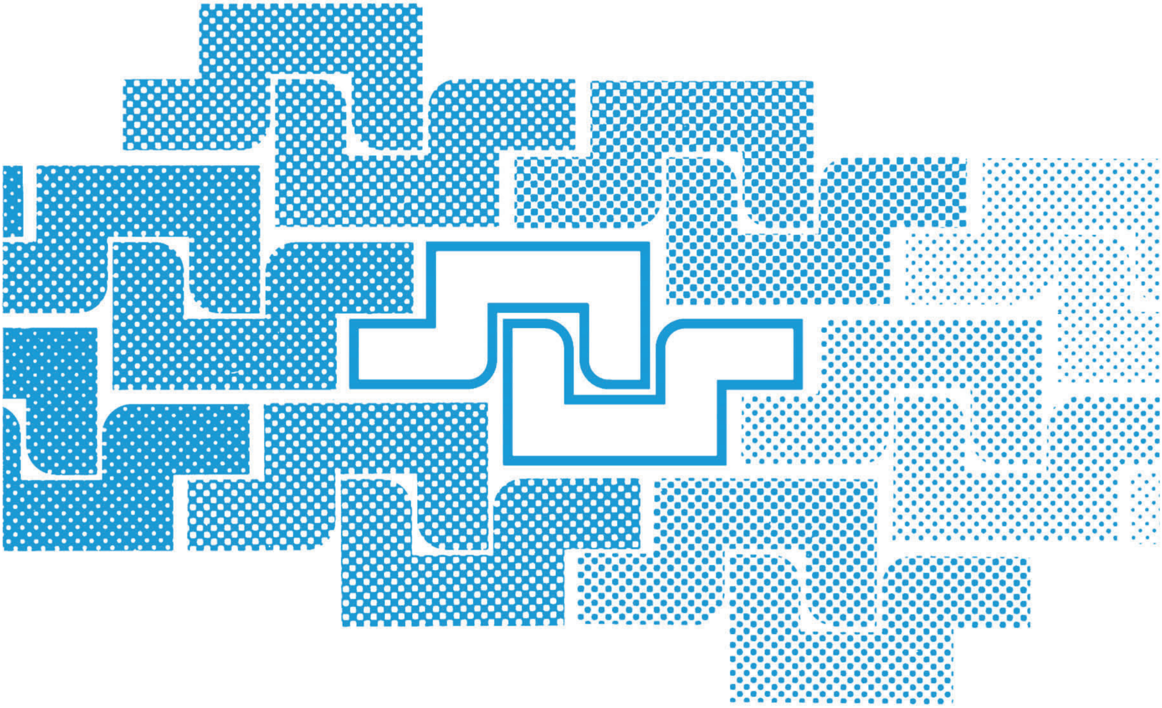


Dynamics of Complex Interconnected Systems: Networks and Bioprocesses

Edited by

Arne T. Skjeltorp and
Alexander V. Belushkin

NATO Science Series

II. Mathematics, Physics and Chemistry – Vol. 232

Dynamics of Complex Interconnected Systems: Networks and Bioprocesses

NATO Science Series

A Series presenting the results of scientific meetings supported under the NATO Science Programme.

The Series is published by IOS Press, Amsterdam, and Springer in conjunction with the NATO Public Diplomacy Division

Sub-Series

I. Life and Behavioural Sciences	IOS Press
II. Mathematics, Physics and Chemistry	Springer
III. Computer and Systems Science	IOS Press
IV. Earth and Environmental Sciences	Springer

The NATO Science Series continues the series of books published formerly as the NATO ASI Series.

The NATO Science Programme offers support for collaboration in civil science between scientists of countries of the Euro-Atlantic Partnership Council. The types of scientific meeting generally supported are “Advanced Study Institutes” and “Advanced Research Workshops”, and the NATO Science Series collects together the results of these meetings. The meetings are co-organized bij scientists from NATO countries and scientists from NATO’s Partner countries – countries of the CIS and Central and Eastern Europe.

Advanced Study Institutes are high-level tutorial courses offering in-depth study of latest advances in a field.
Advanced Research Workshops are expert meetings aimed at critical assessment of a field, and identification of directions for future action.

As a consequence of the restructuring of the NATO Science Programme in 1999, the NATO Science Series was re-organised to the four sub-series noted above. Please consult the following web sites for information on previous volumes published in the Series.

http://www.nato.int/science
http://www.springer.com
http://www.iospress.nl

Series II: Mathematics, Physics and Chemistry – Vol. 232

Dynamics of Complex Interconnected Systems: Networks and Bioprocesses

edited by

Arne T. Skjeltorp
Institute for Energy Technology,
Kjeller, Norway

and

Alexander V. Belushkin
Frank Laboratory of Neutron Physics,
Dubna, Russia

Springer

Published in cooperation with NATO Public Diplomacy Division

Proceedings of the NATO Advanced Study Institute on
Dynamics of Complex Interconnected Biosensor Systems: Networks and Bioprocesses
Geilo, Norway
11–21 April 2005

A C.I.P. Catalogue record for this book is available from the Library of Congress.

ISBN-10 1-4020-5029-1 (PB)
ISBN-13 978-1-4020-5029-9 (PB)
ISBN-10 1-4020-5028-3 (HB)
ISBN-13 978-1-4020-5028-2 (HB)
ISBN-10 1-4020-5030-5 (e-book)
ISBN-13 978-1-4020-5030-5 (e-book)

Published by Springer,
P.O. Box 17, 3300 AA Dordrecht, The Netherlands.

www.springer.com

Printed on acid-free paper

CONTENTS

PREFACE

This volume comprises the proceedings of a NATO Advanced Study Institute (ASI) held at Geilo, Norway, 11-21 April 2005, the eighteenth ASI in a series held every two years since 1971. The objective of this ASI was to identify and discuss areas where synergism between modern physics and biology may be most fruitfully applied to the study of bioprocesses for molecular recognition, and of networks for converting molecular reactions into usable signals and appropriate responses.

Many fields of research are confronted with networks. Genetic and metabolic networks describe how proteins, substrates and genes interact in a cell; social networks quantify the interactions between people in the society; the Internet is a complex web of computers; ecological systems are best described as a web of species. In many cases, the interacting networks manifest so-called emergent properties that are not possessed by any of the individual components. This means that the detailed knowledge of the components is insufficient to describe the whole system. Recent work has indicated that networks in nature have so-called scale-free characteristics, and the associated dynamic network modelling shows unexpected results such as an amazing robustness against accidental failures, a property that is rooted in their inhomogeneous topology. Understanding these phenomena and turning them to use in chemical and biological threat detection and response will require exploring a wide range of network structures as well. Questions related to error and attack tolerance of complex networks and their robustness in particular, and the dynamics of networks in general also have to be addressed. Modelling the signal transduction networks in bioprocesses as in living cells is a challenging interdisciplinary research area. It is now realized that the many features of molecular interaction networks within a cell are shared to a large degree by the other complex systems mentioned above, such as the Internet, computer chips and society. Thus knowledge gained from the study of complex non-biological systems can be applied to the intricate braided relationships that govern cellular functions. Bio-inspired processes provide an attractive option for sensing chemical and biological (CB) agents because nature has solved many of the problems inherent to the sense-and-respond task. For example, many biological responses such as blood clotting, gene expression and the activation of enzymes require enormous amplification of signals carried by as few as a single molecule or ion. Adaptability to local environments, atomic level control of self-assembled structures, benign processing, combinatorial synthesis and complex computation are other features of biological systems that are likely to prove useful in CB sensor development.

The starting point, and the underlying theme throughout the ASI, was a thorough discussion of general network theory. The next focus was on genetic networks and bioprocesses. Finally, focus was placed on the possible universality of network structures and how this knowledge can be combined to attack the urgent problem of rapid detection and diagnosis of CB agents.

The NATO ASI format in Geilo proved very efficient in getting researchers in different areas together and focus on the underlying theme that was common to all of them – that of networks and bioprocesses. In this manner a rapid communication was possible because a common vocabulary was developed during the ASI.

The scientific content of the school was timely and these proceedings should provide a useful definition of the current status. The Institute brought together many lecturers, students and active researchers in the field from a wide range of countries, both NATO and NATO Partner Countries. The lectures fulfilled the aim of the Study Institute in creating a learning environment and a forum for discussion on the topics stated above. They were supplemented by a few contributed seminars and a large number of poster presentations. These seminars and posters were collected in extended abstract form and issued as an open report available at the Institute for Energy Technology, Kjeller, Norway (Report IFE/KR/E-2005/005, ISBN 82-7017-535-8).

Financial support was principally from the NATO Scientific Affairs Division, but also from the Institute for Energy Technology and the nationally coordinated research team COMPLEX in Norway.

The editors are most grateful to M.H. Jensen, J.L. McCauley, R. Pynn and H. Thomas who helped them plan the programme and G. Helgesen for helping with many practical details. Finally, we would like to express our deep gratitude to Trine Løkseth of the Institute for Energy Technology, for all her work and care for all the practical organization before, during, and after the school, including the preparation of these proceedings.

December 2005

Arne T. Skjeltorp Alexander V. Belushkin

LIST OF PARTICIPANTS

Organizing Committee:

Skieltorp, Arne T., Director
Institute for Energy Technology, POB 40, N-2027 Kjeller, Norway

Belushkin, Alexander V, Co-director
Frank Laboratory of Neutron Physics, Joint Institute for Nuclear Research, 141980
Dubna, Moscow region, Russia

Helgesen, Geir, Technical assistant
Institute for Energy Technology, POB 40, N-2027 Kjeller, Norway

Løkseth, Trine, Secretary
Institute for Energy Technology, POB 40, N-2027 Kjeller, Norway

Participants:

Andersson, Anna
Hillerodsgade 69, 2200 Copenhagen, Denmark

Amatori, Andrea
Gruppo di fisica del nucleo Dipartimento di fisica, via celoria 16, 20133
Milano, Italy

Angheluta, Luiza
Peder Skrams Gade, 26, 4tv., 1054 Copenhagen

Apostol, Simona
Physics Department, Faculty of Sciences, Valahia University, 24 Bd
Unirii, 0200 Targoviste, jud Dimbovita, Romania

Bakaeva, Zulfiya
28, Katartal street, 700 135, Tashkent, Uzbekistan

Barabasi, Albert
Department of Physics, 225 Nieuwl and Science Hall, University of Notre
Dame, Notre Dame, IN 46556, USA

Beck, Peter
Sicherheit und Risiko, Austrian Research Centers GmbH – ARC, A-2444
Seibersdorf, Austria

Bernhardsson, Sebastian
c/o J. Hansen, Osterbrogade 95, 2100 Copenhagen, Denmark

Bock Axelsen, Jacob
Niels Bohr Institutet, Blegdamsvej 17, DK-2100 Copenhagen Ø, Denmark

Cernak, Jozef
University of P.J. Safarik, Department of Biophysics, Jesenna 5,
SK-04000 Kosice, Slovak Republic

Christophorov, Leonid
Bogoliubov Institute for Theoretical Physics, NAS Ukraine, 14 B
Metrologichna Str, Kiev 03143, Ukraine

da Silva, Geraldo José
Instituto de Fisica, Universidade de Brasilia, CP 04525 70919-970
Brasilia DF, Brazil

Dmitrochenko, Oleg
Department of Mechanical Design Engineering, RIMT, CAE Lab, Pusan
National University, 30 Jangjeon-Dong, Geumjeong-Gu, Busan 609-735,
South Korea

Duman, Memed
Institude of Graduate and Applied Sciences, Bioengineering Division,
Hacettepe University, Beytepe, 06800 Ankara, Turkey

Eisler, Viktor
Institute for Theoretical Physics, Eotvos University, 1117, Pazmany
setany 1/A, Hungary

Einevoll, Gaute T.
Department of Mathematical Sciences and Technology
Norwegian University of Life Sciences, P.O.Box 5003, N-1432 Aas,
Norway

Elgsaeter, Arnljot
Department of Physics, NTNU, Høgskoleringen 5, N-7491 Trondheim,
Norway

Fossum, Jon Otto
NTNU Department of Physics, Høgskoleringen 5, N-7034 Trondheim, Norway

Garipcan, Bora
Institute of Graduate and Applied Sciences, Bioengineering Division
Hacettepe University, Beytepe, 06800 Ankara, Turkey

Giaever, Ivar
Institute of Science, Rensselaer Polytechnic Institute, Troy, NY 12180, USA

Goksu, Huseyin
Istiklal Mh. Fatih Sk. 21/5, Isparta, 32300, Turkey

Grigoryan, Arsen
Departmetnt of Molecular Physics Faculty of Physics, Yerevan State University, Al. Manoogian Str. 1, Yerevan 375025, Annenia

Hamedi, Mahiar
Inst. för fysik och mätteknik, Linköpings Univesitet/Tekniska Högskolan, 581 83 Linköping, Sweden

Hansen, Alex
Institutt for fysikk, NTNU Gløshaugen, N-7491 Trondheim, Norway

Heiberg-Andersen, Henning
Institute for Energy Technology, POB 40, NO-2027 Kjeller, Norway

Hervoches, Charles
Institute for Energy Technology, POB 40, NO-2027 Kjeller, Norway

Hritz, Jozef
Department of Biophysics, PF-UPJS, Jesenna 5, 04154 Kosice, Slovak Republic

Høgh Jensen, Mogens
Niels Bohr Institute, Blegdarnsvej 27, DK-2100 KØBENHAVN Ø, Denmark

Karlik, Bekir
Department of Computer Engineering, Engineering Faculty, Halic University, Molla Gurani cad. No. 16-18 Findikzacle, 34280-Istanbul, Turkey

Kharlamov, Alexey
3 Krjijanovskiy str., 03142 Kiev, Ukraine

Kharlamova, Ganna
14, Glushkov str., aprt.89., 03187 Kiev, Ukraine

Khizanishvili, Ana
E.Andronikashvili Institute of Physics, 6 Tamarashvili str., Tbilisi, 0177, Georgia

Knudsen, Kenneth D.
Institute for Energy Technology, POB 40, NO-2027 Kjeller, Norway

Kristiansen, Kai de Lange
Fysisk Institutt, University of Oslo, Box 1048 Blindern, 0316 OSLO, Norway

Korraa, Soheir
3 Ahmed El Zomour St. 8th Sector P.O. Box 29 Nasr City, Cairo, Egypt

Krishna, Sandeep
Niels Bohr Institute, Blegdamsvej 17, DK-2100 Copenhagen O, Denmark

Libchaber, Albert
Laboratory of Experimental Condensed Matter Physics, The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA

Lunika, Michael
58 Petropavlovskaja Str., Sumy 40030, Ukraine

Marconi, Daniela
c/o Dipartimento di fisica Campaninini Renato, Viale Berti Pichat 6/2, 40100 Bologna, Italy

Maslov, Sergei
Department of Physics, Brookhaven National Laboratory, Upton, NY 11973, USA

Mathiesen, Joachim
Department of Physics, NTNU, Hogskoleringen 5, 7491 Trondheim, Norway

McCauley, Joseph L.
Tiefetfeld Str. 14, A6632 Ehrwald, Austria

Méheust, Yves
Department of Physics, NTNU, Hogskoleringen 5, 7491 Trondheim, Norway

Micheelsen, Mille Ankerstjeme
The Niels Bohr Institute, University of Copenhagen Blegdamsvej 17, DK-2100 Copenhagen Ø, Denmark

Måløy, Knut Jørgen
Fysisk Institutt, University of Oslo, Box 1048 Blindem, 0316 Oslo, Norway

Muller, Jiri
Institute for Energy Technology, POB 40, NO-2027 Kjeller, Norway

Nawrocki, Waldemar
ul. Piotrowo 3A, PL-60965 Poman, Poland

Nepusz, Tamas
Department of Biophysics, Research Institute for Particle and Nuclear Physics, Konkoly – Thege Miklos u. 29-33, 1121 Budapest, Hungary

Oddershede, Lene
Niels Bohr Institute, Blegdamsvej 17, DK-2100 Copenhagen, Denmark

Oliveira, Fernando A.
International Center for Condensed Matter Physics, Universidade de Brasilia, CP 04513, 70919-970 Brasilia DF, Brazil

Ostrovsky, Mikhail
Institute of Bio-Chemical Physics, Russian Academy of Sciences, Kosygin St 4, 117334 Moscow, Russia

Podolskaya, Olga
Heat Physics Department, Uzbekistan Academy of Sciences, Katartal 28, Tashkent 700135, Uzbekistan

Priezzhev, Vyacheslav, B
Office 203, Sector 14, BLTPJINR, 141980 Dubna, Moscow Region, Russia

Pynn, Roger
Materials Research Lab., UCSB, Santa Barbara, CA 93106-5130, USA

Ramos, Osvanny
Department of Physics, P.O. Box 1048 Blindern, N-0316 Oslo, Norway

Rosvall, Martin
Institutionen för fysikk, Umeä universitet, 90187 Umeä, Sweden

Santucci, Stephane
Department of Physics, P.O.Box 1048 Blindem, N-0316 Oslo, Norway

Shantsev, Daniel
Department of Physics, University of Oslo, POB 1048 Blindern, NO-0316 Oslo, Norway

Sherrington, David
University of Oxford, Theoretical Physics, I Keble Rd. Oxford OXI 3NP, United Kingdom

Sibanf, Paolo
Fysisk Institut, SDU, Campusvej 55, DK5230 Odense M, Denmark
Skau, Karl Isak
Department of Mathematics and Statistics, University of Surrey, Guildford, Surrey, GU2 7XH, United Kingdom

Skoge, Monica
Grad College – Princeton Univ., 88 College Rd., West Princeton, NJ 08544, USA

Skotheim, Jan
Cambridge University, Queens College, Cambridge CB3 9ET, United Kingdom

Stan, Mariana
Sat Straosti nr. 99, Comuna Dragodana, Judet Dambovita, Cod 0184, Romania

Sneppen, Kim
Nordita, Blegdamsvej 17, 2100 Copenhagen OE, Denmark

Stavans, Joel
Department of Physics of Complex Systems, Weimann Institute of Science, PO Box 26, Rehovot 76100, Israel

Steinsvoll, Olav
Institute for Energy Technology, POB 40, NO-2027 Kjeller, Norway

Svåsand, Eldrid
Institute for Energy Technology, POB 40, NO-2027 Kjeller, Norway

Tchesskaya, Tatyana
Department of Information Technology, Odessa State Environmental University, 15 Lvovskaya str., 65016 Odessa, Ukraine

Thomas, Harry
Dept. of Physics, University of Basel, CH-4056 Basel, Switzerland

Tourleigh, Yegor
Leninskiye Gory, 1/12, Dept. of Biophysics, Moscow State University, Russia

Tropin, Timur
FLNP, JINR, 141980 Dubna, Moscow reg, Russia

STRUCTURE AND COMMUNICATION IN COMPLEX NETWORKS

KIM SNEPPEN
Center for Models of Life
Niels Bohr Institute, Blegdamsvej 17,
2100 Copenhagen

1. Introduction

Networks is tool to describe systems composed of many different units which each typically interact with a few of the other units. Networks thus used to quantify complex systems from the intricate interactions of proteins inside a living cell, to ecosystems, social systems and computer networks. In most cases the network quantify communication channels in the system. Thus directly connected nodes communicates easy, while more distant nodes only obtain exchange information through a number of intermediate steps. In fact already in 1982 a detailed study of social networks within university departments revealed that mutual information of one member about another one was decaying exponentially with their distance, and increased linearly with number of common friends (degenerate paths). We will take this viewpoint and consider a Network as a description of who get direct information from who, and which parts that has to resort to second hand or even more inaccurate information: networks quantify the extent to which complex systems operate under the constraints of a limited information horizon.

In the text we will first review a few facts about real world networks, including broad degree distributions and degree correlations and some simple models for how such broad degre distributions may self organize. Secondly we introduce a few measures to characterize the topology of network: Correlation profiles, network motifs, topological hierarchy, search information and a measure for order in topology of the networks. Thirdly we discuss self organization of networks under various degrees of limited information. Finally we discuss biological networks, with focuss on basic physics of gene regulation.

A.T. Skjeltorp and A.V. Belushkin (eds.),
Dynamics of Complex Interconnected Systems: Networks and Bioprocesses, 1–28.

2. Basic Network Concepts

In Figure 1-4 we define a few basic quantities in graph theory. For a pair of nodes one define their distance as the length of the shortest path between them. For a connected graph we can define its diameter as the maximum distance between pairs. Examples of graphs include lattices in any dimension.

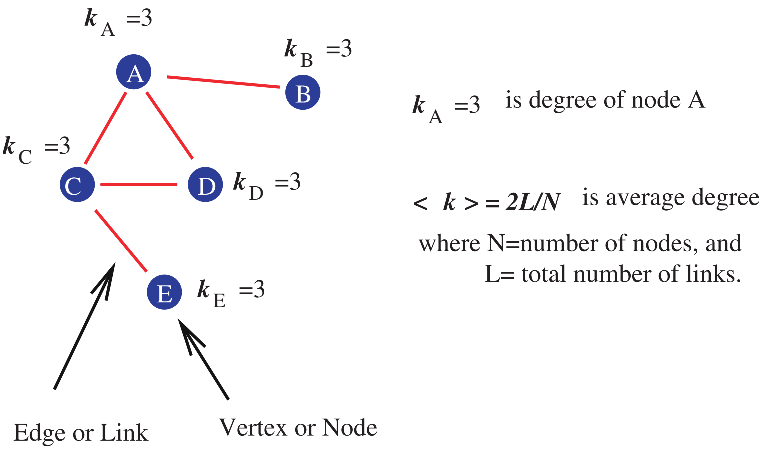


Figure 1. A graph, with nodes and edges.

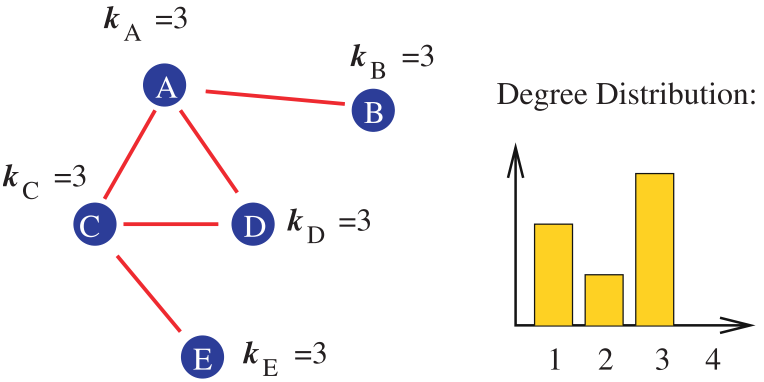


Figure 2. Degree distribution, here for undirected graph.

We now want to consider the simplest possible model for a random graph, the Erdos-Reynei Graph. In this type of graph one have N nodes, each pair connected to each other with probability p. The average (expected number of edges would be $L = p \cdot N(N-1)/2$. The degree distribution (probability that a given node have k links to the remaining N-1 nodes) will be

$$P(k) = C^k_{N-1} p^k (1-p)^k \tag{1}$$

where $C^k_{N-1} = (N-1)!/(k!(N-1-k)!)$. For a random graph one gain the neighborhood of any node increases by factor $\langle k \rangle$ for each step out in the graph (for large graphs, as long as there is essentially zero probability to reach same nodes through two different paths). Thus the network is traversed when

$$\sum_{i=0}^{diam} \langle k \rangle^i \approx N \tag{2}$$

that is when $diam = log(N)/log(\langle k \rangle)$, i.e. the distance between any two points in a random graph grows very slowly with its overall size.

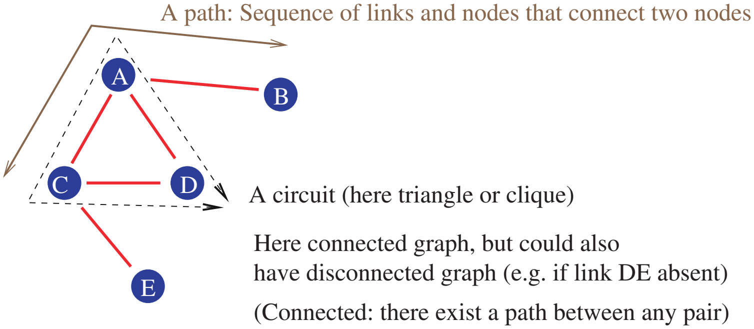
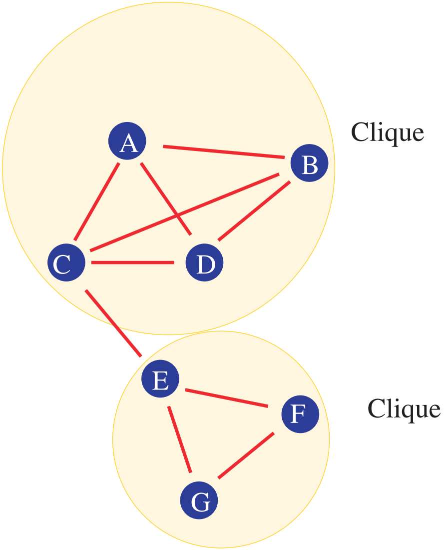


Figure 3. Path's in graphs.

Another quantity which often is used to characterize networks is their cliquishness. For each node this is defined as the fraction shown in Fig 4, meaning that a large cliquishness indicate large locality in the network everybody knows each other locally).

A network is defined as having small world property, when it is having a relatively large cliquishness, while still having a diameter of order $log(N)/log(k)$. Many networks are indeed found to have this interplay between global accessibility and local connectedness.

Finally we would like to stress that a network also have a unique matrix representation, A_{ij} where a link from node i to node j implies that $A_{ij} = 1$. A undirected network, even a symmetric matrix, $A_{ij} = A_{ji}$. The matrix representation opens for some simple manipulation where one for example can calculate the number of triangles in a network $= trace A^3/6$, where the factor $6 = 3 \cdot 2$ comes from going two ways around each triangle, and from starting the triangle a any of the three nodes.



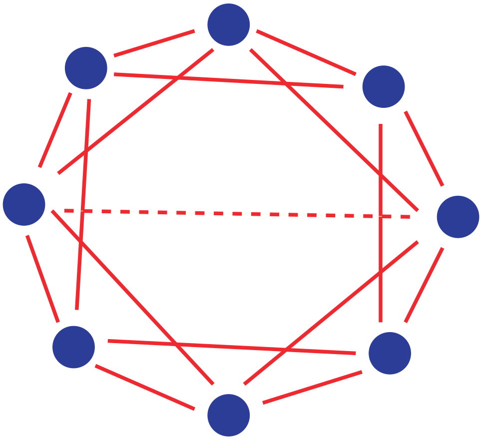
$$C_A = \frac{\text{no. of cliques}}{\text{max no of cliques}}$$

$$= \frac{\text{no. of cliques}}{k_A(k_A - 1)/2}$$

$$= \frac{3}{3} = 1$$

$$C_C = \frac{3}{6}$$

Figure 4. Cliquishness definition: the fraction of possible triangles that a node participate in, given its degree. If all its friends are friends, its cliquishness is 1.



Network with rater large cliquishness

C = 3/6 (except ––––

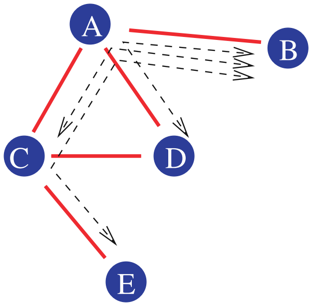
and with few additional links (–––), it also have rather small diameter.

Then SMALL WORLD

Figure 5. Small world network (Watts and Strogatz).

3. Real Networks

From the genetic blueprint in our DNA to the world-wide Internet, information and its dynamic counterpart communication sets the stage for further action. However, we live under the limited information horizon, in the sense that information is often imperfect and communication is always finite. Many complex systems are associated with information transfer. This includes neural networks with their synaptic rewiring, molecular networks



Betweenness:

The betweenness of a node is
number of shortest paths
that goes through the node

β_A = no. path through A = 3

similar definition of link betweenness

(Freeman, Sociometry 1977)

Figure 6. Betweenness (load) on a node, assuming that all transport goes through shortest paths.

evolved to modulate the protein activity in living cells, and social networks exemplified by the Internet. Below we show respectively the worldwide internet, a social network and some examples of molecular networks inside living cells. In all these cases the purpose of the network is to serve as a scaffold for information transfer.

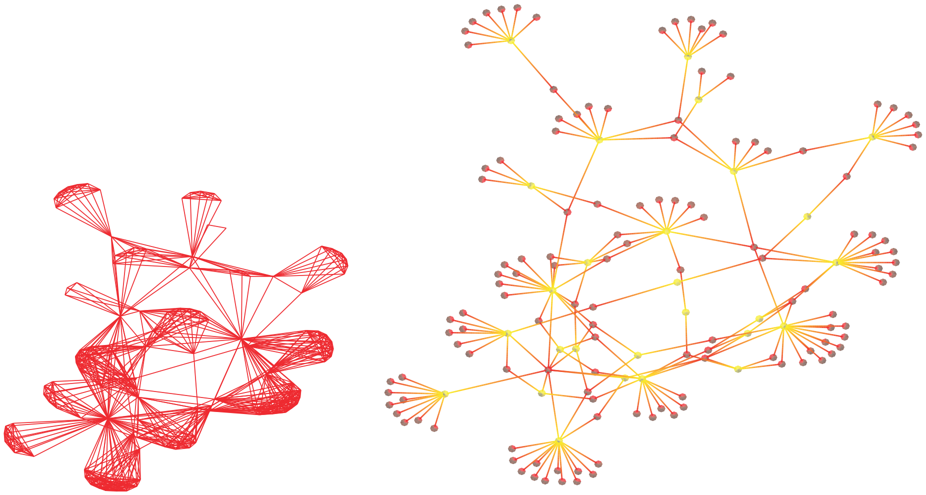


Figure 7. Directors in US: Left representation, connected by link if two nodes in same board. Right representation: Bipartite network representation consist of respective board nodes and member nodes, defining two distinct classes of nodes. In a bipartite graph there are only links from nodes in one class to a node in the other class. The shown network is a small sub-part of the full network of all CEO's in USA.

For many real world networks, the distribution of proteins with a given number of neighbors (connectivity) K may (very crudely) be approximated by a power law

$$N(K) \propto 1/K^{\gamma} \tag{3}$$

with exponent $\gamma \sim 2.5 \pm 0.5$ (Jeong et al. (2001)) for protein-protein binding networks, and exponent $\gamma \sim 1.5 \pm 0.5$ for “out-degree” distribution of transcription regulators. Notice that the distribution of the number of proteins a given protein regulate, the “out-degree”, differs from the much more narrow distribution of “in-degrees”. We would now like to discuss features and possible reasons for why life may have chosen to organize its signaling in this way.

One aspect of a wide distribution of connectivity, is the possible amplification of signals in the network. Consider a signal that enters a node, and assume that it is transmitted along all exit links (unspecific broadcasting). Thus it is amplified by a factor K_{out}. However, not all nodes has equal chance to amplify signals. The probability to enter a node is proportional to K_{in}. Thus one in average visit nodes with probability $\propto K_{in}$ and the weighted average amplification factor in a *directed* network (Newman et al. 2001):

$$\mathcal{A} = \frac{\langle K_{in} K_{out}(given \;\; K_{in}) \rangle}{\langle K_{in} \rangle} = \frac{\langle K_{in} K_{out} \rangle}{\langle K_{in} \rangle} \tag{4}$$

The first equality assumes that there is no correlations between degree of a node and the degree of its neighbors. The second equality assumes that there is no correlations between a given proteins “in” and “out” degree. For undirected random network the amplification would be:

$$\mathcal{A} = \frac{\langle K(K-1) \rangle}{\langle K \rangle} \tag{5}$$

If all nodes has close to the same connectivity we recover the simple result that when $\langle K \rangle = 2$ then $\mathcal{A} = 1$. Thus to have marginal transmission, one input signal in average should lead to one output signal through a new exit. When $\mathcal{A} > 1$ signals tends to be exponentially amplified, and thus most signals will influence signaling over the entire network. For broad connectivity distributions $\mathcal{A}$ typically depend on the node with highest connectivity. To see this, assume that the number degree distribution is power law distributed (eq. 3). Then:

$$\mathcal{A} = \frac{\int_1^N \frac{K^2 dK}{K^{\gamma}}}{\int_1^N \frac{K dK}{K^{\gamma}}} - 1 \sim N^{3-\gamma} \tag{6}$$

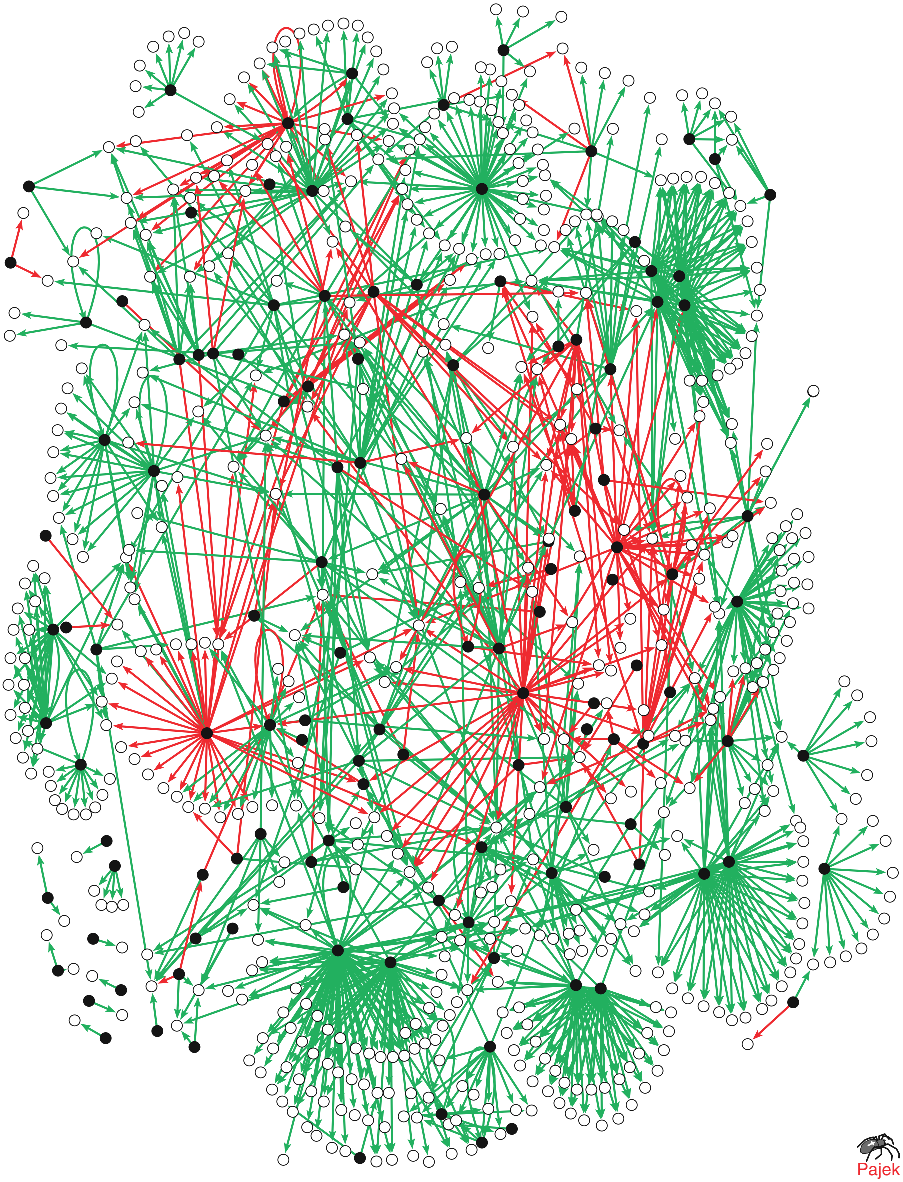


Figure 8. Presently known transcription regulations in Yeast (Sacromyces Cerevisia). Transcription regulation describes how one protein regulate the production of another protein. The network is directed, with both positive and negative regulations (see later for more detailed explanation).