## Algebraic models and finite dynamical systems

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Algebraic Biology

# Fields

## Definition

A set  $\mathbb F$  containing  $1\neq 0$  with addition and multiplication operations is a field if the following three conditions hold:

- $\blacksquare$   $\mathbb F$  is an abelian group under addition.
- $\blacksquare \ \mathbb{F} \setminus \{0\}$  is an abelian group under multiplication.
- The distributive law holds: a(b + c) = ab + ac.

### Examples

- The following sets are fields:  $\mathbb{Q}$ ,  $\mathbb{R}$ ,  $\mathbb{C}$ ,  $\mathbb{F}_p := \mathbb{Z}_p$  (prime p).
- The following sets are *not* fields:  $\mathbb{N}$ ,  $\mathbb{Z}$ ,  $\mathbb{Z}_n$  (composite *n*).

In this course, we will mostly deal with finite fields.

## Proposition (exercise)

- 1. If I is an ideal of a commutative ring R, then R/I is a field iff I is maximal.
- 2. Any finite integral domain is a field.

# Finite fields

### Definition

Let  $\mathbb{F}$  be a finite field. The *characteristic* of  $\mathbb{F}$ , denoted char( $\mathbb{F}$ ), is the smallest positive integer *n* for which  $n1 := \underbrace{1+1+\cdots+1}_{l=0} = 0$ .

n times

## Remarks

- It is elementary to show that  $char(\mathbb{F})$  must be prime.
- $\mathbb{F}$  contains  $\mathbb{F}_p = \{0, 1, \dots, p-1\}$  as a subfield.
- $\mathbb{F}$  is a vector space over  $\mathbb{F}_p$ . Therefore,  $|\mathbb{F}| = p^k$  for some  $k \in \mathbb{Z}$ .

## Proposition

If K and L are finite fields with  $K \subseteq L$  and  $|K| = p^m$  and  $|L| = p^n$ , then m divides n.

## Proof (sketch)

We have  $\mathbb{F}_p \subseteq K \subseteq L$ . Then L is not only a  $\mathbb{F}_p$ -vector space, but also a K-vector space.

Let  $x_1, \ldots, x_k$  be a basis for L over K. Every  $x \in L$  can be written uniquely as  $x = a_1x_1 + \cdots + a_kx_k$ . Now count elements.

# Finite fields

We know that:

- **Z**<sub>p</sub> is a field iff p is prime,
- finite integral domains are fields,
- every finite field has order  $p^k$ .

But what do these "other" finite fields look like?

Let  $R = \mathbb{F}_2[x]$  be the polynomial ring over  $\mathbb{F}_2$ . (Note: we can ignore all negative signs.)

The polynomial  $f(x) = x^2 + x + 1$  is irreducible over  $\mathbb{F}_2$  because it does not have a root. (Note that  $f(0) = f(1) = 1 \neq 0$ .)

Consider the ideal  $I = \langle x^2 + x + 1 \rangle = \{(x^2 + x + 1)h(x) \mid h \in \mathbb{F}_2[x]\}.$ 

In the quotient ring R/I, we have  $x^2 + x + 1 = 0$ , or equivalently,  $x^2 = -x - 1 = x + 1$ .

The quotient has only 4 elements:

$$0+I$$
,  $1+I$ ,  $x+I$ ,  $(x+1)+I$ .

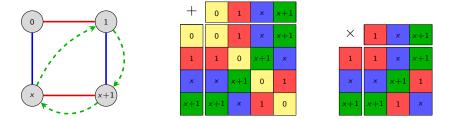
As with the quotient group (or ring)  $\mathbb{Z}/n\mathbb{Z}$ , we usually drop the "I", and just write

$$R/I = \mathbb{F}_2[x]/\langle x^2 + x + 1 \rangle \cong \{0, 1, x, x + 1\}.$$

It is easy to check that this is a field!

# The finite field of order 4

Here is a Cayley diagram, and the operation tables for  $R/I = \mathbb{F}_2[x]/\langle x^2 + x + 1 \rangle$ :



#### Theorem

There exists a finite field  $\mathbb{F}_q$  of order q, which is unique up to isomorphism, iff  $q = p^k$  for some prime p. If k > 1, then this field is isomorphic to the quotient ring

$$\mathbb{F}_p[x]/\langle f \rangle$$
,

where f is any irreducible polynomial of degree k.

Much of the error correcting techniques in coding theory are built using mathematics over  $\mathbb{F}_{2^8} = \mathbb{F}_{256}$ . This is what allows your DVD to play despite scratches.

## Polynomials over finite fields

Let  $\mathbb{F}$  be a field of order  $q = p^k$ . Every  $f \in \mathbb{F}[x]$  defines a function  $\mathbb{F} \to \mathbb{F}$ , by  $c \mapsto f(c)$ .

The set  $\mathbb{F}[x]$  is infinite, but there are only  $q^q$  functions  $\mathbb{F} \to \mathbb{F}$ .

Thus, different polynomials can give the same function. For example, over  $\mathbb{F}_2$ , both  $x^2$  and x define the same function.

#### Remark

The multiplicative group  $\mathbb{F}^* := \mathbb{F} \setminus \{0\}$  is cyclic of order q - 1. Thus,  $a^q = a$  for all  $a \in \mathbb{F}$ .

This means that  $x^q$  and x define the same function over  $\mathbb{F}_q$ .

Elements in the quotient ring  $\mathbb{F}[x]/I$ , where  $I = \langle x^q - x \rangle$ , have the form

$$(a_{q-1}x^{q-1}+\cdots+a_1x+a_0)+I, \qquad a_i \in \mathbb{F}.$$

There are clearly  $q^q$  elements in  $\mathbb{F}[x]/I$ .

#### Summary

- Elements in the (infinite) ring  $\mathbb{F}[x]$  are polynomials over  $\mathbb{F}$ .
- Elements in the (finite) quotient ring  $\mathbb{F}[x]/\langle x^q x \rangle$  are functions  $\mathbb{F} \to \mathbb{F}$ .

We will soon see why every function  $\mathbb{F} \to \mathbb{F}$  can be written like this.

## Multivariate polynomials over finite fields

Let  $\mathbb{F}$  be a field of order  $q = p^k$ . Every  $f \in \mathbb{F}[x_1, \dots, x_n]$  defines a function

$$\mathbb{F}^n \longrightarrow \mathbb{F}, \qquad (c_1, \ldots, c_n) \longmapsto f(c_1, \ldots, c_n).$$

The set  $R = \mathbb{F}[x_1, \ldots, x_n]$  is infinite, but there are only  $q^{(q^n)}$  functions  $\mathbb{F}^n \to \mathbb{F}$ .

Elements in the quotient ring R/I, where  $I = \langle x_1^q - x_1, \dots, x_n^q - x_n \rangle$  are sums of monomials with each exponent from  $0, \dots, q-1$ :

$$f = \sum c_{\alpha} x^{\alpha}, \qquad x^{\alpha} := x_1^{\alpha_1} x_2^{\alpha_2} \cdots x_n^{\alpha_n}, \qquad \alpha = (\alpha_1, \dots, \alpha_n) \in \mathbb{Z}_q^n,$$

where the sum is taken over all  $q^n$  monomials, and  $c_{\alpha} \in \mathbb{F}$ . This is the algebraic normal form of  $f \in R/I$ .

By counting monomials, there are  $q^{(q^n)}$  elements in  $\mathbb{F}[x_1, \ldots, x_n]/\langle x_1^q - x_1, \ldots, x_n^q - x_n \rangle$ .

#### Summary

- Elements in the ring  $\mathbb{F}[x_1, \ldots, x_n]$  are multivariate polynomials over  $\mathbb{F}$ .
- Elements in the quotient ring  $\mathbb{F}[x_1, \ldots, x_n]/\langle x_1^q x_1, \ldots, x_n^q x_n \rangle$  are functions  $\mathbb{F}^n \to \mathbb{F}$ .

We will soon see why *every* function  $\mathbb{F}^n \to \mathbb{F}$  can be written like this.

# A familiar example: Boolean functions

There are several standard ways to write a Boolean function  $f : \mathbb{F}_2^n \to \mathbb{F}_2$ .

- 1. As a logical expression, using  $\land, \lor,$  and  $\neg$  (or  $\overline{\phantom{a}}$  )
- 2. As a "square-free" polynomial in  $\mathbb{F}[x_1, \ldots, x_n]/\langle x_1^2 x_1, \ldots, x_n^2 x_n \rangle$
- 3. As a truth table.

Boolean operation	logical form	polynomial form
AND	$\overline{z = x \wedge y}$	$\overline{z = xy}$
OR	$z = x \lor y$	z = x + y + xy
NOT	$z = \overline{x}$	z = 1 + x

## Example

The following are three different ways to express the function that outputs 0 if x = y = z = 1, and 1 otherwise.

$$f(x,y,z) = \overline{x \wedge y \wedge z}$$

$$f(x, y, z) = 1 + xyz$$

	X	1	1	1	1	0	0	0	0
_	У	1	1	0	0	1	1	0	0
-	Z	1	0	1	0	1	0	1	0
	f(x, y, z)	0	1	1	1	1	1	1	1

Recall that there are  $2^{(2^n)}$  Boolean functions on *n*-variables.

## Boolean networks

Classically, a Boolean network (BN) is an *n*-tuple  $f = (f_1, \ldots, f_n)$  of Boolean functions, where  $f_i : \mathbb{F}_2^n \to \mathbb{F}_2$ . This defines a finite dynamical system (FDS) map

$$f: \mathbb{F}_2^n \longrightarrow \mathbb{F}_2^n, \qquad x = (x_1, \dots, x_n) \longmapsto (f_1(x), \dots, f_n(x)).$$

Any function from a finite set to itself can be described by a directed graph with every node having out-degree 1. For a BN, this is called the *phase space*, or *state space*.

#### Definition

The phase space of a BN is the digraph with vertex set  $\mathbb{F}_2^n$  and edges  $\{(x, f(x)) \mid x \in \mathbb{F}_2^n\}$ .

#### Proposition

Every function  $f: \mathbb{F}_2^n \to \mathbb{F}_2^n$  is the phase space of a Boolean network  $f = (f_1, \dots, f_n)$ .

#### Proof

Clearly, every BN defines a function  $\mathbb{F}_2^n \to \mathbb{F}_2^n$ . We want to prove the converse. It suffices to show that these sets have the same cardinality.

To count functions  $\mathbb{F}_2^n \to \mathbb{F}_2^n$ , we count phase spaces. Each of the  $2^n$  nodes has 1 out-going edge, and  $2^n$  destinations. Thus, there are  $(2^n)^{2^n} = 2^{(n2^n)}$  phase spaces.

To count BNs: there are  $2^{(2^n)}$  choices for each  $f_i$ , and so  $(2^{(2^n)})^n = 2^{(n2^n)}$  possible BNs.

# Local models and FDSs

## Corollary

Every function  $f = \mathbb{F}_2^n \to \mathbb{F}_2^n$  can be written as an *n*-tuple of "square-free" polynomials over  $\mathbb{F}_2$ . That is,

$$f = (f_1, \ldots, f_n), \qquad f_i \in \mathbb{F}_2[x_1, \ldots, x_n]/\langle x_1^2 - x_1, \ldots, x_n^2 - x_n \rangle.$$

This all carries over to generic finite fields, but we will carefully re-define things first.

## Definition

Let  $\mathbb{F}$  be a finite field. A local model over  $\mathbb{F}$  is an *n*-tuple of functions  $f = (f_1, \ldots, f_n)$ , where each  $f_i \colon \mathbb{F}^n \to \mathbb{F}$ .

### Definition

Every local model  $f = (f_1, \ldots, f_n)$  over  $\mathbb{F}$  defines a finite dynamical system (FDS), by iterating the map

$$f: \mathbb{F}^n \longrightarrow \mathbb{F}^n, \qquad x = (x_1, \ldots, x_n) \longmapsto (f_1(x), \ldots, f_n(x)).$$

#### Remark

A classical Boolean network (BN) is just a local model over  $\mathbb{F}_2$ .

# Local models and FDSs

Let  $\mathbb{F}$  be a finite field of order  $q = p^k$ . Recall that

$$R/I = \mathbb{F}[x_1, \ldots, x_n]/\langle x_1^q - x_1, \ldots, x_n^q - x_n \rangle$$

is the set of functions  $\mathbb{F} \to \mathbb{F}$ .

#### Remark

Every local model  $f = (f_1, \ldots, f_n)$  can be associated with an element in  $(R/I) \times \cdots \times (R/I)$ .

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Recall that there are q^{q^n} elements in R/I.
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#### Summary

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(i) There are q^{(nq^n)} local models (f_1, \ldots, f_n) over \mathbb{F}.
(ii) There are q^{(nq^n)} functions \mathbb{F}^n \to \mathbb{F}^n (i.e., FDS maps, or phase spaces).
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In other words, there is a natural bijection between these sets.

Said differently every function  $\mathbb{F}^n \to \mathbb{F}^n$  is indeed the finite dynamical system (FDS) map (i.e., phase space) of a local model  $(f_1, \ldots, f_n)$  over  $\mathbb{F}$ .

## Asynchronous Boolean networks

Consider a Boolean network  $f = (f_1, \ldots, f_n)$ .

Composing the functions synchronously defines the FDS map  $f : \mathbb{F}_2^n \to \mathbb{F}_2^n$ .

We can also compose them asynchronously. For each local function  $f_i$ , define the function

$$F_i: \mathbb{F}_2^n \longrightarrow \mathbb{F}_2^n, \qquad x = (x_1, \dots, x_i, \dots, x_n) \longmapsto (x_1, \dots, f_i(x), \dots, x_n)$$

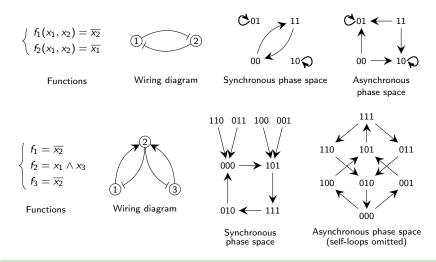
#### Definition

The asynchronous phase space of  $(f_1, \ldots, f_n)$  is the digraph with vertex set  $\mathbb{F}_2^n$  and edges  $\{(x, F_i(x)) \mid i = 1, \ldots, n; x \in \mathbb{F}_2^n\}$ .

### Remarks

- Clearly, this graph has  $n \cdot 2^n$  edges, though self-loops are often omitted.
- Every non-loop edge connect two vertices that differ in exactly one bit. That is, all non-loops are of the form (x, x + e<sub>i</sub>), where e<sub>i</sub> is the i<sup>th</sup> standard unit basis vector.
- Unless we specify otherwise, the term "phase space" refers to the "synchronous phase space."
- It is elementary to extend this concept from BNs to local models over finite fields.

# Examples: synchronous vs. asynchronous



### Remarks

- The 2-cycle in the 1st BN is an "artifact of synchrony."
- In the 2nd asynchronous BN, there is a directed path between any two nodes.

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# Asynchronous local models over finite fields

Recall: every function  $\mathbb{F}^n \to \mathbb{F}^n$  can be realized as the FDS map (i.e., phase space) of a local model over  $\mathbb{F}$ .

Similarly, every digraph with vertex set  $\mathbb{F}^n$  that "could be" the asynchronous phase space of a local model, is one.

#### Theorem

Let  $G = (\mathbb{F}^n, E)$  be a digraph with the following local property (definition):

For every  $x \in \mathbb{F}^n$  and i = 1, ..., n: *E* contains exactly one edge of the form  $(x, x + ke_i)$ , where  $k \in \mathbb{F}$  (possibly a self-loop)

Then G is the asynchronous phase space of some local model  $(f_1, \ldots, f_n)$  over  $\mathbb{F}$ .

#### Proof

It suffices to show there there are  $q^{(nq^n)}$  digraphs  $G = (\mathbb{F}^n, E)$  with the "local property".

Each of the  $q^n$  nodes  $x \in \mathbb{F}^n$  has *n* out-going edges (including loops). Each edge has *q* possible destinations:  $x + ke_i$  for  $k \in \mathbb{F}$ .

This gives  $q^n$  choices at each node, for all  $q^n$  nodes, for  $(q^n)^{q^n} = q^{(nq^n)}$  graphs in total.

Local models over general finite fields: synchronous vs. asynchronous Let  $\mathbb{F}$  be a finite field of order  $q = p^k$ , and let

$$R/I = \mathbb{F}[x_1,\ldots,x_n]/\langle x_1^q - x_1,\ldots,x_n^q - x_n\rangle,$$

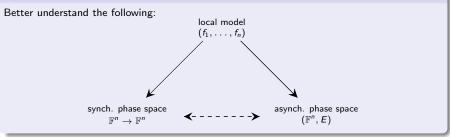
which has cardinality  $q^{(q^n)}$ .

## Summary (updated)

Each of the following sets have cardinality  $q^{(nq^n)}$ :

- local models  $(f_1, \ldots, f_n)$  over  $\mathbb{F}$ .
- **synchronous phase spaces**, i.e., FDS maps  $\mathbb{F}^n \to \mathbb{F}^n$ ;
- **a** asynchronous phase spaces: a digraph  $G = (\mathbb{F}^n, E)$  with the "local property".

## Open-ended question



## Phase spaces: synchronous vs. asynchronous

The synchronous phase space of a local model  $f = (f_1, \ldots, f_n)$  has two types of nodes:

- transient points:  $f^k(x) \neq x$  for all  $k \ge 1$ .
- periodic points:  $f^k(x) = x$  for some  $k \ge 1$ . (k = 1: fixed point)

Thus, the phase space consists of periodic cycles and directed paths leading into these cycles.

The asynchronous phase space of  $f = (f_1, \ldots, f_n)$  can be more complicated.

For  $x, y \in \mathbb{F}^n$ , define  $x \sim y$  iff there is a directed path from x to y and from y to x.

The resulting equivalence classes are the strongly connected components (SCC) of the phase space. An SCC is terminal if it has no out-going edges from it.

A point  $x \in \mathbb{F}^n$ :

- *is transient* if it is not in a terminal SCC.
- *lies on a cyclic attractor* if its terminal SCC is a chordless k-cycle (k = 1: *fixed point*).
- lies on a complex attractor otherwise.

### Proposition

The fixed points of a local model are the same under synchronous and asynchronous update.

# Wiring diagrams

A function  $f_i : \mathbb{F}^n \to \mathbb{F}$  is essential in  $x_i$  if for some  $x \in \mathbb{F}^n$  and  $k \in \mathbb{F}$ ,

$$f_j(x) \neq f(x + ke_i),$$

where  $e_i \in \mathbb{F}^n$  is the *i*<sup>th</sup> standard unit basis vector.

#### Definition

The wiring diagram of a local model  $(f_1, \ldots, f_n)$  over  $\mathbb{F}$  is a directed graph G with vertex set  $x_1, \ldots, x_n$  (or just  $1, \ldots, n$ ) and a directed edge  $(x_i, x_j)$  if  $f_j$  is essential in  $x_i$ .

If  $\mathbb{F} = \mathbb{F}_p$ , then an edge  $x_i \longrightarrow x_j$  is positive if  $a \leq b$  implies

$$f_j(x_1, \ldots, x_{i-1}, a, x_{i+1}, \ldots, x_n) \leq f_j(x_1, \ldots, x_{i-1}, b, x_{i+1}, \ldots, x_n)$$

and negative if the second inequality is reversed.

Negative edges are denoted with circles or blunt arrows instead of traditional arrowheads.

#### Definition

A function  $f_j \colon \mathbb{F}^n \to \mathbb{F}$  is unate (or monotone) if every edge in the wiring diagram is either positive or negative.

# Wiring diagrams in Boolean networks

• A positive edge  $x_i \longrightarrow x_j$  represents a situation where *i* activates *j*.

Examples.

- $f_j = x_i \wedge y$ :  $0 = f_j(x_i = 0, y) \le f_j(x_i = 1, y) \le 1$ .
- $f_j = x_i \lor y$ :  $0 \le f_j(x_i = 0, y) \le f_j(x_i = 1, y) = 1.$
- A negative edge  $x_i \longrightarrow x_j$  represents a situation where *i* inhibits *j*.

Examples.

- $f_j = \overline{x_i} \wedge y$ :  $1 \ge f_j(x_i = 0, y) \ge f_j(x_i = 1, y) = 0.$
- $f_j = \overline{x_i} \lor y$ :  $1 = f_j(x_i = 0, y) \ge f_j(x_i = 1, y) \ge 0$ .

Occasionally, edges are neither positive nor negative:

Example. (The logical "XOR" function):

• 
$$f_j = (x_i \land \overline{y}) \lor (\overline{x_i} \land y)$$
:  
•  $0 = f_j(x_1 = 0, y = 0) < f_j(x_1 = 1, y = 0) = 1$   
 $1 = f_j(x_1 = 0, y = 1) > f_j(x_1 = 1, y = 1) = 0$ 

Most edges in Boolean network models are either positive or negative because most biological interactions are either simple activations or inhibitions.

# Enumerating Boolean networks

## Motivating question

Recall our 9-node Boolean network model of the *lac* operon. For all 4 initial conditions  $(G_e, L_e) \in \mathbb{F}_2^2$ , the phase space had exactly 1 fixed point that made biological sense.

What are the chances that this would have happened purely by coincidence?

To answer this, we need to count the number of Boolean networks, as well as those that have just that one fixed point.

#### Recall

Every graph  $G = (\mathbb{F}^n, E)$  with uniform out-degree 1 is the phase space of some local model  $(f_1, \ldots, f_n)$  over  $\mathbb{F}$ .

## Corollary

Start with a phase space with vertex set  $\mathbb{F}_2^n$ . Remove k edges. There are exactly  $2^{nk}$  local models that "fit this data".

## Proof

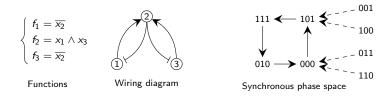
The tail of each "missing edge" is a state  $x \in \mathbb{F}_2^n$ , and there are  $2^n$  possibile destinations  $x \to y$  when replacing it.

# An example

Exercise (easy)

How many Boolean networks contain the 4-cycle 000  $\to$  101  $\to$  111  $\to$  010  $\to$  000 in their phase space?

We saw one of these earlier:



Suppose we remove all of the "dashed edges." Then we can replace each one 8 different ways. Thus, there are  $8^4 = 4096$  possibilities.

## Exercise (harder)

How many Boolean networks contain a 4-cycle in their phase space? What if we require that there is additionally *only one connected component*?

# Counting local models

## Theorem

There are  $q^{(nq^n)}$  local models on *n* nodes. Of these:

- (a)  $q^n!$  have a phase space consisting of a length- $q^n$  chain of transient points.
- (b)  $q^n!$  are invertible (i.e., have no transient points).
- (c)  $(q^n 1)!$  are invertible with a phase space consisting of a single cycle.
- (d)  $(q^n 1)^{q^n}$  have no fixed points.
- (e)  $(q^n)^{q^n-1}$  have a single connected component and fixed point.
- (f)  $(q^n + 1)^{q^n 1}$  have only fixed points (i.e., no longer periodic cycles).

As an example, the number of Boolean networks (that is, q = 2) on n nodes with various properties is shown below.

	<i>n</i> = 2	<i>n</i> = 3	<i>n</i> = 4	<i>n</i> = 5	<i>n</i> = 6
total BNs	256	$1.678  imes 10^7$	$1.845 imes10^{19}$	$1.462 imes10^{48}$	$3.940  imes 10^{115}$
invertible	24	40320	$2.092 imes10^{13}$	$2.631 imes10^{35}$	$1.269 imes10^{89}$
single big cycle	6	5040	$1.308 imes10^{12}$	$8.223\times10^{33}$	$1.983 imes10^{87}$
no fixed points	81	$5.765 imes10^{6}$	$6.568 imes10^{18}$	$5.291 imes10^{47}$	$1.438 imes10^{115}$
1 component & f.p.	64	$2.097 imes10^{6}$	$1.153 imes10^{18}$	$4.567 imes10^{46}$	$6.157  imes 10^{113}$
only fixed points	125	$4.782 imes10^{6}$	$2.862\times10^{18}$	$1.189  imes 10^{47}$	$1.635 imes10^{114}$

# Counting local models

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- (e)  $(q^n)^{q^n-1}$  have a single connected component and fixed point.
- (f)  $(q^n + 1)^{q^n 1}$  have only fixed points (i.e., no longer periodic cycles).

# Proof (sketch)

- (a)–(d) are elementary counting arguments.
- (e) is just the number labeled rooted trees on  $q^n$  nodes.

For (f), use a bijection between phase spaces and labeled unrooted trees on  $q^n+1$  nodes.  $\Box$ 

# Cayley's formula (and corollaries)

- #{labeled unrooted trees on n nodes} =  $n^{n-2}$ .
- #{labeled rooted trees on n nodes} =  $n^{n-1}$ .
- The number of labeled forests on n labeled vertices is  $(n+1)^{n-1}$ .

## Back to the *lac* operon

### Motivating question

Recall our 9-node Boolean network model of the *lac* operon. For all 4 initial conditions  $(G_e, L_e) \in \mathbb{F}_2^2$ , the phase space had exactly 1 fixed point that made biological sense.

What are the chances that this would have happened purely by coincidence?

There are  $(2^9)^{(2^9)}=512^{512}\approx 1.400\times 10^{1387}$  Boolean networks on 9 nodes.

Of these,  $(2^9)^{2^9-1} = 512^{511} \approx 2.735 \times 10^{1384}$  have a single component and fixed point.

Of these,  $(2^9)^{2^9-2} = 512^{510} \approx 5.342 \times 10^{1381}$  have the "correct" fixed point.

In other words, 1 in 262,141 Boolean networks on n nodes have this property.

Thus, the probability that each  $(G_e, L_e) \in \mathbb{F}_2^2$  would yield such a phase space purely by chance is approximately

$$\left(\frac{1}{262,141}\right)^4 \approx 2.118 \times 10^{-22}.$$