Boolean Networks And Their Dynamics

IWBN2020

Concepción, Chile
January 6, 2020

Reinhard Laubenbacher
Center for Quantitative Medicine
UConn School of Medicine
Jackson Laboratory for Genomic Medicine

reinhard.laubenbacher@gmail.com

The New York Times

DEADLY GERMS, LOST CURES

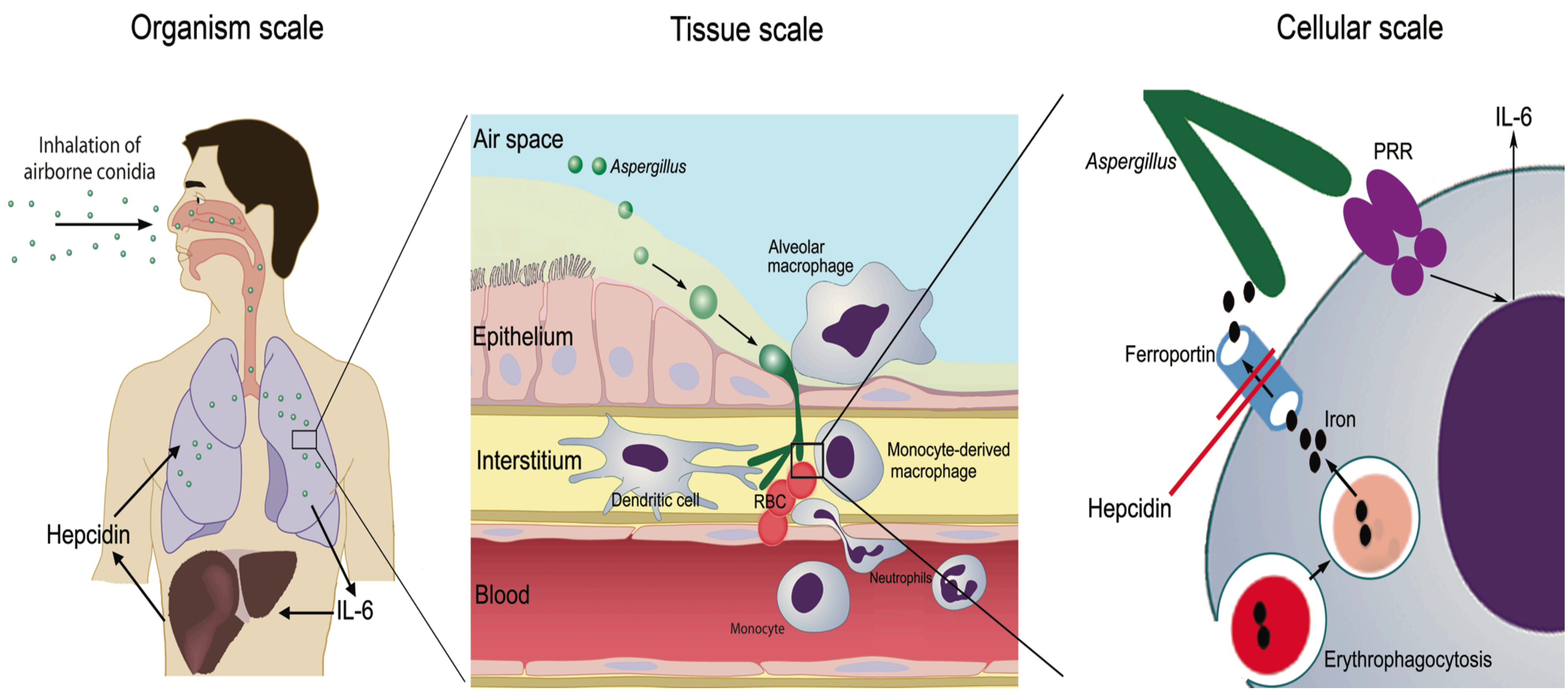
A Mysterious Infection, Spanning the Globe in a Climate of Secrecy

The rise of Candida auris embodies a serious and growing public health threat: drug-resistant germs.

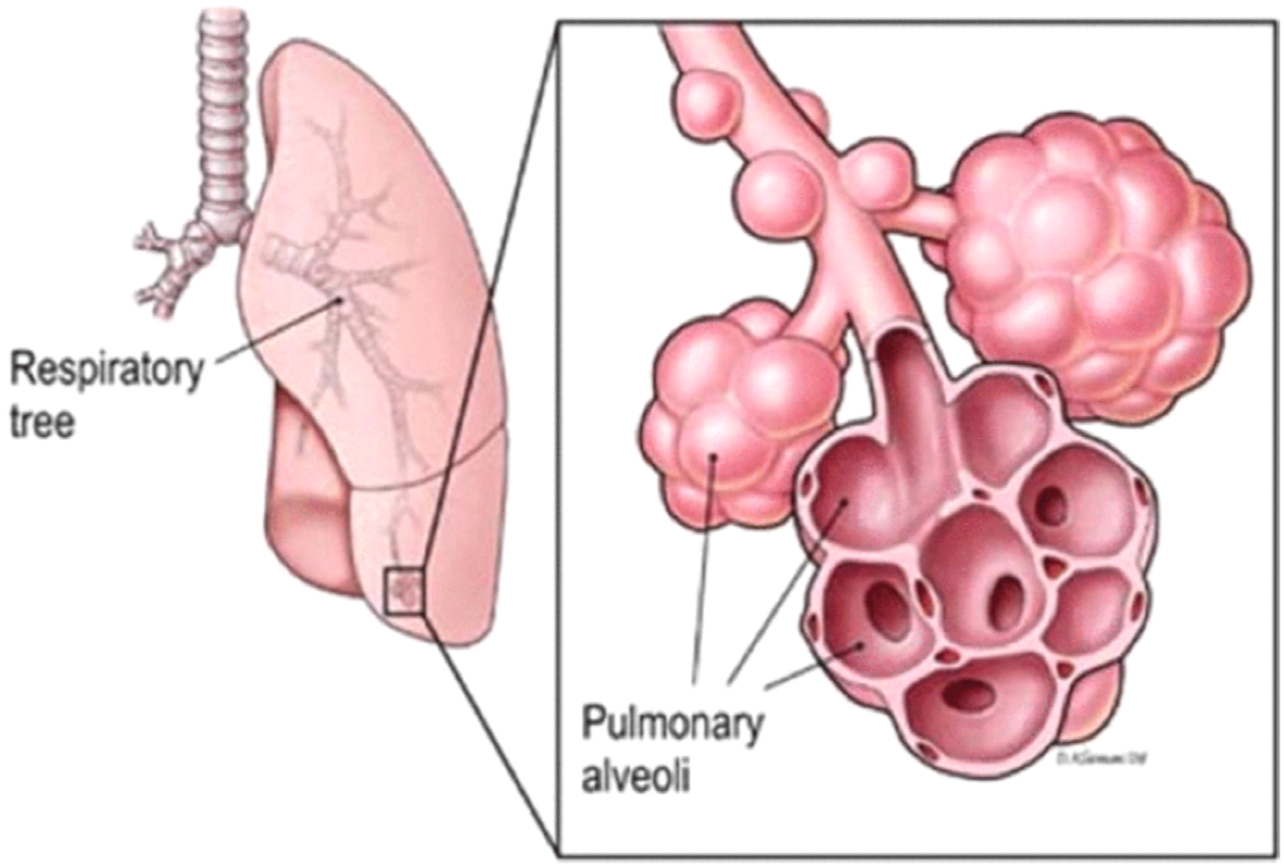
By Matt Richtel and Andrew Jacobs

April 6, 2019

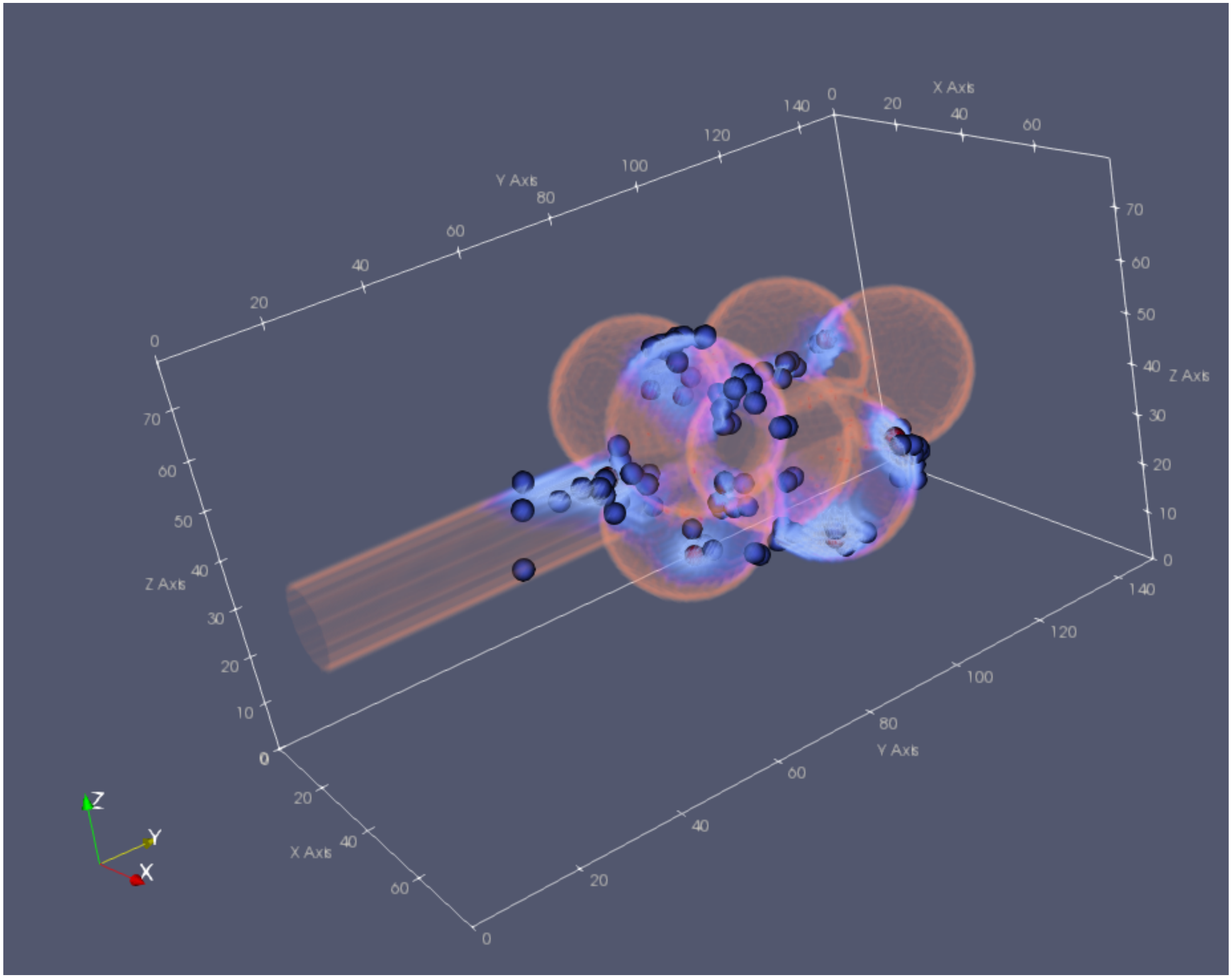
Nutritional immunity and fungal infections



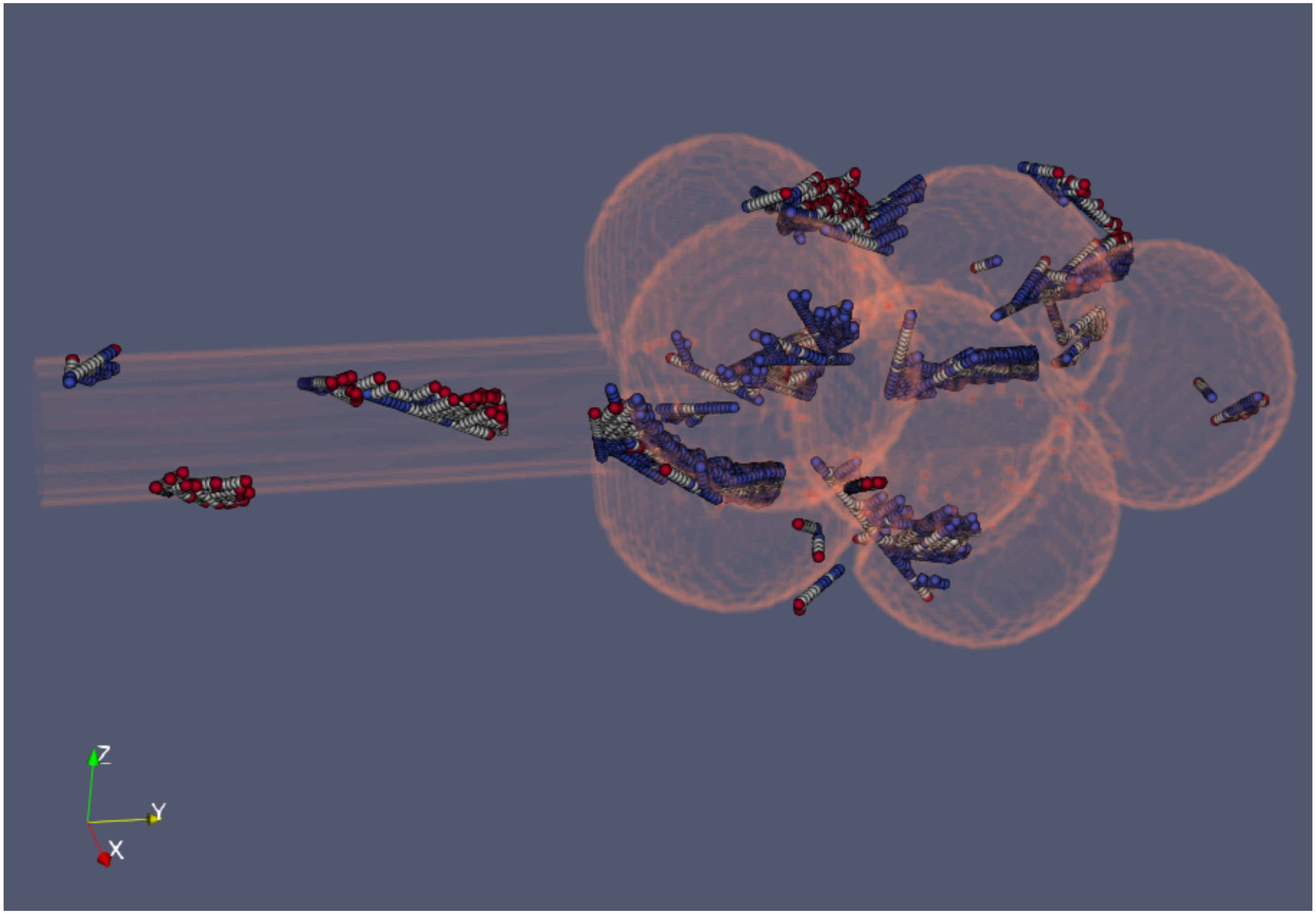
S.J. Park et al., *J. Immunol.*, 2006



Y.-S. Sun et al., Biomicrofluidics, 2012

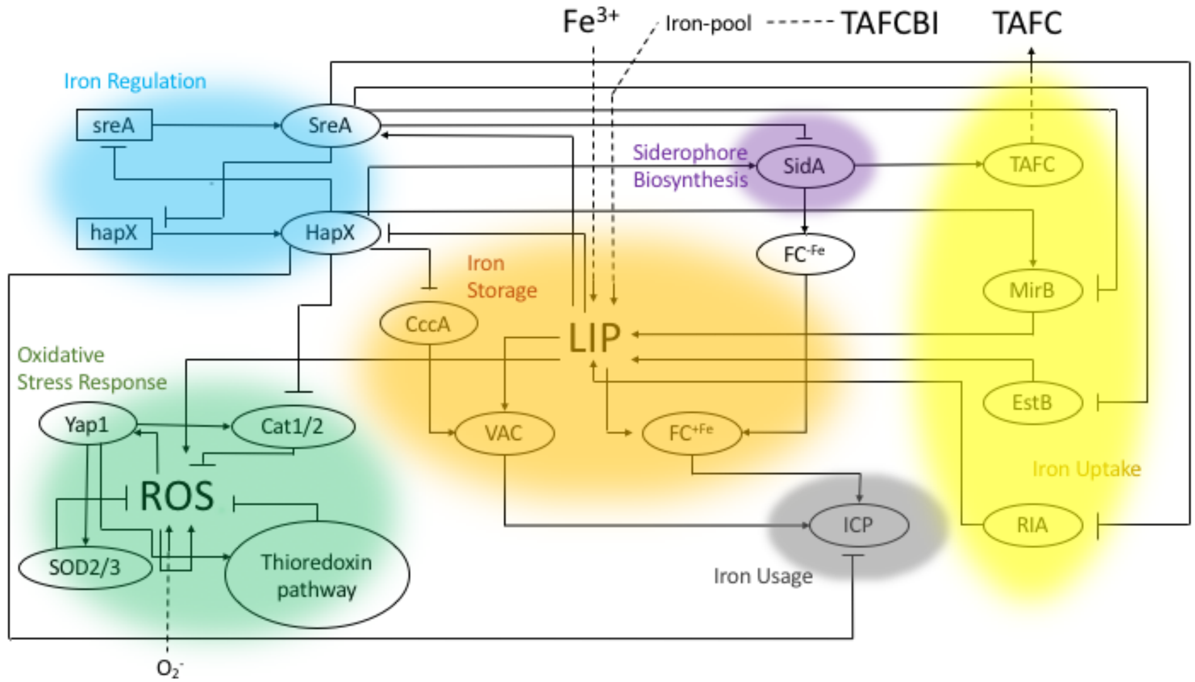


X Axis
Y Axis
Z Axis
0
20
40
60
80
100
120
140
10
30
50
70
Z
Y
X

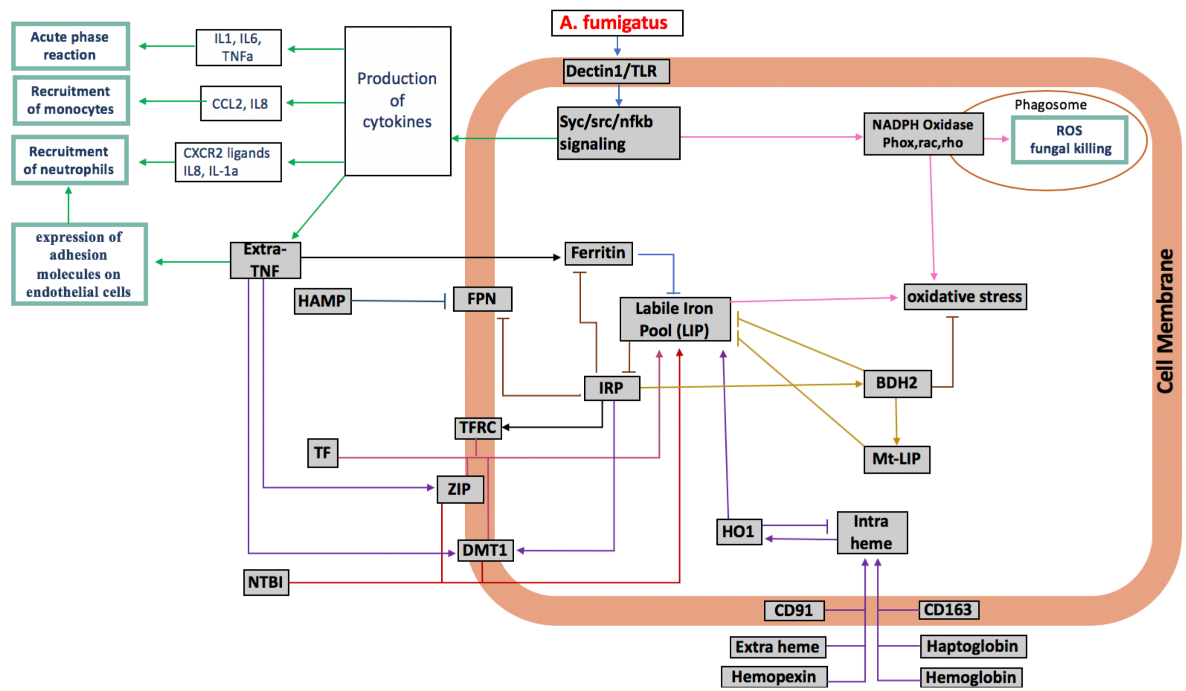

Z
Y
X

Aspergillus fumigatus

Brandon *et al.*,
*BMC Sys. Biol.*2015



Macrophage
(preliminary)



The Team:

***UConn SOM*: **B. Adhikari, A. Conan, H. DeAssis, L. Flores, J. Masison, E. Mei, L. Poudel

***Jackson Laboratory*: **L. Sordo Vieira

U Florida SOM: B. Mehrad, N. Yang, Y. Scindia

Kitware Inc.: W. Schroeder, M. Grauer, B. Helba, S. Arikatla, J. Beezley

Boolean Networks

Computation

Structure ⟷ **Dynamics**

Theory

Computation

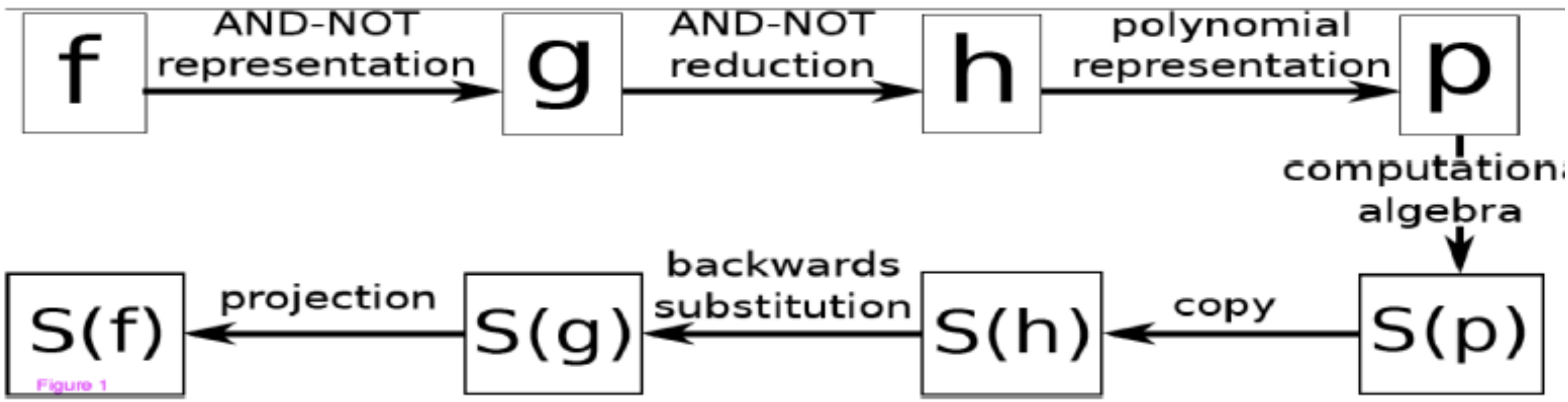
Veliz-Cuba et al. BMC Bioinformatics 2014, 15:221
http://www.biomedcentral.com/1471-2105/15/221

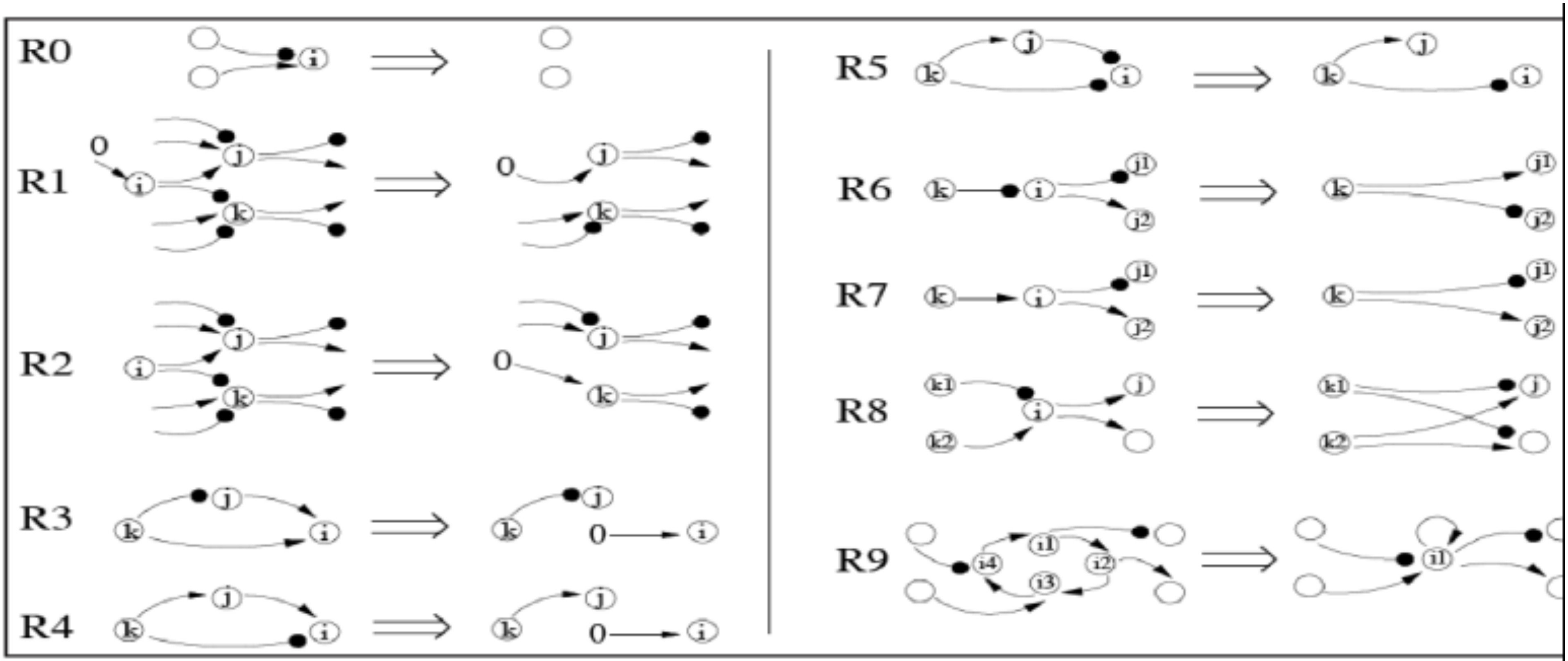
BMC Bioinformatics

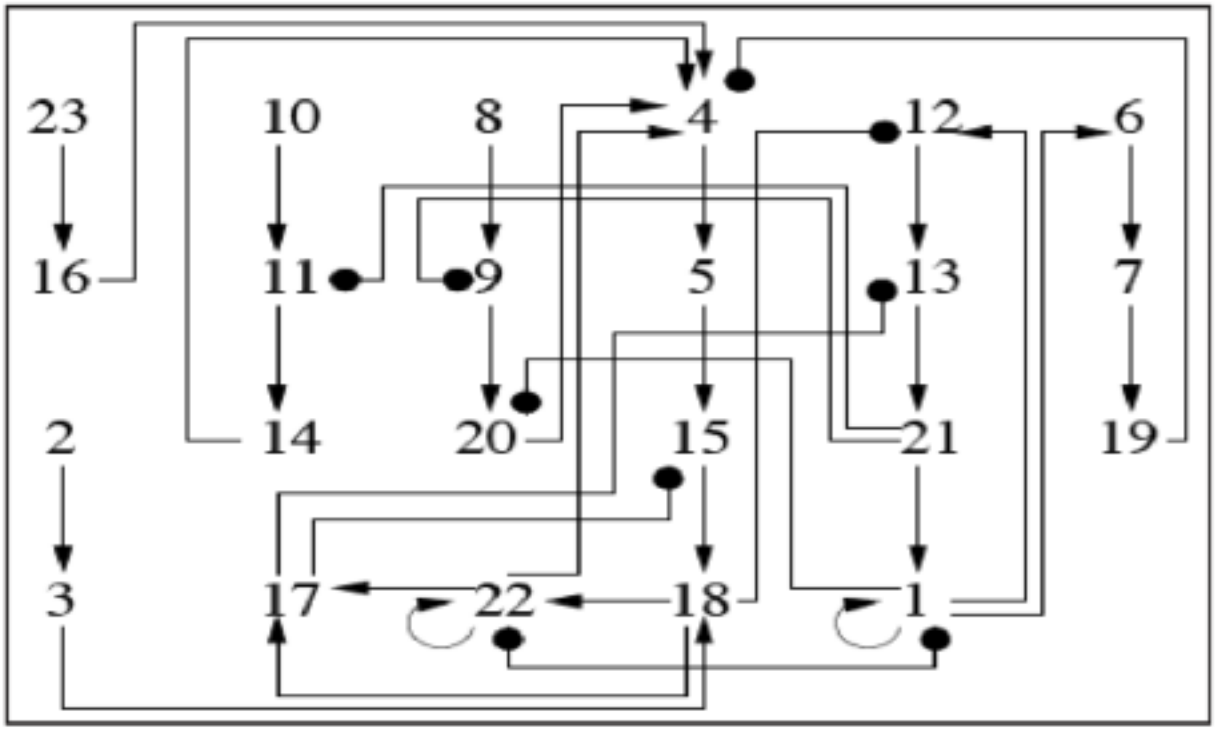
METHODOLOGY ARTICLE Open Access

Steady state analysis of Boolean molecular network models via model reduction and computational algebra

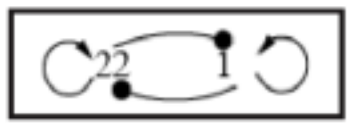
Alan Veliz-Cuba[1,2*], Boris Aguilar[3], Franziska Hinkelmann[4] and Reinhard Laubenbacher[5]


f
AND-NOT representation
g
AND-NOT reduction
h
polynomial representation
p
computationa
algebra
S(p)
copy
S(h)
backwards substitution
S(g)
projection
S(f)
Figure 1


R0
R1
R2
R3
R4
R5
R6
R7
R8
R9



Mendoza, Xenarios, Theor. Biol. And Med., 2006


22
1

- “Dynamic equivalence” of networks
- AND-NOT networks
- Transformation to a graph-theoretic problem
- Transformation into polynomial systems

Theory

Communications in Algebra®, 33: 2977–2989, 2005

ISSN: 0092-7872 print/1532-4125 online
DOI: 10.1081/AGB-200066211

Taylor & Francis
Taylor & Francis Group

LINEAR FINITE DYNAMICAL SYSTEMS#

René A. Hernández Toledo
Mathematics Department, University of Puerto Rico at Cayey, Cayey, Puerto Rico

Commun. Math. Phys. 93, 219–258 (1984)

Communications in
Mathematical
Physics

Algebraic Properties of Cellular Automata

Olivier Martin[1,★], Andrew M. Odlyzko[2], and Stephen Wolfram[2,3,★★]

1 California Institute of Technology, Pasadena, CA 91125, USA
2 Bell Laboratories, Murray Hill, NJ 07974, USA
3 The Institute for Advanced Study, Princeton, NJ 08540, USA

Bulletin of Mathematical Biology (2010)
DOI 10.1007/s11538-010-9501-z

ORIGINAL ARTICLE

The Dynamics of Conjunctive and Disjunctive Boolean Network Models

Abdul Salam Jarrah[a,b,*], Reinhard Laubenbacher[a], Alan Veliz-Cuba[a]

[a] *Virginia Bioinformatics Institute, Virginia Tech, Blacksburg, VA 24061-0477, USA*
[b] *Present address: Department of Mathematics and Statistics, American University of Sharjah, Sharjah, UAE*

The number of periodic points

Theorem 3 *Let f be a conjunctive Boolean network whose dependency graph is strongly connected and has loop number c. If $c = 1$, then f has the two fixed points $(0, 0, \ldots, 0)$ and $(1, 1, \ldots, 1)$ and no other limit cycles of any length. If $c > 1$ and m is a divisor of c, then the number of periodic states of period m is*

$$|A(m)| = \sum_{i_1=0}^{1} \cdots \sum_{i_r=0}^{1} (-1)^{i_1+i_2+\cdots+i_r} 2^{p_1^{k_1-i_1} p_2^{k_2-i_2} \cdots p_r^{k_r-i_r}},$$

where $m = \prod_{i=1}^{r} p_i^{k_i}$ is the prime factorization of m, that is $p_1, \ldots, p_r$ are distinct primes and $k_i \geq 1$ for all i.

Theorem 6.2. *Consider the function*

$$\mathcal{L}(z_1, \ldots, z_t) := \sum_{\mathcal{J} \subseteq \Omega} (-1)^{|\mathcal{J}|+1} \prod_{j \in \bigcap_{J \in \mathcal{J}} J} z_i .$$

Then for any conjunctive Boolean network f with subnetworks $h_1, \ldots, h_t$ and Ω its set of maximal antichains in the poset of f, we have

$$\mathcal{L}\big(\mathcal{C}(h_1), \ldots, \mathcal{C}(h_t)\big) \leq \mathcal{C}(f). \tag{9}$$

Here, the function $\mathcal{L}$ is evaluated using the "multiplication" described in Corollary 3.5. This inequality provides a sharp lower bound on the number of limit cycles of f of a given length.

There is no sharp upper bound in the form of a polynomial function in terms of the cycle structure of the strongly connected components and the structure of the partially ordered set of components.

Automatica 99 (2019) 167–174

Contents lists available at ScienceDirect

Automatica

journal homepage: www.elsevier.com/locate/automatica

Brief paper

Dynamics of semilattice networks with strongly connected dependency graph[☆]

Alan Veliz-Cuba[a,*], Reinhard Laubenbacher[b,c]

[a] University of Dayton, Dayton, OH, USA
[b] Center for Quantitative Medicine, University of Connecticut Health Center, USA
[c] Jackson Laboratory for Genomic Medicine, USA

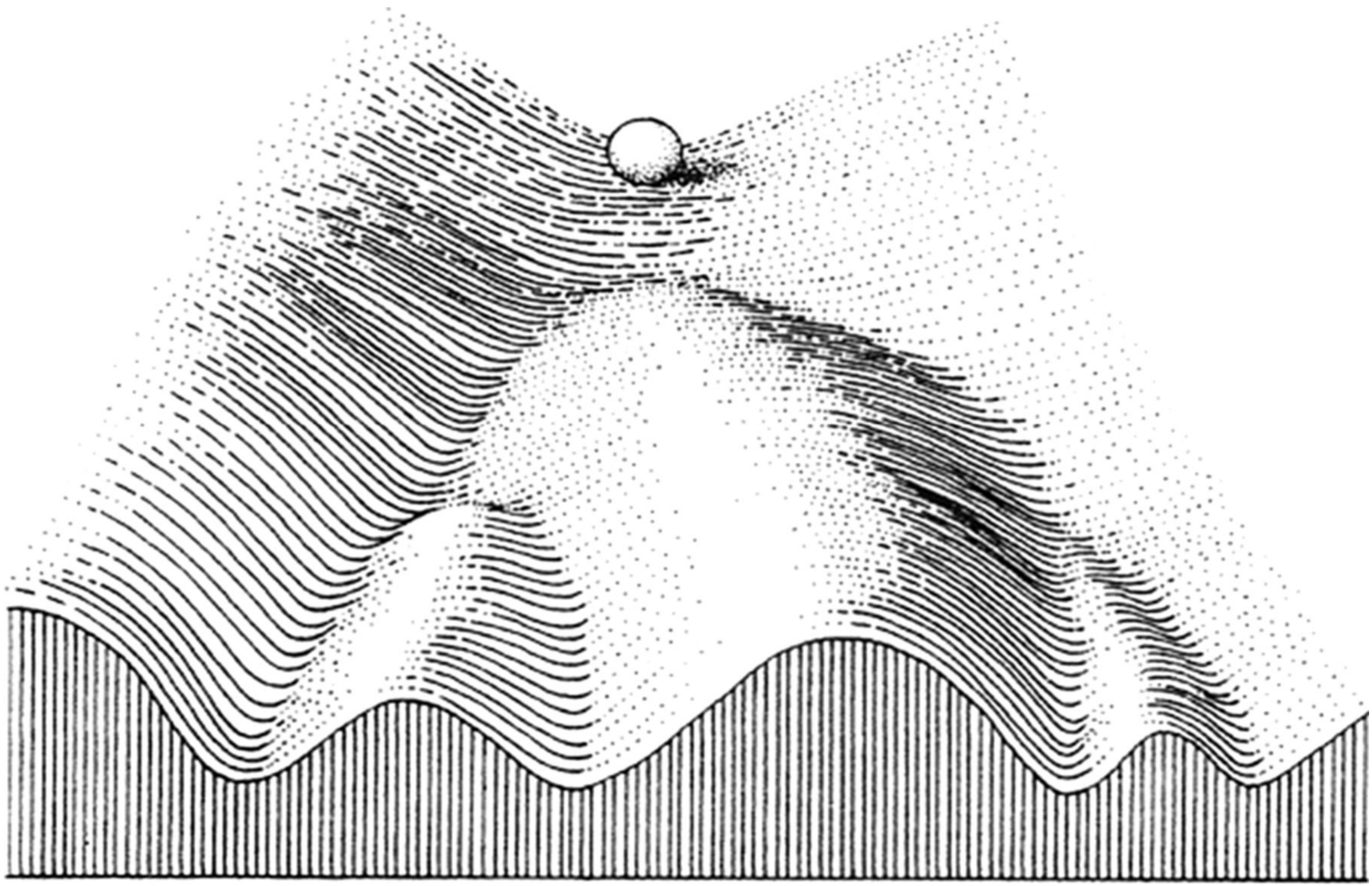
A “Hölder Program” for BNs

- Identify a class of BNs that are “simple” and sufficiently “rich.”
- Define a notion of “quotient” of a BN by a subnetwork.
- Show that each BN has a filtration by subnetworks so that each successive quotient is a product of simple networks.
- Classify the different ways in which BNs can be built as extensions of two BNs that are simpler.
- Rigorous definition of “dynamic equivalence” of BNs.
- Develop a category-theoretic foundation for this program.

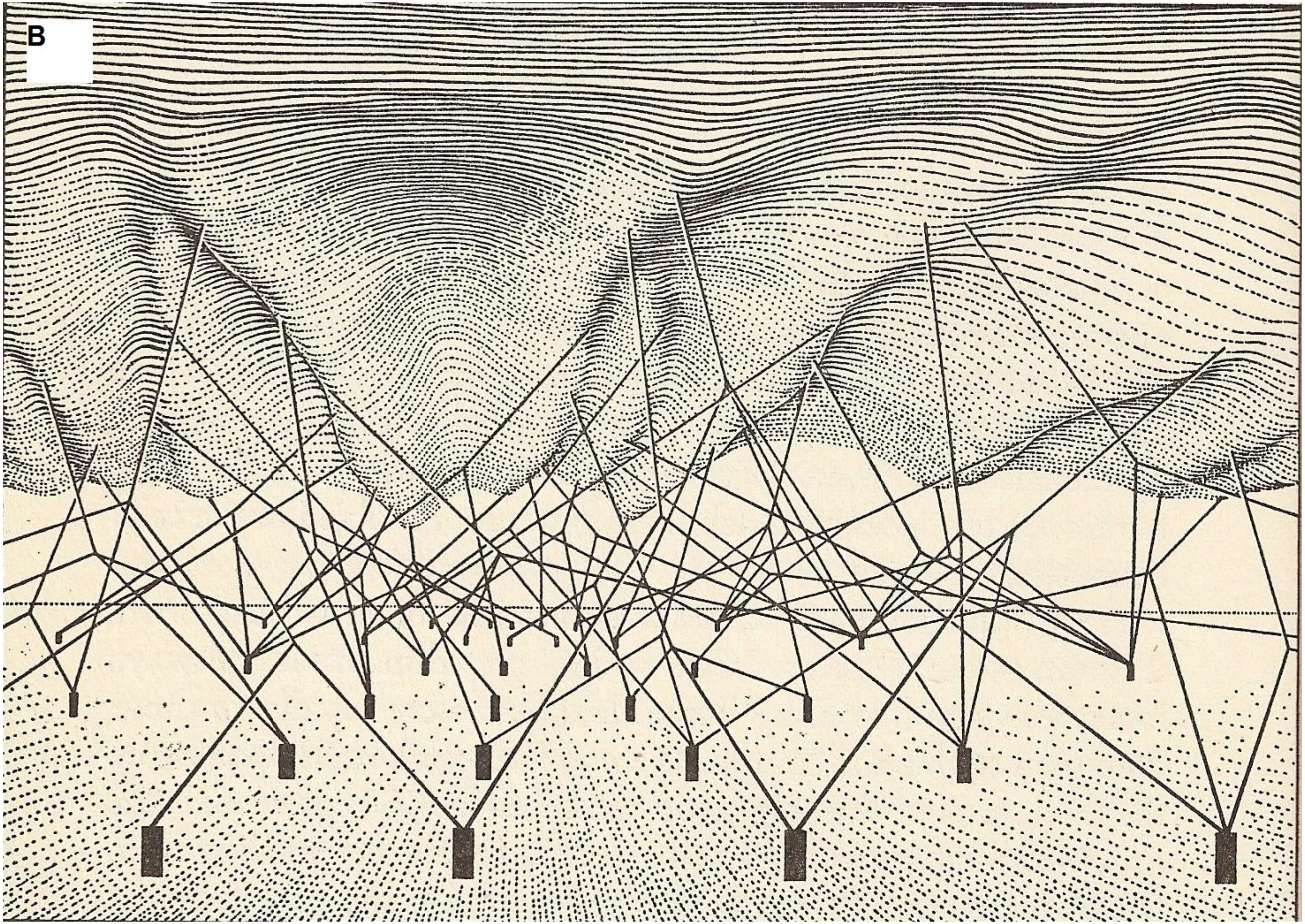
Journal of Theoretical Biology
Volume 22, Issue 3, March 1969, Pages 437-467

Metabolic stability and epigenesis in randomly constructed genetic nets

S.A. Kauffman [a, b]



C. Waddington, The Strategy of the Genes, 1957



C. Waddington, The Strategy of the Genes, 1957

Physica D 314 (2016) 1–8

Contents lists available at ScienceDirect

Physica D

journal homepage: www.elsevier.com/locate/physd

Stratification and enumeration of Boolean functions by canalizing depth

Qijun He, Matthew Macauley *

Department of Mathematical Sciences, Clemson University, Clemson, SC 29634-0975, USA

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

Physica D 233 (2007) 167–174

PHYSICA D

www.elsevier.com/locate/physd

Nested canalyzing, unate cascade, and polynomial functions☆

Abdul Salam Jarrah[a,*], Blessilda Raposa[b], Reinhard Laubenbacher[a]

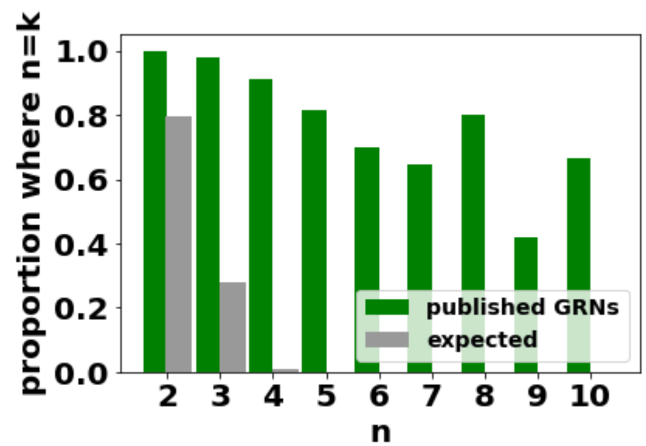
[a] *Virginia Bioinformatics Institute (0477), Virginia Tech, Blacksburg, VA 24061, USA*

[b] *Mathematics Department, De La Salle University, 2401 Taft Avenue, Manila, Philippines*

Prevalence of canalization

observed

n \ k	0	1	2	3	4	5	6	7	8	9	10
0	2										
1	0	1688									
2	0	0	744								
3	6	1	0	411							
4	23	2	0	0	251						
5	19	8	2	0	0	133					
6	17	5	6	0	1	0	66				
7	7	4	3	1	1	0	0	27			
8	4	1	0	2	0	0	0	0	26		
9	2	3	3	0	0	3	0	0	0	7	
10	0	0	1	0	1	0	0	0	0	0	4



- Nested canalizing functions (and therefore? canalizing functions) are overrepresented in GRNs.

Courtesy C. Kadelka

Available at WWW.MATHEMATICSWEB.ORG
POWERED BY SCIENCE @ DIRECT

ACADEMIC PRESS

Advances in Applied Mathematics 30 (2003) 655–678

ADVANCES IN Applied Mathematics

www.elsevier.com/locate/yaama

Decomposition and simulation of sequential dynamical systems

Reinhard Laubenbacher [a,*] and Bodo Pareigis [b]

[a] *Virginia Bioinformatics Institute, Blacksburg, VA 24061, USA*
[b] *Mathematisches Institut, Universität München, Theresienstr. 39, D-80333 München, Germany*

Proposal

Carry out the Hölder Program for synchronous AND-NOT networks.

Research supported by:

NIH 1R011AI135128-01
NIH 1U01EB024501-01
NIH 1R21AI101619-01
NSF CBET-1750183
NSF DMS 1460967
NSF CMMI-0908201
U.S. Dept. Defense W911NF-14-1-0486