A Useful Links

Note that URL addresses were checked as of January 2009.

Groups Working on Networks and Complex Systems

Adam P. Arkin	`http://genomics.lbl.gov/`
László A. Barabási	`http://www.barabasilab.com/`
Yaneer Bar-Yam	`http://necsi.org/publications/dcs/`
Eric L. Berlow	`http://www.ericlberlow.net/`
György Buzsáki	`http://osiris.rutgers.edu/frontmid/indexmid.html`
Gerald M. Edelman	`http://www.scripps.edu/nb/chair.html`
Jennifer H. Fewell	`http://sfi.cyberbee.net/jennifer.html`
Murray Gell-Mann	`http://www.santafe.edu/∼mgm/`
John Gerhart	`http://mcb.berkeley.edu/faculty/CDB/gerhartj.html`
Mark Granovetter	`http://www.stanford.edu/dept/soc/` `people/mgranovetter/index.html`
Stuart A. Kauffman	`http://en.wikipedia.org/wiki/Stuart_Kauffman`
János Kertész	`http://www.phy.bme.hu/∼kertesz/`
Marc W. Kirschner	`http://sysbio.med.harvard.edu/faculty/kirschner/`
Susan Lindquist	`http://www.wi.mit.edu/research/faculty/` `lindquist.html`
Kevin S. McCann	`http://www.uoguelph.ca/zoology/` `department/people/faculty/k_mccann.htm`
Mark J. Newman	`http://www-personal.umich.edu/∼mejn/`
Zoltán N. Oltvai	`http://path.upmc.edu/people/faculty/oltvai-lab/`
Sándor Pongor	`http://www.icgeb.org/sandor-pongor.html`
Nikos A. Salingaros	`http://www.math.utsa.edu/sphere/salingar/`
Ricard V. Solé	`http://complex.upf.es/`
Steven H. Strogatz	`http://tam.cornell.edu/Strogatz.html`
Tamás Vicsek	`http://angel.elte.hu/∼vicsek/` `http://www.cfinder.org`
Duncan J. Watts	`http://www.sociology.columbia.edu/` `fac-bios/watts/faculty.html`

Libraries and General Databases

E-libraries

`http://www.arxiv.org`
`http://www.santafe.edu/research/publications/`
`publications-working-papers.php`
`http://cogprints.org`
`http://comdig.com`
`http://www.nslij-genetics.org/wli/1fnoise/`

Mathematical Tools

Network map
construction

`http://vlado.fmf.uni-lj.si/pub/networks/pajek`
`http://biodata.mshri.on.ca/osprey/servlet/Index`
`http://strc.herts.ac.uk/bio/maria/NetBuilder/`
`http://paup.csit.fsu.edu`
`http://taxonomy.zoology.gla.ac.uk/rod/`
`treeview.html`

Network modules

`http://www.cfinder.org`

Digital organism
development programs

`http://physis.sourceforge.net`

Protein Networks

Protein interaction databases
(mostly yeast)

`http://www-unix.mcs.anl.gov/compbio`
`http://yeast.cellzome.com`
`http://www.bind.ca`
`http://dip.doe-mbi.ucla.edu/`

Human protein reference
database

`http://hprd.org`

Subnetwork analysis

`http://networks.gersteinlab.org/`

Metabolic Networks

Modeling of biochemical reactions   `http://www.gepasi.org/`

Whole cell simulation   `http://www.nrcam.uchc.edu/`

Metabolic networks (general)   `http://metacyc.org`

Metabolic networks (yeast)   `http://www.genome.ad.jp/kegg/`
`http://systemsbiology.ucsd.edu/`
`organisms/yeast.html`

Metabolic networks
(*Escherichia coli*)

`http://gcrg.ucsd.edu/organisms/`
`ecoli.html`

Red blood cell   `http://systemsbiology.ucsd.edu/`
`organisms/rbc.html`

Transcriptional Networks

Gene interactions and pathways	`http://www.biocarta.com/genes/`
	`allpathways.asp`
	`http://www.cifn.unam.mx/`
	`Computational_Genomics/regulondb`
	`http://strc.herts.ac.uk/bio/maria/`
	`NetBuilder/`

Escherichia coli transcriptional network	`http://www.weizmann.ac.il/mcb/UriAlon`
Yeast sporulation network	`http://cmgm.stanford.edu/pbrown/` `sporulation`

Gene expression databases	`http://www.ebi.ac.uk/arrayexpress`
	`http://www.ncbi.nih.gov/geo`
	`http://transcriptome.ens.fr`
	`http://www.gene-regulation.com`

Specific Biological Databases

Bacterial chemotaxis simulation program	`http://www.pdn.cam.ac.uk/groups/` `comp-cell`
Homepage of complex physiological signals	`http://www.physionet.org`

Neuronal networks	`http://www.cocomac.org/databases.htm`
	`http://www.ncl.ac.uk/biol/research/`
	`psychology/nsg/neuroinformatics.htm`

Social Nets

Social network analysis	`http://www.sfu.ca/~insna/`
Business networks	`http://www.theyrule.net`
Dark networks	`http://www.orgnet.com/hijackers.html`
Zachary friendship network	`http://vlado.fmf.uni-lj.si/pub/` `networks/data/UciNet/zachary.dat`
Internet	`http://moat.nlanr.net/AS/`
Textual networks	`www.textarc.org`
Network visualizations	`www.visualcomplexity.com`

B Glossary

This glossary explains a few of the key words used in the book. I would like to apologize if a specific meaning is sometimes given for a word to define it in a way which is used only in this book and slightly restricts or modifies the definition of the same word used in other contexts. Glossary items are marked with *italics* in the explanations for cross-reference.

Allometric scaling laws. Allometric scaling laws cover a wide variety of empirical scaling relationships where the given property is a power law function of the mass. The defining equation of allometric scaling laws is $P = cM^\alpha$, where P means the property, c is a constant, M is the mass of the organism or organelle, and α is a scaling exponent which varies depending on the nature of P. In the most studied example, viz., Kleiber's law (1932), P is the basal metabolic rate and the scaling exponent α is $3/4$. In other examples, the value of the exponent may be different, e.g., the dependence of heart rate ($\alpha = -1/4$), life span ($\alpha = 1/4$), the radii of aortas and tree trunks ($\alpha = 3/8$), the unicellular genome length ($\alpha = 1/4$), and RNA concentration ($\alpha = -1/4$), on the mass all have different exponents in their scaling relationship.

Assortativity. We call a *network* assortative, if similar *elements* of the network are selectively and preferentially linked. The elements may be similar by their *degree* or by any other property.

Attractor. The attractor is a set of *network* states on the *stability* mono- or multi-*landscapes* which behaves as a focus where members of a much larger set of network states converge as the network undergoes dynamical changes.

Betweenness centrality. The betweenness centrality of an *element* i is the fraction of shortest paths between any pair of elements in the

network which pass through the i th element. (For the definition of the shortest path, see *path length*.)

Canalization. Canalization refers to a reduced sensitivity of an organism to noise from the environment or towards changes in its genotype. In Waddington's formulation, canalization is "the capacity to produce a particular definite end-result in spite of a certain variability both in the initial situation from which development starts and in the conditions met with during its course."

Chaperone. A chaperone, or molecular chaperone, is a protein which helps the folding of other proteins by preventing their aggregation or by partially unfolding them to give them a new opportunity to refold. Chaperones may be RNAs. Both protein- and RNA-chaperones may help the folding of RNAs, besides their help in protein folding. A chaperone is often a stress protein or heat shock protein, which means that its synthesis is induced by *stress* or heat shock, respectively.

Clustering (coefficient). Clustering occurs if neighbors of an *element* have a good chance of being connected. The clustering coefficient is the probability that two neighbors of a given element are also neighbors of each other. The clustering coefficient C for an element is the number of links between all the neighbors of the element (n) divided by the number of links that could possibly exist between all the neighbors of the element (N), i.e., $C = n/N$ (Watts, 1999). Clustering is also often called network transitivity. The range of the clustering coefficient varies between 0 and 1, and the average of all clustering coefficients gives a general measure of the cluster (triangle) formation in a network (Barabasi and Oltvai, 2004).

Cognitive dimensions. In the context of the present book, cognitive dimensions refer to the number of different views (personalities) a person can simultaneously accommodate and evaluate. This process requires the internalization, relative separation and internal conflicts of the intentions, drives, words and deeds of the real or imagined persons, groups of persons or value sets. A typical sentence to reflect this complexity is the following: I believe that A supposes that B intends to guess how C understands what D thinks. Dunbar (2005) shows that the typical average cognitive limit is around 5 cognitive dimensions. However, exceptional minds can think to the 6th or higher order. The

cognitive dimensions probably reflect the number of stable oscillation sets a certain person's brain sections can simultaneously accommodate and process.

Creative elements. Creative elements are special elements, or element sets of the networks, which occupy a central position, a structural hole in the network integrating the communication of the entire network. Creative elements are very dynamic, performing a partially random sampling of the whole network, and connecting distant network modules. Creative elements have transient, weak links leading to important positions (often hubs) in the network, and become especially important when the whole system experiences an atypical situation requiring a novel, creative solution. Typical examples of creative elements are the active centres of proteins, the stress proteins of cells, stem cells of organisms, practically any neuron in our brain, and (last but not least) creative people, or groups. Creative elements play a key role in the development, survival and evolvability of complex systems (Csermely, 2008).

Degeneracy. A *network* is degenerate if structurally different elements of the network show a functional identity under special circumstances. (See also *redundancy*.)

Degree (distribution). The degree of a network element corresponds to the number of *links* of this element. The degree distribution is the histogram of the total number of elements of the network with a given degree. The degree distribution is a Poissonian distribution for the Erdős–Rényi *random graph* and exponential for single-scaled graphs. It follows a power law for *scale-free* graphs (Barabasi and Oltvai, 2004). The average degree is usually called the coordination number of the network. The origin of the expression 'coordination number' refers to regular lattices where all elements have the same degree.

Element. The element is a single building block of a *network*. The element is also called a vertex in graph theory, site in physics, or actor in sociology. The number of elements is called the order of the graph.

Emergent property. The emergent property of a *network* is derived from the interaction of the network *elements*, and is not observable or

inherent in any element of the network considered separately.

Epigenetic inheritance. We call inheritance epigenetic if the inheritable property is not transmitted via a DNA sequence but is inherited by means of other molecular mechanisms. Such a mechanism may use the modulation of DNA accessibility by DNA methylation or histone modification. Epigenetic molecular mechanisms also include RNA- and protein-based inheritance.

Evolvability. Evolvability is the ability of random genetic variation to produce phenotypic changes that can increase *fitness* (intrinsic evolvability), or the ability of a population to respond to selection (extrinsic evolvability). Extrinsic evolvability depends on intrinsic evolvability as well as on external variables such as the history, size and structure of the population (Rutherford, 2003). In the present book, evolvability is mostly used in a broader context, accommodating all mechanisms which determine the ability of a network to respond to changes in the environment.

Exponential cutoff (decay). Most natural scale-free distributions lose their scale-free pattern after a few orders of magnitude. Beyond the scale-free distribution, the probability of the extreme value decays very sharply, usually in an exponential manner.

Fitness. The survival value and reproductive capacity of a given phenotype as compared with the average of the population or other genotypes of the population.

Fractal. Fractal objects are generated by a recursive process in which self-similar objects of different size are repeated. The self-similar objects have a *scale-free* size distribution. The distribution is characterized by the *fractal dimension*. Fractal behavior can be defined in time intervals as well (see *multifractal*).

Fractal dimension (Hausdorff dimension, Hurst exponent). Elements of self-similar, fractal objects have a scale-free size distribution. If we try to fill a larger object with smaller objects, we get the equation $N = (L/l)^d$, where N is the number of smaller objects fitted into the larger object, L/l is the ratio of the characteristic measure of the two objects of different size, and d is the exponent, which is cal-

led the fractal dimension. The fractal dimension in space is also called the Hausdorff dimension, and in time the Hurst exponent. In fractal objects, d is not an integer.

Fringe area. The fringe area is an overlap between two *modules* or two independent *networks*. It may either facilitate or prevent communication between the two connected modules or networks. This property of the fringe area can be tightly regulated and may change from time to time (Agnati et al., 2004).

Genetic drift. Genetic drift is a random change in allele frequency within a population. If the population is isolated and genetic drift continues for long enough, it may lead to specitation.

Genome cleansing. The cleansing of the genome occurs, when *stress* makes the consequences of otherwise *silent mutations* visible at the level of the phenotype. Under stress, organisms that have mutations with unfavorable consequences will be sorted out by natural selection. As a consequence the average genome of the whole population will be more uniform, and will 'shed' many of the unfavorable silent mutations.

Giant component. The giant component is the largest part of the *network*, where all *elements* are connected to each other. The giant component contains most of the network elements and appears after the *percolation* threshold.

Hub. A hub is a highly connected *element* of the *network*. A hub usually has more than 1% of total connections.

Keystone species. The keystone species is an important *hub* of an ecosystem whose removal triggers many secondary extinctions and may cause the fragmentation of the whole *network*.

Le Chatelier principle. The Le Chatelier–Brown principle describes the behavior of a system when its equilibrium is perturbed. If a system in equilibrium suffers an effect which changes its conditions, the system will adjust itself to minimize this change.

Link. A link is a connection between two *network elements*. In graph theory, the link is called an edge of the graph. In molecular networks, the link is a bond, and in social networks, the word 'tie' is more often used. The number of links is the size of the graph.

Module. Modules are groups of network *elements* that are relatively isolated from the rest of the network and are functionally or physically linked to each other. Modules may arise from parcellation of a larger network, or from integration of several smaller networks.

Molecular crowding. Molecular crowding occurs if a significant volume of a solution, e.g., the cytoplasm, is occupied by macromolecules. Under such conditions, a large amount of water molecules are transiently bound to the macromolecules present and several phenomena will be drastically changed. As an example of this, protein–protein interactions will be grossly favored in crowded solutions.

Motif. Motifs, network blocks, or patterns are small groups of network *elements* with characteristic linkage patterns. Typical motifs are the feed-forward loops and feedback loops. (See also *negative feedback*.)

Multifractal. This is a distribution in time or space which displays a complex *scale-free* pattern with several scale-free distributions superimposed upon each other and in which the overall distribution has more than one scaling exponent. Multifractal behavior is usually found in time series. More precisely, time dependence in mathematical analysis is typically continuous with continuous derivatives. It can thus be approximated in the vicinity of a time t_i by a so-called Taylor series or power series:

$$f(t) = a_0 + a_1(t - t_i) + a_2(t - t_i)^2 + \cdots + a_h(t - t_i)^h + \cdots ,$$

where h is an integer. In contrast, most time series found in 'real' experiments cannot be approximated by the above formula. If a non-integer number of h is enough to quantify a local singularity in a noisy time series, we call the time series a fractal series. If we find a single value $h = H$ for all singularities t_i in the signal, then the signal is a monofractal. If we need several distinct values to describe the time series, than the signal is multifractal.

Negative feedback. Negative feedback is a common regulatory *network motif*, in which an increase in the quantity or function of a network *element* provokes an inhibition of the network elements which caused the increase.

Nested sync. This expression is used in the present book to denote the highly hypothetical induction of synchrony between oscillations at different *network* levels. In other words, nested sync occurs if an element of a top network synchronizes its oscillations with the oscillation of the whole top network, and this phenomenon continues through at least three hierarchical levels of networks. (See also *syntalansis*.)

Nestedness. The *elements* of most real *networks* are not points, but complex networks themselves. This means that real networks are often nested. However, the elements of abstract mathematical networks, known as graphs, are points with no internal structure.

Netquake. A netquake occurs if a *network* has a restricted relaxation and, after the gradual build-up of a tension, the network reaches a state of *self-organized criticality*. Restricted relaxation means that a perturbation of the network is not easily dissipated in the network. In the self-organized critical state, the probability and extent – size and duration – of netquakes often follow a *scale-free* distribution. (See also *pink noise*.)

Netsistance. The netsistance of a *network* refers to its stability against the removal of its *elements* or *links*. Whilst the network is able to preserve its *giant component* and *percolation*, it can be said to have maintained its netsistance. Loss of netsistance implies the death of the network if it is a biological system like a cell or other living organism.

Network. A network is a set of *elements* which are connected to each other by *links*. The elements of most real networks are not points, but complex networks themselves. This means that real networks are often *nested*. However, the elements of abstract mathematical networks, called graphs, are points with no internal structure.

Network diameter. The *network* diameter is the maximal number of *links* in the shortest *path* between any pair of network *elements*.

Node. A node is a *network element* with more than three *links*.

Path length. The path length is the number of *links* we have to pass along when we travel between two *network elements*. The shortest path length is the length of the shortest route between the two elements. The characteristic path length is the average of all the shortest path lengths in the network, and gives a good measure of the navigability of the network (Barabasi and Oltvai, 2004). (See also *network diameter*.)

Percolation (threshold). Percolation is the status of the *network* when it has a *giant component*, so that most of the network *elements* are connected with each other and can therefore communicate. The percolation threshold is the number of *links* when the network reaches percolation.

Pink noise. Noise is usually characterized as a sum of sinusoidal waves. The distribution of the constituent sinusoidal waves follows the equation $P = cD^{-\alpha}$, where P is the contribution of the sinusoidal wave, c is a constant, D is the frequency, and α is a scaling exponent. We call the noise pink if α lies between zero and two. The zero and two exponents correspond to white and brown noise, respectively. Pink noise is also called colored noise, flicker noise, crackling noise or Barkhausen noise. The names $1/f$, $1/t$ or $1/\tau$ noise refer to the situation where α is exactly unity. In pink noise, rare events have a greater effect on the noise than frequent events. This is the reason why this noise is said to be pink. The spectrum of pink noise is biased towards the low frequencies, which correspond to the red light in the spectral analogy with visible light. Therefore the spectrum of pink noise is 'reddened' compared to white noise, i.e., it is pink. Pink noise contains disturbances equally on all time scales, which means that pink noise is *scale-free*. In other words, *netquakes* of *self-organized critical* events are pink-noise processes.

Punctuated equilibrium. Punctuated equilibrium originally referred to a model of evolution in which change occurs in relatively rapid bursts followed by longer periods of stasis (Gould and Eldredge, 1993). In the present book, the expression is used in a more general context. Here, punctuated equilibrium refers to changes of a network on a 'rough' *stability landscape*, where the probability of transition between local minima is relatively low. This gives the same rapid burst and stasis dynamics that characterize the original description, but makes the expression useful to describe changes on the protein energy land-

scape, the evolutionary fitness landscape, the innovation landscape, software design landscape, scientific progress landscape, the landscape of economic markets, the diegetic landscape of plays, films and novels and any other 'rough' landscapes.

Random graph. The random graph is a mathematical representation of a *network* in which network *elements* are connected at random. The random graph has a Poissonian ('single scale') degree distribution, in which nodes with *degree* deviating significantly from the average degree are extremely rare (Barabasi and Oltvai, 2004).

Redundancy. Two structurally identical *network elements* are redundant. These elements double a certain function. Redundancy is different from *degeneracy*, where the functional identity is displayed only under special circumstances and arises from structurally different elements.

Regular lattice. The regular lattice is a *network* in which all elements have the same *degree*, and are arranged in highly periodical manner.

Resilience. The resilience of a *network* refers to its resistance against the removal of its *elements* or *links*. Resilience is usually measured by the disturbance of network communication (*percolation*). The expression 'resilience' is mainly used for ecological networks. In the present book, this form of network stability is generalized to all networks and called *netsistance*.

Robustness. A *network* is said to be robust if it displays a low sensitivity to environmental fluctuations (network perturbations). In ecosystems, robustness against the removal of *links* and *elements* is called *resilience* or (in the present book) *netsistance*.

Scale-free. A *network* is scale-free if its the *degree distribution* follows a power law. Generally, the distribution of scale-free systems can be written as $P = cM^{-\alpha}$, where P is the probability, c a constant, M the measure, and α a scaling exponent. The names Hurst exponent or *fractal dimension* are used for the scaling exponent when the scale-free distribution is observed in time or space, respectively. Scale-free distributions are best visualized if we take the logarithm of the above equation to obtain $\log P = \log c - \alpha \log M$, which shows that the

logarithm of the probability is a linear function of the logarithm of the measure. If we plot the data with this log–log representation (see Fig. 2.5 of Sect. 2.2), we get a straight line. Exceedingly large numbers have a non-zero probability in scale-free distributions. For an order of magnitude higher value, we always have a probability just an order of magnitude lower (Barabasi and Oltvai, 2004). (See also *pink noise*.)

Self-organized criticality. Self-organized criticality lacks a clear-cut definition. In the present book, the expression refers to *networks* where improper relaxation and an increasing tension spontaneously develop long-range correlations between network *elements*. The increasing correlations lead to a statistical steady state of criticality which is characterized by the occurrence of collective behavior manifested by avalanches. The avalanches display a *scale-free* size distribution and occur with a scale-free probability. (See also *pink noise*.)

Silent mutations (hidden mutations). Mutations of the DNA remain silent if their effect is not exposed at the level of the phenotype. Silent mutations may occur in DNA sequences which do not code proteins and are not involved in gene regulation. These mutations may remain silent forever. Silent mutations may also be conditional. These silent mutations may be revealed under specific (*stressful*) conditions, where the rest of the cellular networks cannot substitute the missing function by *redundant* or *degenerate network* segments. A specific form of silent mutation is hidden by *chaperones*. Here the mutation-induced changes in protein structure are repaired by chaperones. This repair becomes compromised after stress, when chaperones become occupied by damaged proteins. Thus, stress often exposes silent mutations at the level of the phenotype and makes them the subject of natural selection. This may cause a *cleansing of the genome* (where the occurrence of the silent mutation in the genome of the population is decreased) or derail *canalization* and give rise to a new dominant phenotype. In extreme cases, the exposure of silent mutations may even cause a jump in evolution.

Small world. We call a *network* a small world when its characteristic *path length* is close to the rather small path length of an Erdős–Rényi *random graph*, but its *clustering coefficient* is much higher than that of the random graph (Watts, 1999).

Social dimensions. The social dimension is the number of features of a social actor, i.e., a person or an element of a social *network*, which helps the classification of this element by other elements of the network. People often use social dimensions to direct and define efficient search and communication in social networks. Social dimensions are also used as an organizational pattern for *clustering*, *motif* and *module* formation in *assortative* social networks.

Stability landscape. On the stability landscape, each state (parameter set) of the *network* is plotted as a function of a 'goodness value'. The stability landscape may characterize any networks, such as proteins (energy landscape), ecosystems (fitness landscape), social networks (economy, innovation, design, scientific progress, etc., landscapes), informational, textual networks (the diegetic landscape of dramas, films and novels), etc. The 'goodness value' depends on the form of the stability landscape. The goodness value may be energy, fitness, market value, story integrity, etc. 'Rough' landscapes have very high goodness values, making high saddles between their local minima. High saddles make the probability of transition low. In contrast, 'buffed' landscapes have low saddles, which make the transition probability high. Rough landscapes often produce a *punctuated equilibrium* and may give rise to *self-organized criticality*.

Stress. Stress is any unexpected, large and sudden perturbation in the life of the *network*, (1) to which the network does not have a prepared adaptive response, or (2) where the network does not have time to mobilize an adaptive response. Stress in this book is used differently from stress in the usual sense in physics, where it is a force that produces strain on a physical body.

Syntalansis. Syntalansis is the extensive synchronization of the oscillators of *network elements*. The development of syntalansis displays a phase transition. As the difference between the frequencies of different oscillators is decreased below a certain threshold, they will suddenly all become synchronized, thereby achieving syntalansis. This phenomenon is similar to the *percolation threshold*.

Topological phase transition. A topological phase transition occurs if a continuous increase in the number of perturbations provokes a singular change in the global topology of the network. The global

topology is best monitored by the measure G/N, where G is the size of the largest connected component of the network and N is the total number of links. Alternatively, the measure $k_{\max}/M$ can also be used, where $k_{\max}$ is the largest degree of the network and M is the number of edges in the network (Derenyi et al., 2004; Palla et al., 2004).

Weak links. A *link* of a *network* is weak if its addition or removal does not change the mean value of a target measure, which is usually an *emergent property* of the network, in a statistically discernible way. Weak links stabilize most networks. The effects of weak links are described in every chapter of the present book.

References

The systematic update of the reference list is complete up to 31 August 2005. Additional key references have been added as of 31 January 2009. Before some of the references you will find one or two asterisks:

∗ a very interesting piece of work, from which I learned a lot;
∗∗ a seminal contribution, which you should read.

I would like to apologize for not including several groundbreaking papers in these categories. I restricted these signs to those papers which are necessary to understand the main message of this book: weak links stabilize complex systems. Moreover, I would like to apologize to those whose papers are not cited in the following list. The reference list is already rather voluminous. If I had inserted more papers, the text of the book would have become an appendix to the reference list and not vice versa.

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