Chapter 1 Random Boolean Networks

Complex system theory deals with dynamical systems containing a very large number of variables. The resulting dynamical behavior can be arbitrary complex and sophisticated. It is therefore important to have well controlled benchmarks, dynamical systems which can be investigated and understood in a controlled way for large numbers of variables.

Networks of interacting binary variables, i.e. boolean networks, constitute such canonical complex dynamical system. They allow the formulation and investigation of important concepts like phase transition in the resulting dynamical state. They are also recognized to be the starting points for the modeling of gene expression and protein regulation networks; the fundamental networks at the basis of all life.

1.1 Introduction

Boolean Networks In this chapter, we describe the dynamics of a set of N binary variables.

Boolean Variables. A boolean or binary variable has two possible values, typically 0 and 1.

The actual values chosen for the binary variable are irrelevant; ± 1 is an alternative popular choice. These elements interact with each other according to some given interaction rules denoted as coupling functions.

Boolean Coupling Functions. A boolean function $\{0,1\}^K \to \{0,1\}$ maps K boolean variables onto a single one.

The dynamics of the system is considered to be discrete, t = 0, 1, 2, ...The value of the variables at the next time step are determined by the choice of boolean coupling functions.



Fig. 1.1 Illustration of a boolean network with N = 4 sites. $\sigma_1(t+1)$ is determined by $\sigma_2(t)$, $\sigma_3(t)$ and $\sigma_4(t)$ (K = 3). The controlling elements of σ_2 are σ_1 and σ_3 (K = 2). The connectivity of σ_3 and σ_4 is K = 1

The Boolean Network. The set of boolean coupling functions interconnecting the N boolean variables can be represented graphically by a directed network, the boolean network.

In Fig. 1.1 a small boolean network is illustrated. Boolean networks at first sight seem to be quite esoteric, devoid of the practical significance for real-world phenomena. Why are they then studied so intensively?

Cell Differentiation in Terms of Stable Attractors The field of boolean networks was given the first big boost by the seminal study of Kauffman in the late 1960s. Kauffman casted the problem of gene expression in terms of a gene regulation network and introduced the so-called N-K model in this context. All cells of an animal contain the same genes and cell differentiation, i.e. the fact that a skin cell differs from a muscle cell, is due to differences in the gene activities in the respective cells. Kauffman proposed that different stable attractors, viz cycles, in his random boolean gene expression network correspond to different cells in the bodies of animals.

The notion is then that cell types correspond to different dynamical states of a complex system, i.e. of the gene expression network. This proposal by Kauffman has received on one side strong support from experimental studies. In Sect. 4.5.2 we will discuss the case of the yeast cell division cycle, supporting the notion that gene regulation networks constitute the underpinnings of life. Regarding the mechanisms of cell differentiation in multicellular organisms, the situation is, on the other side, less clear. Cell types are mostly determined by DNA methylation, which affects the respective gene expression on long time scales.

Boolean Networks are Everywhere Kauffman's original work on gene expression networks was soon generalized to a wide spectrum of applications, such as, to give a few examples, the modeling of neural networks by random boolean networks and of the "punctuated equilibrium" in long-term evolution; a concept that we will discuss in Chap. ??.

Dynamical systems theory (see Chap. ??) deals with dynamical systems containing a relatively small number of variables. General dynamical systems with large numbers of variables are very difficult to analyze and control. Ran-

1.2 Random Variables and Networks

dom boolean networks can hence be considered, in a certain sense, as being of prototypical importance in this field, as they provide well defined classes of dynamical systems for which the thermodynamical limit $N \to \infty$ can be taken. They show chaotic as well as regular behavior, despite their apparent simplicity, and many other typical phenomena of dynamical systems. In the thermodynamic limit there can be phase transitions between chaotic and regular regimes. These are the issues studied in this chapter.

N-K Networks There are several types of random boolean networks. The most simple realization is the N-K model. It is made up of N boolean variables, each variable interacting exactly with K other randomly chosen variables. The respective coupling functions are also chosen randomly from the set of all possible boolean functions mapping K boolean inputs onto one boolean output.

There is no known realization of N-K models in nature. All real physical or biological problems have very specific couplings determined by the structure and the physical and biological interactions of the system considered. The topology of the couplings is, however, often very complex and, in many instances, completely unknown. It is then often a good starting point to model the real-world system by a generic model, like the N-K model.

Binary Variables Modeling real-world systems by a collection of interacting binary variables is often a simplification, as real-world variables are often continuous. For the case of the gene expression network, one just keeps two possible states for every single gene: active or inactive.

Thresholds, viz parameter regimes at which the dynamical behavior changes qualitatively, are wide-spread in biological systems. Examples are neurons, which fire or do not fire depending on the total strength of presynaptic activity. Similar thresholds occur in metabolic networks in the form of activation potentials for the chemical reactions involved. Modeling real-world systems based on threshold dynamics with binary variables is, then, a viable first step towards an understanding.

1.2 Random Variables and Networks

Boolean networks have a rich variety of possible concrete model realizations and we will discuss in the following the most important ones.

1.2.1 Boolean Variables and Graph Topologies

Boolean Variables and State Space We denote by

$$\sigma_i \in \{0, 1\}, \qquad i = 1, 2, \dots, N$$

the N binary variables and by Σ_t the state of the system at time t,

$$\Sigma_t = \{\sigma_1(t), \sigma_2(t), \dots, \sigma_N(t)\}.$$
(1.1)

 Σ_t can be thought of as a vector pointing to one of the $\Omega = 2^N$ edges of an N-dimensional hypercube, where Ω is the number of possible configurations. For numerical implementations and simulations it is useful to consider Σ_t as the binary representation of an integer number $0 \leq \Sigma_t < 2^N$.

Time Dependence Time is assumed to be discrete,

$$\sigma_i = \sigma_i(t), \qquad t = 1, 2, \dots$$

The value of a given boolean element σ_i at the next time step is determined by the values of K controlling variables.

Controlling Elements. The controlling elements $\sigma_{j_1(i)}, \sigma_{j_2(i)}, \ldots, \sigma_{j_{K_i}(i)}$ of a boolean variable σ_i determine its time evolution by

$$\sigma_i(t+1) = f_i(\sigma_{j_1(i)}(t), \sigma_{j_2(i)}(t), \dots, \sigma_{j_{K_i}(i)}(t)) .$$
(1.2)

Here f_i is a boolean function associated with σ_i . The set of controlling elements might include σ_i itself. Some exemplary boolean functions are given in Table 1.1.

Model Definition For a complete definition of the model we then need to specify several parameters:

- The Connectivity: The first step is to select the connectivity K_i of each element, i.e. the number of its controlling elements. With

Table 1.1 Examples of boolean functions of three arguments. (a) A particular random function. (b) A canalizing function of the first argument. When $\sigma_1 = 0$, the function value is 1. If $\sigma_1 = 1$, then the output can be either 0 or 1. (c) An additive function. The output is 1 (active) if at least two inputs are active. (d) The generalized XOR, which is true when the number of 1-bits is odd

			$f(\sigma_1, \sigma_2, \sigma_3)$			
σ_1	σ_2	σ_3	Random	Canalizing	Additive	Gen. XOR
0	0	0	0	1	0	0
0	0	1	1	1	0	1
0	1	0	1	1	0	1
0	1	1	0	1	1	0
1	0	0	1	0	0	1
1	0	1	0	1	1	0
1	1	0	1	0	1	0
1	1	1	1	0	1	1

1.2 Random Variables and Networks



Fig. 1.2 Translational invariant linkages for a completely ordered one-dimensional lattice with connectivities K = 2, 4, 6

$$\langle K \rangle = \frac{1}{N} \sum_{i=1}^{N} K_i$$

the average connectivity is defined. Here we will consider mostly the case in which the connectivity is the same for all nodes: $K_i = K, i = 1, 2, ..., N$.

- The Linkages: The second step is to select the specific set of controlling elements $\{\sigma_{j_1(i)}, \sigma_{j_2(i)}, \ldots, \sigma_{j_{K_i}(i)}\}$ on which the element σ_i depends. See Fig. 1.1 for an illustration.
- The Evolution Rule: The third step is to choose the boolean function f_i determining the value of $\sigma_i(t+1)$ from the values of the linkages $\{\sigma_{j_1(i)}(t), \sigma_{j_2(i)}(t), \ldots, \sigma_{j_{K_i}(i)}(t)\}$.

The Geometry of the Network The way the linkages are assigned determines the topology of the network and networks can have highly diverse topologies, see Chap. ??. It is custom to consider two special cases:

Lattice Assignment. The boolean variables σ_i are assigned to the nodes of a regular lattice. The K controlling elements $\{\sigma_{j_1(i)}, \sigma_{j_2(i)}, \ldots, \sigma_{j_K(i)}\}$ are then chosen in a regular, translational invariant manner, see Fig. 1.2 for an illustration.

Uniform Assignment. In a uniform assignment the set of controlling elements are randomly drawn from all N sites of the network. This is the case for the N-K model, also called the *Kauffman net*. In terms of graph theory one also speaks of an Erdös–Rényi random graph.

All intermediate cases are possible. Small-world networks, to give an example, with regular short-distance links and random long-distance links are popular models in network theory, as discussed extensively in Chap. ??.

1.2.2 Coupling Functions

Number of Coupling Functions The coupling function

$$f_i: \{\sigma_{j_1(i)}, \dots, \sigma_{j_K(i)}\} \to \sigma_i$$

has 2^K different arguments. To each argument value one can assign either 0 or 1. Thus there are a total of

 \mathcal{B}

$$N_f = 2^{\binom{2^K}{}} = 2^{2^K} = \begin{cases} 2 & K = 0\\ 4 & K = 1\\ 16 & K = 2\\ 256 & K = 3 \end{cases}$$
(1.3)

possible coupling functions. In Table 1.1 we present several examples for the case K = 3, out of the $2^{2^3} = 256$ distinct K = 3 boolean functions.

Classification of Coupling Functions For small numbers of connectivity K one can completely classify all possible coupling functions:

- K = 0

There are only two constant functions, f = 1 and f = 0. - K = 1Apart from the two constant functions.

Apart from the two constant functions which one may denote together by \mathcal{A} , the are the identity 1 and the negation – which one can lump together into a classical statement.

e together by \mathcal{A} , there σ Class \mathcal{A} Class	ass
and the negation $\neg \sigma$, $0 0 1 0 1$	L
together into a class $1 0 1 1 0$)

 $- \overset{\mathcal{B}.}{K} = 2$

There are four classes of functions $f(\sigma_1, \sigma_2)$, compare Table 1.2, with each class being invariant under the interchange $0 \leftrightarrow 1$ in either the arguments or the value of f:

 \mathcal{A} (constant functions),

 \mathcal{B}_1 (fully canalizing functions for which one of the arguments determines the output deterministically),

 \mathcal{B}_2 (normal canalizing functions, see also Table 1.1),

 ${\mathcal C}$ (non-canalizing functions, sometimes also denoted "reversible functions").

Types of Coupling Ensembles There are a range of different possible choices for the probability distribution of coupling functions. The following are some examples:

– Uniform Distribution: As introduced originally by Kauffman, the uniform distribution specifies all possible coupling functions to occur with the same probability $1/N_f$.

σ_1	σ_2	Clas	ss \mathcal{A}	Clas	Class \mathcal{B}_1 Class \mathcal{B}_2							Class \mathcal{C}					
0	0	1	0	0	1	0	1	1	0	0	0	0	1	1	1	1	0
0	1	1	0	0	1	1	0	0	1	0	0	1	0	1	1	0	1
1	0	1	0	1	0	0	1	0	0	1	0	1	1	0	1	0	1
1	1	1	0	1	0	1	0	0	0	0	1	1	1	1	0	1	0

Table 1.2 The 16 boolean functions for K = 2. For the definition of the various classes see Sect. 1.2.2 and ?

- 1.2 Random Variables and Networks
- Magnetization Bias¹: The probability of a coupling function to occur is proportional to p if the outcome is 0 and proportional to 1 p if the outcome is 1.
- Forcing Functions: Forcing functions are also called "canalizing function". The function value is determined when one of its arguments, say $m \in \{1, \ldots, K\}$, is given a specific value, say $\sigma_m = 0$ (compare Table 1.1). The function value is not specified if the forcing argument has another value, here when $\sigma_m = 1$.
- Additive Functions: In order to simulate the additive properties of interneural synaptic activities one can choose

$$\sigma_i(t+1) = \Theta(\tilde{f}_i(t)), \qquad \tilde{f}_i(t) = -h + \sum_{j=1}^N w_{ij} \,\sigma_j(t)$$

where $\Theta(x)$ is the Heaviside step function, h the threshold for activating the neuron and w_{ij} the synaptic weight connecting the pre-/ and postsynaptic neurons j and i. The value of $\sigma_i(t+1)$ depends only on a weighted sum of its controlling elements at time t.

1.2.3 Dynamics

Model Realizations A given set of linkages and boolean functions $\{f_i\}$ defines what one calls a *realization* of the model. The dynamics then follows from Eq. (1.2). For the updating of all elements during one time step one has several choices:

- Synchronous Update: All variables $\sigma_i(t)$ are updated simultaneously.
- Serial Update (or asynchronous update):Only one variable is updated at every step. This variable may be picked at random or by some predefined ordering scheme.

The choice of updating does not affect thermodynamic properties, like the phase diagram discussed in Sect. 1.3.2. The occurrence and the properties of cycles and attractors, as discussed in Sect. 1.4, however, crucially depends on the form of update.

Selection of the Model Realization There are several alternatives for choosing the model realization during numerical simulations.

¹ Magnetic moments often have only two possible directions (up or down in the language of spin-1/2 particles). A compound is hence magnetic when more moments point into one of the two possible directions, viz if the two directions are populated unequally.

- The Quenched Model²: One specific realization of coupling functions is selected at the beginning and kept throughout all time.
- The Annealed Model³: A new realization is randomly selected after each time step. Then either the linkages or the coupling functions or both change with every update, depending on the choice of the algorithm.
- The Genetic Algorithm: If the network is thought to approach a predefined goal, one may employ a genetic algorithm in which the system slowly modifies its realization with passing time.

Real-world systems are normally modeled by quenched systems with synchronous updating. All interactions are then fixed for all times.

Cycles and Attractors Boolean dynamics correspond to a trajectory within a finite state space of size $\Omega = 2^N$. Any trajectory generated by a dynamical system with unmutable dynamical update rules, as for the quenched model, will eventually lead to a cyclical behavior. No trajectory can generate more than Ω distinct states in a row. Once a state is revisited,

$$\Sigma_t = \Sigma_{t-T}, \qquad T < \Omega ,$$

part of the original trajectory is retraced and cyclic behavior follows. The resulting cycle acts as an attractor for a set of initial conditions.

Cycles of length 1 are fixpoint attractors. The fixpoint condition $\sigma_i(t+1) = \sigma_i(t)$ (i = 1, ..., N) is independent of the updating rules, viz synchronous vs. asynchronous. The order of updating the individual σ_i is irrelevant when none of them changes.

An Example In Fig. 1.3 a network with N = 3 and K = 2 is fully defined. The time evolution of the $2^3 = 8$ states Σ_t is given for synchronous updating. One can observe one cycle of length 2 and two cycles of length 1 (fixpoints).

1.3 The Dynamics of Boolean Networks

We will now examine how we can characterize the dynamical state of boolean networks in general and of N–K nets in particular. Two concepts will turn out to be of central importance, the relation of robustness to the flow of information and the characterization of the overall dynamical state, which we will find to be either frozen, critical or chaotic.

8

 $^{^2}$ An alloy made up of two or more substances is said to be "quenched" when it is cooled so quickly that it remains stuck in a specific atomic configuration, which does not change anymore with time.

 $^{^3}$ A compound is said to be "annealed" when it has been kept long enough at elevated temperatures such that the thermodynamic stable configuration has been achieved.



Fig. 1.3 A boolean network with N = 3 sites and connectivities $K_i \equiv 2$. Left: Definition of the network linkage and coupling functions. Right: The complete network dynamics (From ?)

1.3.1 The Flow of Information Through the Network

The Response to Changes For random models the value of any given variable σ_i , or its change with time, is, per se, meaningless. Of fundamental importance, however, for quenched models is its response to changes. We may either change the initial conditions, or some specific coupling function, and examine its effect on the time evolution of the variable considered.

Robustness Biological systems need to be robust. A gene regulation network, to give an example, for which even small damage routinely results in the death of the cell, will be at an evolutionary disadvantage with respect to a more robust gene expression set-up. Here we will examine the sensitivity of the dynamics with regard to the initial conditions. A system is robust if two similar initial conditions lead to similar long-time behavior.

The Hamming Distance and the Divergence of Orbits We consider two different initial states,

$$\Sigma_0 = \{ \sigma_1(0), \sigma_2(0), \dots, \sigma_N(0) \}, \qquad \tilde{\Sigma}_0 = \{ \tilde{\sigma}_1(0), \tilde{\sigma}_2(0), \dots, \tilde{\sigma}_N(0) \}$$

Typically we are interested in the case when Σ_0 and $\tilde{\Sigma}_0$ are close, viz when they differ in the values of only a few elements. A suitable measure for the distance is the "Hamming distance" $D(t) \in [0, N]$,

$$D(t) = \sum_{i=1}^{N} \left(\sigma_i(t) - \tilde{\sigma}_i(t) \right)^2 , \qquad (1.4)$$

which is just the sum of elements that differ in Σ_0 and $\tilde{\Sigma}_0$. As an example we consider

$$\Sigma_1 = \{1, 0, 0, 1\}, \qquad \Sigma_2 = \{0, 1, 1, 0\}, \qquad \Sigma_3 = \{1, 0, 1, 1\}$$

We have 4 for the Hamming distance Σ_1 - Σ_2 and 1 for the Hamming distance Σ_1 - Σ_3 . If the system is robust, two close-by initial conditions will never move far apart with time passing time, in terms of the Hamming distance.

The Normalized Overlap The normalized overlap $a(t) \in [0, 1]$ between two configurations is defined as

$$a(t) = 1 - \frac{D(t)}{N} = 1 - \frac{1}{N} \sum_{i=1}^{N} \left(\sigma_i^2(t) - 2\sigma_i(t)\tilde{\sigma}_i(t) + \tilde{\sigma}_i^2(t) \right)$$
$$\approx \frac{2}{N} \sum_{i=1}^{N} \sigma_i(t)\tilde{\sigma}_i(t) , \qquad (1.5)$$

where we have assumed the absence of any magnetization bias, namely

$$\frac{1}{N}\sum_i \sigma_i^2 \approx \frac{1}{2} \approx \frac{1}{N}\sum_i \tilde{\sigma}_i^2 \ ,$$

in the last step. The normalized overlap Eq. (1.5) is then like a normalized scalar product between Σ and $\tilde{\Sigma}$. Two arbitrary states have, on the average, a Hamming distance of N/2 and a normalized overlap a = 1 - D/N of 1/2.

Information Loss/Retention for Long Time Scales The difference between two initial states Σ and $\tilde{\Sigma}$ can also be interpreted as an information for the system. One then has than two possible behaviors:

- Loss of Information: $\lim_{t\to\infty} a(t) \to 1$

 $a(t) \rightarrow 1$ implies that two states are identical, or that they differ only by a finite number of elements, in the thermodynamic limit. This can happen when two states are attracted by the same cycle. All information about the starting states is lost.

- Information Retention: $\lim_{t \to \infty} a(t) = a^* < 1$

The system "remembers" that the two configurations were initially different, with the difference measured by the respective Hamming distance.

The system is very robust when information is routinely lost. Robustness depends on the value of a^* when information is kept. If $a^* > 0$ then two trajectories retain a certain similarity for all time scales.

Percolation of Information for Short Time Scales Above we considered how information present in initial states evolves for very long times. Alternatively one may ask, and this a typical question in dynamical system theory, how information is processed for short times. We write

$$D(t) \approx D(0) \,\mathrm{e}^{\lambda t} \,\,, \tag{1.6}$$

10

where $0 < D(0) \ll N$ is the initial Hamming distance and where λ is called the "Lyapunov exponent", which we discussed in somewhat more detail in Chap. ??.

The question is then whether two initially close trajectories, also called "orbits" within dynamical systems theory, converge or diverge initially. One may generally distinguish between three different types of behaviors or phases:

– The Chaotic Phase: $\lambda > 0$

The Hamming distance grows exponentially, i.e. information is transferred to an exponential large number of elements. Two initially close orbits soon become very different. This behavior is found for large connectivities K and is not suitable for real-world biological systems.

– The Frozen Phase: $\lambda < 0$

Two close trajectories typically converge, as they are attracted by the same attractor. This behavior arises for small connectivities K. The system is locally robust.

- The Critical Phase: $\lambda = 0$

An exponential time dependence, when present, dominates all other contributions. There is no exponential time dependence when the Lyapunov exponent vanishes and the Hamming distance then typically depends algebraically on time, $D(t) \propto t^{\gamma}$.

All three phases can be found in the N-K model when $N \to \infty$. We will now study the N-K model and determine its phase diagram.

1.3.2 The Mean-Field Phase Diagram

A mean-field theory, also denoted "molecular-field theory" is a simple treatment of a microscopic model by averaging the influence of many components, lumping them together into a single mean- or molecular-field. Mean-field theories are ubiquitous and embedded into the overall framework of the "Landau Theory of Phase Transitions", which we are going to discuss in Sect. ??.

Mean-Field Theory We consider two initial states

$$\Sigma_0, \qquad \tilde{\Sigma}_0, \qquad D(0) = \sum_{i=1}^N \left(\sigma_i - \tilde{\sigma}_i\right)^2.$$

We remember that the Hamming distance D(t) measures the number of elements differing in Σ_t and $\tilde{\Sigma}_t$.

For the N-K model, every boolean coupling function f_i is as likely to occur and every variable is, on the average, a controlling element for K other variables. Therefore, the variables differing in Σ_t and $\tilde{\Sigma}_t$ affect on the aver-



Fig. 1.4 The time evolution of the overlap between two states Σ_t and $\tilde{\Sigma}_t$. The vertices (given by the *squares*) can have values 0 or 1. Vertices with the same value in both states Σ_t and $\tilde{\Sigma}_t$ are highlighted by a *gray* background. The values of vertices at the next time step, t + 1, can only differ if the corresponding arguments are different. Therefore, the vertex with *gray* background at time t + 1 must be identical in both states. The vertex with the *star* can have different values in both states at time, t + 1, with a probability 2p(1-p), where p/(1-p) are the probabilities of having vertices with 0/1, respectively

age KD(t) coupling functions, see Fig. 1.4 for an illustration. Every coupling function changes with probability half of its value, in the absence of a magnetization bias. The number of elements different in Σ_{t+1} and $\tilde{\Sigma}_{t+1}$, viz the Hamming distance D(t+1) will then be

$$D(t+1) = \frac{K}{2} D(t), \qquad D(t) = \left(\frac{K}{2}\right)^t D(0) = D(0) e^{t \ln(K/2)} .$$
(1.7)

The connectivity K then determines the phase of the N-K network:

- Chaotic K > 2Two initially close orbits diverge, the number of different elements, i.e. the relative Hamming distance grows exponentially with time t.

- Frozen (K < 2)

The two orbits approach each other exponentially. All initial information contained D(0) is lost.

- Critical $(K_c = 2)$

The evolution of Σ_t relative to $\tilde{\Sigma}_t$ is driven by fluctuations. The power laws typical for critical regimes cannot be deduced within mean-field theory, which discards fluctuations.

The mean-field theory takes only average quantities into account. The evolution law D(t + 1) = (K/2)D(t) holds only on the average. Fluctuations, viz the deviation of the evolution from the mean-field prediction, are however of importance only close to a phase transition, i.e. close to the critical point K = 2.

The mean-field approximation generally works well for lattice physical systems in high spatial dimensions and fails in low dimensions. The Kauffman network has no dimension per se, but the connectivity K plays an analogous role.

Phase Transitions in Dynamical Systems and the Brain The notion of a "phase transition" originally comes from physics, where it denotes the transition between two or more different physical phases, like ice, water and gas, see Chap.??, which are well characterized by their respective order parameters.

The term phase transition therefore classically denotes a transition between two stationary states. The phase transition discussed here involves the characterization of the overall behavior of a dynamical system. They are well defined phase transitions in the sense that $1 - a^*$ plays the role of an order parameter; its value uniquely characterizes the frozen phase and the chaotic phase in the thermodynamic limit.

An interesting, completely open and unresolved question is then, whether dynamical phase transitions play a role in the most complex dynamical system known, the mammalian brain. It is tempting to speculate that the phenomena of consciousness may result from a dynamical state characterized by a yet unknown order parameter. Were this true, then this phenomena would be "emergent" in the strict physical sense, as order parameters are rigorously defined only in the thermodynamic limit.

Let us stress, however, that these considerations are very speculative at this point. In Chap. ??, we will discuss a somewhat more down-to-earth approach to cognitive systems theory in general and to aspects of the brain dynamics in particular.

1.3.3 The Bifurcation Phase Diagram

In deriving Eq. (1.7) we assumed that the coupling functions f_i of the system acquire the values 0 and 1 with the same probability p = 1/2. We generalize this approach and consider the case of a magnetic bias in which the coupling functions are

$$f_i = \begin{cases} 0, & \text{with probability } p \\ 1, & \text{with probability } 1 - p \end{cases}$$

For a given value of the bias p and connectivity K, there are critical values

$$K_c(p), \qquad p_c(K) ,$$

such that for $K < K_c$ ($K > K_c$) the system is in the frozen phase (chaotic phase). When we consider a fixed connectivity and vary p, then $p_c(K)$ separates the system into a chaotic phase and a frozen phase.

The Time Evolution of the Overlap We note that the overlap a(t) = 1 - D(t)/N between two states Σ_t and $\tilde{\Sigma}_t$ at time t is the probability that two vertices have the same value both in Σ_t and in $\tilde{\Sigma}_t$. The probability that all arguments of the function f_i will be the same for both configurations is then

$$\rho_K = \left[a(t) \right]^K \,. \tag{1.8}$$



Fig. 1.5 Solution of the self-consistency condition $a^* = 1 - [1 - (a^*)^K]/K_c$, see Eq. (1.11). *Left*: Graphical solution equating both sides. *Right*: Numerical result for a^* for $K_c = 3$. The fixpoint $a^* = 1$ becomes unstable for $K > K_c = 3$

As illustrated by Fig. 1.4, the values at the next time step differ with a probability 2p(1-p), but only if the arguments of the coupling functions are non-different. Together with the probability that at least one controlling element has different values in Σ_t and $\tilde{\Sigma}_t$, $1 - \rho_K$, this gives the probability, $(1 - \rho_K)2p(1 - p)$, of values being different in the next time step. We then have

$$a(t+1) = 1 - (1 - \rho_K) 2p(1-p) = 1 - \frac{1 - [a(t)]^K}{K_c} , \qquad (1.9)$$

where K_c is given in terms of p as

$$K_c = \frac{1}{2p(1-p)}, \qquad p_c^{1,2} = \frac{1}{2} \pm \sqrt{\frac{1}{4} - \frac{1}{2K}}.$$
 (1.10)

The fixpoint a^* of Eq. (1.9) obeys

$$a^* = 1 - \frac{1 - [a^*]^K}{K_c} . \tag{1.11}$$

This self-consistency condition for the normalized overlap can be solved graphically or numerically by simple iterations, see Fig. 1.5.

Stability Analysis The trivial fixpoint

$$a^* = 1$$

always constitutes a solution of Eq. (1.11). We examine its stability under the time evolution equation (1.9) by considering a small deviation $\delta a_t > 0$ from the fixpoint solution, $a_t = a^* - \delta a_t$:

$$1 - \delta a_{t+1} = 1 - \frac{1 - [1 - \delta a_t]^K}{K_c}, \qquad \delta a_{t+1} \approx \frac{K \,\delta a_t}{K_c} \,. \tag{1.12}$$

The trivial fixpoint $a^* = 1$ therefore becomes unstable for $K/K_c > 1$, viz when $K > K_c = (2p(1-p))^{-1}$.



Fig. 1.6 Phase diagram for the N-K model. The *curve* separating the chaotic phase from the ordered (frozen) phase is $K_c = [2p(1-p)]^{-1}$. The *insets* are simulations for N = 50 networks with K = 3 and p = 0.60 (chaotic phase), p = 0.79 (on the critical line) and p = 0.90 (frozen phase). The site index runs horizontally, the time vertically. Notice the fluctuations for p = 0.79 (From ?)

Bifurcation Equation (1.11) has two solutions for $K > K_c$, a stable fixpoint $a^* < 1$ and the unstable solution $a^* = 1$. One speaks of a bifurcation, which is shown in Fig. 1.5. We note that

$$K_c\Big|_{p=1/2} = 2$$

in agreement with our previous mean-field result, Eq. (1.7), and that

$$\lim_{K \to \infty} a^* = \lim_{K \to \infty} \left(1 - \frac{1 - [a^*]^K}{K_c} \right) = 1 - \frac{1}{K_c} = 1 - 2p(1 - p)$$

since $a^* < 1$ for $K > K_c$, compare Fig. 1.5. Notice that $a^* = 1/2$ for p = 1/2 corresponds to the average normalized overlap for two completely unrelated states in the absence of the magnetization bias, p = 1/2. Two initial similar states then become completely uncorrelated for $t \to \infty$ in the limit of infinite connectivity K.

Rigidity of the Kauffman Net We can connect the results for the phase diagram of the N-K network illustrated in Fig. 1.6 with our discussion on robustness, see Sect. 1.3.1.

- The Chaotic Phase: $K > K_c$

The infinite time normalized overlap a^* is less than 1 even when two trajectories Σ_t and $\tilde{\Sigma}_t$ start out very close to each other. a^* , however, always remains above the value expected for two completely unrelated states.



Fig. 1.7 Normalized Hamming distance D(t)/N for a Kauffman net (*left*) and a square lattice (*right*) with N = 10,000 variables, connectivity K = 4 and D(0) = 100, viz D(0)/N = 0.01. *Left*: (*top*) Frozen phase (p = 0.05), critical ($p_c \simeq 0.1464$) and chaotic (p = 0.4) phases, plotted with a logarithmic scale; (*bottom*) Hamming distance for the critical phase ($p = p_c$) but in a non-logarithmic graph. *Right*: Frozen phase (p = 0.1), critical ($p_c \simeq 0.27$) and chaotic (p = 0.4) phases, plotted with a logarithmic scale. Note that $a^* = \lim_{t\to\infty} (1 - D(t)/N) < 1$ in the frozen state of the lattice system, compare Fig. 1.5 (From ?)

This is so as the two orbits enter two different attractors consecutively, after which the Hamming distance remains constant, modulo small-scale fluctuations that do not contribute in the thermodynamic limit $N \to \infty$. The Frozen Phase: $K < K_c$

The infinite time overlap a^* is exactly one. All trajectories approach essentially the same configuration independently of the starting point, apart from fluctuations that vanish in the thermodynamic limit. The system is said to "order".

Lattice Versus Random Networks The complete loss of information in the ordered phase observed for the Kauffman net does not occur for lattice networks, for which $a^* < 1$ for any K > 0. This behavior of lattice systems is born out by the results of numerical simulations presented in Fig. 1.7. The finite range of the linkages in lattice systems allows them to store information about the initial data in spatially finite proportions of the system, specific to the initial state. For the Kauffman graph every region of the network is equally close to any other and local storage of information is impossible.

Percolation Transition in Lattice Networks For lattice boolean networks the frozen and chaotic phases cannot be distinguished by examining the value of the long-term normalized overlap a^* , as it is always smaller than unity. The lattice topology, however, allows for a connection with percolation theory. One considers a finite system, e.g. a 100×100 square lattice, and two states Σ_0 and $\tilde{\Sigma}_0$ that differ only along one edge. If the damage, viz the difference in between Σ_t and $\tilde{\Sigma}_t$ spreads for long times to the opposite

edge, then the system is said to be percolating and in the chaotic phase. If the damage never reaches the opposite edge, then the system is in the frozen phase. Numerical simulations indicate, e.g. a critical $p_c \simeq 0.298$ for the twodimensional square lattice with connectivity K = 4, compare Fig. 1.7.

Numerical Simulations The results of the mean-field solution for the Kauffman net are confirmed by numerical solutions of finite-size networks. In Fig. 1.7 the normalized Hamming distance, D(t)/N, is plotted for both Kauffman graphs and a two-dimensional squared lattice, both containing N = 10,000 elements and connectivity K = 4.

For both cases results are shown for parameters corresponding to the frozen phase and to the chaotic phase, in addition to a parameter close to the critical line. Note that $1 - a^* = D(t)/N \to 0$ in the frozen phase for the random Kauffman network, but not for the lattice system.

1.3.4 Scale-Free Boolean Networks

The Kauffman model is a reference model which can be generalized in various ways, e.g. by considering small-world or scale-free networks.

Scale-Free Connectivity Distributions Scale-free connectivity distributions

$$P(K) = \frac{1}{\zeta(\gamma)} K^{-\gamma}, \qquad \zeta(\gamma) = \sum_{K=1}^{\infty} K^{-\gamma}, \qquad \gamma > 1 \qquad (1.13)$$

abound in real-world networks, as discussed in Chap. ??. Here P(K) denotes the probability to draw a coupling function $f_i(\cdot)$ having Z arguments. The distribution Eq. (1.13) is normalizable for $\gamma > 1$.

The average connectivity $\langle K \rangle$ is

$$\langle K \rangle = \sum_{K=1}^{\infty} KP(K) = \begin{cases} \infty & \text{if } 1 < \gamma \le 2\\ \frac{\zeta(\gamma-1)}{\zeta(\gamma)} < \infty & \text{if } \gamma > 2 \end{cases}$$
(1.14)

where $\zeta(\gamma)$ is the Riemann zeta function.

Annealed Approximation We consider again two states Σ_t and $\tilde{\Sigma}_t$ and the normalized overlap

$$a(t) = 1 - D(t)/N ,$$

which is identical to the probability that two vertices in Σ and $\dot{\Sigma}$ have the same value. In Sect. 1.3.3 we derived, for a magnetization bias p,

$$a(t+1) = 1 - (1 - \rho_K) 2p(1-p) \tag{1.15}$$

for the time-evolution of a(t), where

$$\rho_K = [a(t)]^K \quad \to \quad \sum_{K=1}^{\infty} [a(t)]^K P(K) \tag{1.16}$$

is the average probability that the K = 1, 2, ... controlling elements of the coupling function $f_i()$ are all identical. In Eq. (1.16) we have generalized Eq. (1.8) to a non-constant connectivity distribution P(K). We then find

$$a(t+1) = 1 - 2p(1-p) \left\{ 1 - \sum_{K=1}^{\infty} a^{K}(t) P(K) \right\} \equiv F(a(t)) , \qquad (1.17)$$

compare Eq. (1.9). Effectively we have used here an annealed model, due to the statistical averaging in Eq. (1.16).

Fixpoints Within the Annealed Approximation In the limit $t \to \infty$, Eq. (1.17) becomes the self-consistency equation

$$a^* = F(a^*) ,$$

for the fixpoint a^* , where F(a) is defined as the right-hand-side of Eq. (1.17). Again, $a^* = 1$ is always a fixpoint of Eq. (1.17), since $\sum_K P(K) = 1$ per definition.

Stability of the Trivial Fixpoint We repeat the stability analysis of the trivial fixpoint $a^* = 1$ of Sect. 1.3.3 and assume a small deviation $\delta a > 0$ from a^* :

$$a^* - \delta a = F(a^* - \delta a) = F(a^*) - F'(a^*)\delta a, \qquad \delta a = F'(a^*)\delta a.$$

The fixpoint a^* becomes unstable if $F'(a^*) > 1$. We find for $a^* = 1$

$$1 = \lim_{a \to 1^{-}} \frac{\mathrm{d}F(a)}{\mathrm{d}a} = 2p(1-p) \sum_{k=1}^{\infty} KP(K)$$
$$= 2p(1-p) \langle K \rangle . \tag{1.18}$$

For $\lim_{a\to 1^-} dF(a)/da < 1$ the fixpoint $a^* = 1$ is stable, otherwise it is unstable. The phase transition is then given by

$$2p(1-p)\langle K \rangle = 1$$
. (1.19)

For the classical N-K model all elements have the same connectivity, $K_i = \langle K \rangle = K$, and Eq. (1.19) reduces to Eq. (1.12).

The Frozen and Chaotic Phases for the Scale-Free Model For $1 < \gamma \leq 2$ the average connectivity is infinite, see Eq. (1.14). $F'(1) = 2p(1-p) \langle K \rangle$ is then always larger than unity and $a^* = 1$ unstable, as illustrated in

18



Fig. 1.8 Phase diagram for a scale-free boolean network with connectivity distribution $\propto K^{-\gamma}$, as given by (1.19). The average connectivity diverges for $\gamma < 2$ and the network is chaotic for all p (From ?)

Fig. 1.8. Equation (1.17) then has a stable fixpoint $a^* \neq 1$; the system is in the chaotic phase for all $p \in]0, 1[$.

For $\gamma > 2$ the first moment of the connectivity distribution P(K) is finite and the phase diagram is identical to that of the N-K model shown in Fig. 1.6, with K replaced by $\zeta(\gamma_c - 1)/\zeta(\gamma_c)$. The phase diagram in $\gamma-p$ space is presented in Fig. 1.8. One finds that $\gamma_c \in [2, 2.5]$ for any value of p. There is no chaotic scale-free network for $\gamma > 2.5$. It is interesting to note that $\gamma \in [2, 3]$ for many real-world scale-free networks.

1.4 Cycles and Attractors

We have emphasized so far the general properties of boolean networks, such as the phase diagram. We now turn to a more detailed inspection of the dynamics, particulary regarding the structure of the attractors.

1.4.1 Quenched Boolean Dynamics

Self-Retracting Orbits From now on we consider quenched systems for which the coupling functions $f_i(\sigma_{i_1}, \ldots, \sigma_{i_K})$ are fixed for all times. Any orbit eventually partly retraces itself, since the state space $\Omega = 2^N$ is finite. The long-term trajectory is therefore cyclic.



Fig. 1.9 Cycles and linkages. Left: Sketch of the state space where every bold point stands for a state $\Sigma_t = \{\sigma_1, \ldots, \sigma_N\}$. The state space decomposes into distinct attractor basins for each cycle attractor or fixpoint attractor. Right: Linkage loops for an N = 20 model with K = 1. The controlling elements are listed in the center column. Each arrow points from the controlling element toward the direct descendant. There are three modules of uncoupled variables (From ?)

Attractors. An attractor A_0 of a discrete dynamical system is a region $\{\Sigma_t\} \subset \Omega$ in phase space that maps completely onto itself under the time evolution $A_{t+1} = A_t \equiv A_0$.

Attractors are typically cycles

 $\Sigma^{(1)} \rightarrow \Sigma^{(2)} \rightarrow \dots \rightarrow \Sigma^{(1)}$

see Figs. 1.3 and 1.9 for some examples. Fixed points are cycles of length 1.

The Attraction Basin. The attraction basin B of an attractor A_0 is the set $\{\Sigma_t\} \subset \Omega$ for which there is a time $T < \infty$ such that $\Sigma_T \in A_0$.

The probability to end up in a given cycle is directly proportional, for randomly drawn initial conditions, to the size of its basin of attraction. The three-site network illustrated in Fig. 1.3 is dominated by the fixpoint $\{1, 1, 1\}$, which is reached with probability 5/8 for random initial starting states.

Attractors are Everywhere Attractors and fixpoints are generic features of dynamical systems and are very important for their characterization, as they dominate the time evolution in state space within their respective basins of attraction. Random boolean networks allow for very detailed studies of the structure of attractors and of the connection to network topology. Of special interest in this context is how various properties of the attractors, like the cycle length and the size of the attractor basins, relate to the thermodynamic differences between the frozen phase and the chaotic phase. These are the issues that we shall now discuss. Linkage Loops, Ancestors and Descendants Every variable σ_i can appear as an argument in the coupling functions for other elements; it is said to act as a controlling element. The collections of all such linkages can be represented graphically by a directed graph, as illustrated in Figs. 1.1, 1.3 and 1.9, with the vertices representing the individual binary variables. Any given element σ_i can then influence a large number of different states during the continued time evolution.

Ancestors and Descendants. The elements a vertex affects consecutively via the coupling functions are called its descendants. Going backwards in time one find ancestors for each element.

In the 20-site network illustrated in Fig. 1.9 the descendants of σ_{11} are σ_{11} , σ_{12} and σ_{14} .

When an element is its own descendant (and ancestor) it is said to be part of a "linkage loop". Different linkage loops can overlap, as is the case for the linkage loops

$$\sigma_1 \to \sigma_2 \to \sigma_3 \to \sigma_4 \to \sigma_1, \qquad \sigma_1 \to \sigma_2 \to \sigma_3 \to \sigma_1$$

shown in Fig. 1.1. Linkage loops are disjoint for K = 1, compare Fig. 1.9.

Modules and Time Evolution The set of ancestors and descendants determines the overall dynamical dependencies.

Module. The collection of all ancestors and descendants of a given element σ_i is called the module (or component) to which σ_i belongs.

If we go through all variables σ_i , $i = 1, \ldots, N$ we find all modules, with every element belonging to one and only one specific module. Otherwise stated, disjoint modules correspond to disjoint subgraphs, the set of all modules constitute the full linkage graph. The time evolution is block-diagonal in terms of modules; $\sigma_i(t)$ is independent of all variables not belonging to its own module, for all times t.

In lattice networks the clustering coefficient (see Chap. ??) is large and closed linkage loops occur frequently. For big lattice systems with a small mean linkage K we expect far away spatial regions to evolve independently, due the lack of long-range connections.

Relevant Nodes and Dynamic Core Taking a look at dynamics of the 20-site model illustrated in Fig. 1.9, we notice that, e.g., the elements σ_{12} and σ_{14} just follow the dynamics of σ_{11} , they are "enslaved" by σ_{11} . These two elements do not control any other element and one could just delete them from the system without qualitative changes to the overall dynamics.

Relevant Nodes. A node is termed relevant if its state is not constant and if it controls at least one other relevant element (eventually itself).

An element is constant if it evolves, independently of the initial conditions, always to the same state and not constant otherwise. The set of relevant nodes, the dynamic core, controls the overall dynamics. The dynamics of all other nodes can be disregarded without changing the attractor structure. The node σ_{13} of the 20-site network illustrated in Fig. 1.9 is relevant if the boolean function connecting it to itself is either the identity or the negation.

The concept of a dynamic core is of great importance for practical applications. Gene expression networks may be composed of thousands of nodes, but contain generally a relatively small dynamic core controlling the overall network dynamics. This is the case, e.g., for the gene regulation network controlling the yeast cell cycle discussed in Sect. 1.5.2.

Lattice Nets versus Kauffman Nets For lattice systems the linkages are short-ranged and whenever a given element σ_j acts as a controlling element for another element σ_i there is a high probability that the reverse is also true, viz that σ_i is an argument of f_j .

The linkages are generally non-reciprocal for the Kauffman net; the probability for reciprocality is just K/N and vanishes in the thermodynamic limit for finite K. The number of disjoint modules in a random network therefore grows more slowly than the system size. For lattice systems, on the other hand, the number of modules is proportional to the size of the system. The differences between lattice and Kauffman networks translate to different cycle structures, as every periodic orbit for the full system is constructed out of the individual attractors of all modules present in the network considered.

1.4.2 The K = 1 Kauffman Network

We start our discussion of the cycle structure of Kauffman nets with the case K = 1, which can be solved exactly. The maximal length for a linkage loop l_{max} is on the average of the order of

$$l_{\rm max} \sim N^{1/2}$$
 . (1.20)

The linkage loops determine the cycle structure together with the choice of the coupling ensemble. As an example we discuss the case of an N = 3 linkage loop.

The Three-site Linkage Loop with Identities For K = 1 there are only two non-constant coupling functions, i.e. the identity I and the negation \neg . We start by considering the case of all the coupling functions being the identity:

$$ABC \rightarrow CAB \rightarrow BCA \rightarrow ABC \rightarrow \dots$$
,

where we have denoted by A, B, C the values of the binary variables σ_i , i = 1, 2, 3. There are two cycles of length 1, in which all elements are identical. When the three elements are not identical, the cycle length is 3. The complete dynamics is then, as illustrated in Fig. 1.10,

22



Fig. 1.10 An example of a K = 1 linkage loop with N = 3 sites and identities as Boolean coupling functions

$000 \rightarrow 000$	$100 \rightarrow 010 \rightarrow 001 \rightarrow 100$
$111 \rightarrow 111$	$011 \rightarrow 101 \rightarrow 110 \rightarrow 011$

Three-Site Linkage Loops with Negations Let us consider now the case that all three coupling functions are negations:

$$ABC \to \overline{C}\overline{A}\overline{B} \to BCA \to \overline{A}\overline{B}\overline{C} \to \dots \qquad \overline{A} = \neg A, \text{etc.}$$

The cycle length is 2 if all elements are identical

$$000 \rightarrow 111 \rightarrow 000$$

and of length 6 if they are not.

$$100 \rightarrow 101 \rightarrow 001 \rightarrow 011 \rightarrow 010 \rightarrow 110 \rightarrow 100 .$$

The complete state space $\Omega = 2^3 = 8$ decomposes into two cycles, one of length 6 and one of length 2.

Three-Site Linkage Loops with a Constant Function Let us see what happens if any of the coupling functions is a constant function. For illustration purposes we consider the case of two constant functions 0 and 1 and the identity:

$$ABC \to 0A1 \to 001 \to 001 . \tag{1.21}$$

Generally it holds that the cycle length is 1 if any of the coupling functions is an identity and that there is then only a single fixpoint attractor. Equation (1.21) holds for all $A, B, C \in \{0, 1\}$; the basin of attraction for 001 is therefore the whole state space, and 001 is a global attractor.

The Kauffman net can contain very large linkage loops for K = 1, see Eq. (1.20), but then the probability that a given linkage loop contains at least one constant function is also very high. The average cycle length therefore remains short for the K = 1 Kauffman net.

Loops and Attractors The attractors are made up of the set of linkage loops. As an example we consider a five-site network with two linkage loops,

$$A \xrightarrow{I} B \xrightarrow{I} C \xrightarrow{I} A, \qquad D \xrightarrow{I} E \xrightarrow{I} D,$$

with all coupling functions being the identity I. The states

00000, 00011, 11100, 11111

are fixpoints in phase space $\Sigma = ABCDE$. Examples of cyclic attractors of length 3 and 6 are

$$10000 \rightarrow 01000 \rightarrow 00100 \rightarrow 10000$$

and

$$10010 \rightarrow 01001 \rightarrow 00110 \rightarrow 10001 \rightarrow 01010 \rightarrow 00101 \rightarrow 10010$$

In general, the length of an attractor is given by the least common multiple of the periods of the constituent loops. This relation holds for K = 1 Boolean networks, for general K the attractors are composed of the cycles of the constituent set of modules.

Critical K = 1 **Boolean networks** When the coupling ensemble is selected uniformly, compare Sect. 1.2.2, the K = 1 network is in the frozen state. If we do however restrict our coupling ensemble to the identity I and to the negation \neg , the value of one node is just copied or inverted to exactly one other node. There is no loss of information anymore, when disregarding the two constant K = 1 coupling functions (see Sect. 1.2.2). The information is not multiplied either, being transmitted to exactly one and not more nodes. The network is hence critical, as pointed out in Sect. 1.3.1.

1.4.3 The K = 2 Kauffman Network

The K = 2 Kauffman net is critical, as discussed in Sects. 1.3.1 and 1.3.2. When physical systems undergo a (second-order) phase transition, power laws are expected right at the point of transition for many response functions; see the discussion in Chap. ??. It is therefore natural to expect the same for critical dynamical systems, such as a random boolean network.

This expectation was indeed initially born out of a series of mostly numerical investigations, which indicated that both the typical cycle lengths, as well as the mean number of different attractors, would grow algebraically with N, namely like \sqrt{N} . It was therefore tempting to relate many of the power laws seen in natural organisms to the behavior of critical random boolean networks.

Undersampling of the State Space The problem to determine the number and the length of cycles is, however, numerically very difficult. In order to extract power laws one has to simulate systems with large N. The state space $\Omega = 2^N$, however, grows exponentially, so that an exhaustive enumeration of all cycles is impossible. One has therefore to resort to a weighted sampling of the state space for any given network realization and to extrapolate from the

1.4 Cycles and Attractors

small fraction of states sampled to the full state space. This method yielded the \sqrt{N} dependence referred to above.

The weighted sampling is, however, not without problems; it might in principle undersample the state space. The number of cycles found in the average state space might not be representative for the overall number of cycles, as there might be small fractions of state space with very high number of attractors dominating the total number of attractors.

This is indeed the case. One can prove rigorously that the number of attractors grows faster than any power for the K = 2 Kauffman net. One might still argue, however, that for biological applications the result for the "average state space" is relevant, as biological systems are not too big anyway. The hormone regulation network of mammals contains of the order of 100 elements, the gene regulation network of the order of 20,000 elements.

Observational Scale Invariance Experimental observations of a dynamical system are typically equivalent to a random sampling of its phase space. Experimental results will hence reflect the properties of the attractors with large basins of attractions, which dominate phase space. For the case of the K = 2 Kauffman net an external observer would hence find scale invariance. The response of the system to a random perturbation will also involve the dominating attractors and may hence be considered as "effectively scale free".

1.4.4 The K = N Kauffman Network

Mean-field theory holds for the fully connected network K = N and we can evaluate the average number and length of cycles using probability arguments.

The Random Walk Through Configuration Space We consider an orbit starting from an arbitrary configuration Σ_0 at time t = 0. The time evolution generates a series of states

$$\Sigma_0, \Sigma_1, \Sigma_2, \ldots$$

through the configuration space of size $\Omega = 2^N$. We consider all Σ_t to be uncorrelated, viz we consider a random walk. This assumption holds due to the large connectivity K = N.

Closing the Random Walk The walk through configuration space continues until we hit a previously visited point, see Fig. 1.11. We define by

 $-q_t$: the probability that the trajectory remains unclosed after t steps;

- P_t : the probability of terminating the excursion exactly at time t.

If the trajectory is still open at time t, we have already visited t + 1 different sites (including the sites Σ_0 and Σ_t). Therefore, there are t + 1 ways of



Fig. 1.11 A random walk in configuration space. The relative probability of closing the loop at time t, $\rho_t = (t+1)/\Omega$, is the probability that $\Sigma_{t+1} \equiv \Sigma_{t'}$, with a certain $t' \in [0, t]$

terminating the walk at the next time step. The relative probability of termination is then $\rho_t = (t+1)/\Omega$ and the overall probability P_{t+1} to terminate the random walk at time t+1 is

$$P_{t+1} = \rho_t \, q_t = \frac{t+1}{\Omega} \, q_t \; .$$

The probability of still having an open trajectory after t + 1 steps is

$$q_{t+1} = q_t(1-\rho_t) = q_t\left(1-\frac{t+1}{\Omega}\right) = q_0\prod_{i=1}^{t+1}\left(1-\frac{i}{\Omega}\right), \qquad q_0 = 1$$

The phase space $\varOmega = 2^N$ diverges in the thermodynamic limit $N \to \infty$ and the approximation

$$q_t = \prod_{i=1}^t \left(1 - \frac{i}{\Omega} \right) \approx \prod_{i=1}^t e^{-i/\Omega} = e^{-\sum_i i/\Omega} = e^{-t(t+1)/(2\Omega)}$$
(1.22)

becomes exact in this limit. For large times t we have $t(t+1)/(2\Omega) \approx t^2/(2\Omega)$ in Eq. (1.22). The probability

$$\sum_{t=1}^{\Omega} P_t \simeq \int_0^\infty dt \, \frac{t}{\Omega} \, e^{-t^2/(2\Omega)} = 1$$

for the random walk to close at all is unity.

Cycle Length Distribution The average number $\langle N_c(L) \rangle$ of cycles of length L is

$$\langle N_c(L) \rangle = \frac{q_{t=L-1}}{\Omega} \frac{\Omega}{L} = \frac{\exp[-L^2/(2\Omega)]}{L} , \qquad (1.23)$$

where we used Eq. (1.22). $\langle \cdots \rangle$ denotes an ensemble average over realizations. In deriving Eq. (1.23) we used the following considerations:

(i) The probability that Σ_{t+1} is identical to Σ_0 is $1/\Omega$.

(ii) There are Ω possible starting points (factor Ω).

1.4 Cycles and Attractors

(iii) Factor 1/L corrects for the overcounting of cycles when considering the L possible starting sites of the L-cycle.

Average Number of Cycles We are interested in the mean number \bar{N}_c of cycles,

$$\bar{N}_c = \sum_{L=1}^N \langle N_c(L) \rangle \simeq \int_1^\infty dL \, \langle N_c(L) \rangle \,. \tag{1.24}$$

When going from the sum \sum_{L} to the integral $\int dL$ in Eq. (1.24) we neglected terms of order unity. We find

$$\bar{N}_{c} = \int_{1}^{\infty} \mathrm{d}L \ \frac{\exp[-L^{2}/(2\Omega)]}{L} = \underbrace{\int_{1/\sqrt{2\Omega}}^{1} \mathrm{d}u \ \frac{e^{-u^{2}}}{u}}_{\equiv I_{1}} + \underbrace{\int_{1}^{\infty} \mathrm{d}u \ \frac{e^{-u^{2}}}{u}}_{\equiv I_{2}} \ ,$$

where we rescaled the variable by $u = L/\sqrt{2\Omega}$. For the separation $\int_{1/\sqrt{2\Omega}}^{\infty} = \int_{1/\sqrt{2\Omega}}^{c} + \int_{c}^{\infty}$ of the integral above we used c = 1 for simplicity; any other finite value for c would do also the job.

The second integral, I_2 , does not diverge as $\Omega \to \infty$. For I_1 we have

$$I_{1} = \int_{1/\sqrt{2\Omega}}^{1} \mathrm{d}u \, \frac{e^{-u^{2}}}{u} = \int_{1/\sqrt{2\Omega}}^{1} \mathrm{d}u \, \frac{1}{u} \left(1 - u^{2} + \frac{1}{2}u^{4} + \dots \right)$$

 $\approx \ln(\sqrt{2\Omega}) , \qquad (1.25)$

since all further terms $\propto \int_{1/\sqrt{2\Omega}}^{1} \mathrm{d} u \, u^{n-1} < \infty$ for $n = 2, 4, \ldots$ and $\Omega \to \infty$. The average number of cycles is then

$$\bar{N}_c = \ln(\sqrt{2^N}) + O(1) = \frac{N \ln 2}{2} + O(1)$$
 (1.26)

for the N = K Kauffman net in thermodynamic limit $N \to \infty$.

Mean Cycle Length The average length \overline{L} of a random cycle is

$$\bar{L} = \frac{1}{\bar{N}_c} \sum_{L=1}^{\infty} L \langle N_c(L) \rangle \approx \frac{1}{\bar{N}_c} \int_1^{\infty} dL L \frac{\exp[-L^2/(2\Omega)]}{L}$$
$$= \frac{1}{\bar{N}_c} \int_1^{\infty} dL \ e^{-L^2/(2\Omega)} = \frac{\sqrt{2\Omega}}{\bar{N}_c} \int_{1/\sqrt{2\Omega}}^{\infty} du \ e^{-u^2}$$
(1.27)

after rescaling with $u = L/\sqrt{2\Omega}$ and using Eq. (1.23). The last integral on the right-hand-side of Eq. (1.27) converges for $\Omega \to \infty$ and the mean cycle length \bar{L} consequently scales as

$$\bar{L} \sim \Omega^{1/2} / N = 2^{N/2} / N$$
 (1.28)

for the K = N Kauffman net, when using Eq. (1.24), $\bar{N}_c \sim N$.

1.5 Applications

1.5.1 Living at the Edge of Chaos

Gene Expression Networks and Cell Differentiation Kauffman introduced the N-K model in the late 1960s for the purpose of modeling the dynamics and time evolution of networks of interacting genes, i.e. the gene expression network. In this model an active gene might influence the expression of any other gene, e.g. when the protein transcripted from the first gene influences the expression of the second gene.

The gene expression network of real-world cells is not random. The web of linkages and connectivities among the genes in a living organism is, however, very intricate, and to model the gene–gene interactions as randomly linked is a good 0-th order approximation. One might then expect to gain a generic insight into the properties of gene expression networks; insights that are independent of the particular set of linkages and connectivities realized in any particular living cell.

Dynamical Cell Differentiation Whether random or not, the gene expression network needs to result in a stable dynamics in order for the cell to keep functioning. Humans have only a few hundreds of different cell types in their bodies. Considering the fact that every single cell contains the identical complete genetic material, in 1969 Kauffman proposed an, at that time revolutionary, suggestion that every cell type corresponds to a distinct dynamical state of the gene expression network. It is natural to assume that these states correspond to attractors, viz in general to cycles. The average length \bar{L} of a cycle in a N-K Kauffman net is

 $\bar{L} \sim 2^{\alpha N}$

in the chaotic phase, e.g. for N = K where $\alpha = 1/2$, see Eq. (1.28), The mean cycle length \overline{L} is exponentially large; consider that $N \approx 20,000$ for the human genome. A single cell would take the universe's lifetime to complete a single cycle, which is an unlikely setting. It then follows that gene expression networks of living organisms cannot be operational in the chaotic phase.

Living at the Edge of Chaos If the gene expression network cannot operate in the chaotic phase there are but two possibilities left: the frozen phase or the critical point. The average cycle length is short in the frozen phase, see Sect. 1.4.2, and the dynamics stable. The system is consequently very resistant to damage of the linkages.

1.5 Applications

But what about Darwinian evolution? Is too much stability good for the adaptability of cells in a changing environment? Kauffman suggested that gene expression networks operate at the edge of chaos, an expression that has become legendary. By this he meant that networks close to criticality may benefit from the stability properties of the close-by frozen phase and at the same time exhibit enough sensitivity to changes in the network structure so that Darwinian adaption remains possible.

But how can a system reach criticality by itself? For the N-K network there is no extended critical phase, only a single critical point K = 2. In Chap. ?? we will discuss mechanisms that allow certain adaptive systems to evolve their own internal parameters autonomously in such a way that they approach the critical point. This phenomenon is called "self-organized criticality".

One could then assume that Darwinian evolution trims the gene expression networks towards criticality: Cells in the chaotic phase are unstable and die; cells deep in the frozen phase cannot adapt to environmental changes and are selected out in the course of time.

1.5.2 The Yeast Cell Cycle

The Cell Division Process Cells have two tasks: to survive and to multiply. When a living cell grows too big, a cell division process starts. The cell cycle has been studied intensively for the budding yeast. In the course of the division process the cell goes through a distinct set of states

$$G_1 \to S \to G_2 \to M \to G_1$$
,

with G_1 being the "ground state" in physics slang, viz the normal cell state and the chromosome division takes place during the M phase. These states are characterized by distinct gene activities, i.e. by the kinds of proteins active in the cell. All eukaryote cells have similar cell division cycles.

The Yeast Gene Expression Network From the ≈ 800 genes involved only 11–13 core genes are actually regulating the part of the gene expression network responsible for the division process; all other genes are more or less just descendants of the core genes. The cell dynamics contains certain checkpoints, where the cell division process can be stopped if something were to go wrong. When eliminating the checkpoints a core network with only 11 elements remains. This network is shown in Fig. 1.12.

Boolean Dynamics The full dynamical dependencies are not yet known for the yeast gene expression network. The simplest model is to assume



Fig. 1.12 The N = 11 core network responsible for the yeast cell cycle. Acronyms denote protein names, solid arrows excitatory connections and dashed arrows inhibitory connections. Cln3 is inactive in the resting state G_1 and becomes active when the cell reaches a certain size (top), initiating the cell division process (compare ?)

$$\sigma_i(t+1) = \begin{cases} 1 \text{ if } a_i(t) > 0\\ 0 \text{ if } a_i(t) \le 0 \end{cases}, \qquad a_i(t) = \sum_j w_{ij} \sigma_j(t) , \qquad (1.29)$$

i.e. a boolean dynamics⁴ for the binary variables $\sigma_i(t) = 0, 1$ representing the activation/deactivation of protein *i*, with couplings $w_{ij} = \pm 1$ for an excitatory/inhibitory functional relation.

Fixpoints The 11-site network has 7 attractors, all cycles of length 1, viz fixpoints. The dominating fixpoint has an attractor basin of 1,764 states, representing about 72 % of the state space $\Omega = 2^{11} = 2,048$. Remarkably, the protein activation pattern of the dominant fixpoint corresponds exactly to that of the experimentally determined G_1 ground state of the living yeast cell.

The Cell Division Cycle In the G_1 ground state the protein Cln3 is inactive. When the cell reaches a certain size it becomes expressed, i.e. it becomes active. For the network model one then just starts the dynamics by setting

$$\sigma_{Cln3} \to 1, \qquad \text{at} \quad t = 0$$

in the G_1 state. The ensuing simple boolean dynamics, induced by Eq. (1.29), is depicted in Fig. 1.13.

⁴ Genes are boolean variables in the sense that they are either expressed or not. The quantitative amount of proteins produced by a given active gene is regulated via a separate mechanism involving microRNA, small RNA snippets.

1.5 Applications



Fig. 1.13 The yeast cell cycle as an attractor trajectory of the gene expression network. Shown are the 1,764 states (green dots, out of the $2^{11} = 2,048$ states in phase space Ω) making up the basin of attraction of the biologically stable G_1 state (at the bottom). After starting with the excited G_1 normal state (the first state in the biological pathway represented by blue arrows), compare Fig. 1.12, the boolean dynamics runs through the known intermediate states (blue arrows) until the G_1 states attractor is again reached, representing the two daughter cells (From ?)

The remarkable result is that the system follows an attractor pathway that runs through all experimentally known intermediate cell states, reaching the ground state G_1 in 12 steps.

Comparison with Random Networks The properties of the boolean network depicted in Fig. 1.12 can be compared with those of a random boolean network. A random network of the same size and average connectivity would have more attractors with correspondingly smaller basins of attraction. Living cells clearly need a robust protein network to survive in harsh environments.

Nevertheless, the yeast protein network shows more or less the same susceptibility to damage as a random network. The core yeast protein network has an average connectivity of $\langle K \rangle = 27/11 \simeq 2.46$. The core network has only N = 11 sites, a number far too small to allow comparison with the properties of N-K networks in the thermodynamic limit $N \to \infty$. Nevertheless, an average connectivity of 2.46 is remarkably close to K = 2, i.e. the critical connectivity for N-K networks.

Life as an Adaptive Network Living beings are complex and adaptive dynamical systems; a subject that we will further dwell on in Chap. ??. The here discussed preliminary results on the yeast gene expression network indicate that this statement is not just an abstract notion. Adaptive regulative networks constitute the core of all living.



Fig. 1.14 Illustration of ensemble (a) and time (b) encoding. Left: All receptor neurons corresponding to the same class of input signals are combined, as occurs in the nose for different odors. Right: The primary input signals are mixed together by a random neural network close to criticality and the relative weights are time encoded by the output signal

1.5.3 Application to Neural Networks

Time Encoding by Random Neural Networks There is some debate in neuroscience whether, and to which extent, time encoding is used in neural processing.

- Ensemble Encoding: Ensemble encoding is present when the activity of a sensory input is transmitted via the firing of certain ensembles of neurons. Every sensory input, e.g. every different smell sensed by the nose, has its respective neural ensemble.
- Time Encoding: Time encoding is present if the same neurons transmit more than one piece of sensory information by changing their respective firing patterns.

Cyclic attractors in a dynamical ensemble are an obvious tool to generate time encoded information. For random boolean networks as well as for random neural networks appropriate initial conditions, corresponding to certain activity patterns of the primary sensory organs, will settle into a cycle, as discussed in Sect. 1.4. The random network may then be used to encode initial firing patterns by the time sequence of neural activities resulting from the firing patterns of the corresponding limiting cycle, see Fig. 1.14.

Critical Sensory Processing The processing of incoming information is qualitatively different in the various phases of the N-K model, as discussed in Sect. 1.3.1.

The chaotic phase is unsuitable for information processing, any input results in an unbounded response and saturation. The response in the frozen phase is strictly proportional to the input and is therefore well behaved, but also relatively uninteresting. The critical state, on the other hand, has the possibility of nonlinear signal amplification.

Sensory organs in animals can routinely process physical stimuli, such as light, sound, pressure or odorant concentrations, which vary by many orders



Fig. 1.15 The primary response of sensory receptors can be enhanced by many orders of magnitude using the non-linear amplification properties of a random neural network close to criticality

of magnitude in intensity. The primary sensory cells, e.g. the light receptors in the retina, have, however a linear sensibility to the intensity of the incident light, with a relatively small dynamical range. It is therefore conceivable that the huge dynamical range of sensory information processing of animals is a collective effect, as it occurs in a random neural network close to criticality. This mechanism, which is plausible from the view of possible genetic encoding mechanisms, is illustrated in Fig. 1.15.