
 interaction number of interactions in a pathnet
 connection downstream/interaction

Lower in SF than in RND and SW.
 Higher in SF than in RND and SW.
 Negative relationship between a structure feature and TP or TN.
 Positive relationship between a structure feature and TP or TN.
 No relationship between a structure feature and TP or TN.
 X Not applicable.
 Structure-edge relationships related to reverse engineering performance in scale-free networks.