THE INFORMATIONAL ARCHITECTURE OF BIOLOGICAL NETWORKS. H.Kim[1], P.C.W. Davies[1], and S.I. Walker[1,2,3,*], [1]Beyond Center for Fundamental Concepts in Science, Arizona State University Tempe AZ USA; [2]School of Earth and Space Exploration, Arizona State University, Tempe AZ USA, [3]Blue Marble Space Institute of Science, Seattle WA USA.
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Life seems distinctive in its ability to process and store information [1]. An important question is whether information is merely a useful analogy for describing biological systems or intrinsic to biological function. To address this question we provide a rigorous case study of the informational architecture of two representative biological networks. We do so by utilizing information theoretic analyses to detail how information is stored, processed and distributed in the execution of biological function.

Our study focuses on two model systems: the cell-cycle regulatory network of the fission yeast *Schizosaccharomyces Pombe* [2] and that of the budding yeast *Saccharomyces cerevisiae* [3]. For both cell-cycle regulatory networks, we calculate the storage and processing of information among nodes. We compare the results for the biologically functional cell-cycle networks with randomly constructed Boolean networks of similar architecture. We utilize two types of random network in our analysis: random networks with global constraints (RNGC) and random networks with local constraints (RNLC). Networks constructed with the global constraint are equivalent in network size (in terms of number of nodes and edges) to the reference biological network. Networks constructed with the local constraint additionally share topological properties with the reference biological network, including degree distribution.

Our results demonstrate that both biological networks share commonalities in their informational structure that set them far apart from their random network counterparts. Among these distinctive features, the biological networks exhibit a previously uncharacterized scaling law for the distribution of transfer entropy between nodes (Fig. 1). For both biological networks, the fit to a power law has an exponent close to ~1: 1.01 for the *S. cerevisiae* cell-cycle network and 0.95 for *S. Pombe*, whereas for RNLC these scalings are 0.6 and 0.51, respectively and even smaller for RNGC. Thus the scaling of transfer entropy has a distribution that is nearly Zipfian. Additionally, the biological networks are also outliers in that they contain nodes specialized for storage of information about the global state space. To characterize this feature, we introduce a new information-theoretic measure we call preservation entropy *PE*, which roughly captures the

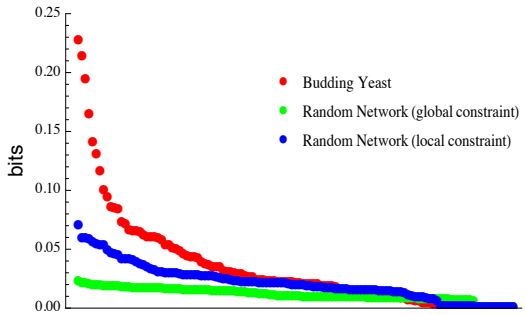

Fig 1: Transfer entropy scaling for biological and random networks, shown for the budding yeast cell-cycle regulatory network (similar results for the fission yeast cell-cycle regulatory network are not shown).

degree to which the dynamics of a node is dominated by information storage in its own past versus the transfer of information with other nodes. Nearly all individual nodes in the random networks have $PE(X) > 0$, indicating their dynamics are dominated by their own history. In contrast, in the two biologically functional cell-cycle networks nearly all nodes have $PE(X) < 0$, with the exception of four nodes in each network with positive preservation entropy. Intriguingly, these nodes have previously been identified to play a unique functional role in each network as control kernel nodes [4], suggesting a connection between local information storage and biological control.

These results show that both biological networks are similar in their informational architecture, but are very distinct from random networks. This is suggestive of previously unidentified information-based organizational principles that go beyond topological considerations, such as degree distribution (captured by our RNLC networks), which may be critical to biological function. Thus, information may be intrinsic to the operation of living systems, where the informational architecture of biologically evolved networks has the potential to distinguish biological networks from other classes of network architecture that do not exhibit these informational properties.

References: [1] Walker, S.I. and Davies, P.C.W. (2013) J. Roy Soc. Interface, *6, 20120869.* [2] Davidich, M.I. and Bornholdt, S. (2008). *PLoS ONE*, 3, e1672. [3] Li, F. *et al.* (2004) PNAS, *101, 4781.* [4] Kim, J. *et al.* (2013) *Sci. Rep., 3, 2223.*