biologically-inspired computing

lecture 8



course outlook



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final project schedule

Projects

bit.lv/atBIC

Due by May 7th in Brightspace, "Final Project 483/583" assignment

ALIFE 2025

- Not necessarily to submit to actual conference due date
 - May 4 full paper, July 4, abstract
- https://2025.alife.org/
- Max 8 pages, author guidelines:
- https://2025.alife.org/calls#paper-call
- MS Word and Latex/Overleaf templates
- Preliminary ideas by March 7
 - Submit to "Project Idea" assignment in Brightspace.
- Individual or group
 - With very definite tasks assigned per member of group

ALIFE 2025

Tackle a real problem using bio-inspired algorithms, such as those used in the labs.



Reusing and expanding labs is highly encouraged.

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readings for this class

Additional information

- Floreano, D. and C. Mattiussi [2008]. *Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies*. MIT Press. Preface, Sections 4.1, 4.2. **Chapter 2.**
 - Nunes de Castro, Leandro [2006]. Fundamentals of Natural Computing: Basic Concepts, Algorithms, and Applications. Chapman & Hall. Chapter 1, pp. 1-23. Sections 7.1 to 7.4, Appendix B.3.1. Chapter 2, Sections 8.1, 8.2, 8.3.10

Lecture notes

- Chapter 1: What is Life?
- Chapter 2: The logical Mechanisms of Life
- Chapter 3: Formalizing and Modeling the World
- Chapter 4: Self-Organization and Emergent Complex Behavior
 - posted online @ casci.binghamton.edu/academics/i-bic
- Papers and other materials
 - Optional
 - Prusinkiewicz and Lindenmeyer [1996] The algorithmic beauty of plants.
 - Chapter 1
 - Flake's [1998], *The Computational Beauty of Life*. MIT Press.
 - Chapters 1, 5, 6 (7-9).
 - Chapters 10, 11, 14





What's a CA?

more formally



Langton's parameter

Finding the structure of all possible transition functions

- Statistical analysis
 - Identify classes of transition functions with similar behavior
 - Similar dynamics (statistically)
 - Via Higher level statistical observables
 - Like Kauffman
- The Lambda Parameter (similar to bias in BN)
 - Select a subset of D characterized by λ
 - Arbitrary quiescent state: s_q
 - Usually 0
 - A particular function Δ has *n* transitions to this state and (*K*^{*N*}-*n*) transitions to other states *s* of Σ
 - $(1-\lambda)$ is the probability of having a s_{α} in every position of the rule table



- $\lambda = 0$: all transitions lead to s_q (n =K^N)
- λ = 1: no transitions lead to s_q (n =0)
- $\lambda = 1-1/K$: equally probable states (n=1/K . K^N)

Range: from most homogeneous to most heterogeneous

Langton, C.G. [1990]. "Computation at the edge of chaos: phase transitions and emergent computation". *Artificial Life II*. Addison-Wesley.

Langton's observations







Langton's results











Approximate time when density is within 1% of long-term behavior

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Langton's results

 $\lambda = 0.70$

Approximate time when density is within 1% of longterm behavior





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- Transient growth in the vicinity of phase transitions
 - Length of CA lattice only relevant around phase transition (λ =0.5)
- Conclusion: more complicated behavior found in the phase transition between order and chaos
 - Patterns that move across the lattice

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Computation at the edge of chaos?



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evolution requires life in critical regime which is small, how come life is not chaotic? 0.8 Kauffman, S. A. (1984). *Phys. D* Waddington CH (1942). 0.6 Nonlinear Phen.10,145-156. **Chaotic Phase** D Nature.150 (3811):563-565 0.4 robustness of phenotypes is the result of a *buffering* of 0.2 the developmental process. 0 + 0 20 60 40 dynamics of gene networks provides buffering (self-K organization). But still easily chaotic. Aldana, M. [2003]. Physica D. 185: 45-66 The Criticality Hypothesis rocha@binghamton.edu BINGHAMTON UNIVERSITY casci.binghamton.edu/academics/i-bic

self-organization easily chaotic

self-organization easily chaotic

evolution requires life in critical regime which is small, how come life is not chaotic?





self-organization easily chaotic



criticality in Boolean networks





Marques-Pita & Rocha, [2013]. PLoS ONE, 8(3): e55946.

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Interaction graph typically obtained from (qualitative) pairwise estimation of interaction. No dynamics represented in graph; many dynamics fit same structure.

Effective graph redundancy in dynamics is integrated probabilistically (not estimated). Reveals network of nonlinear interactions that escapes pairwise estimation. Provides **causal explanation** of how dynamical perturbation and control signals propagate in biochemical pathways.

Gates, Correia, Wang & Rocha [2021]. PNAS. 118 (12): e2022598118.

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redundant pathways are ubiquitous in biochemical regulation



Gates, Correia, Wang & Rocha [2021]. PNAS. 118 (12): e2022598118.







Costa, Rozum, Marcus, & Rocha[2023]. *Entropy*. **25**(2):374. Manicka, Marques-Pita, & Rocha, [2021]. *J. Royal Society Interface*. **19**(186):20210659.











Thaliana control pathways (using structure and dynamics information)

control and the cybernetics of life

Boolean networks, control, sound, art, and education



control and the cybernetics of life

Boolean networks, control, sound, art, and education



discrete modeling of cancer networks

predicting drug and therapy targets in causal models

discrete modeling of within-cell **oncogenic signal transduction**, recapitulates known resistance PI3K inhibitors. Suggests novel combinatorial interventions.



A network modeling approach to elucidate drug resistance mechanisms and predict combinatorial drug treatments in breast cancer Jorge G. T. Zañudo^{1,2,3,*} and Réka Albert^{1,4,&}





HER3_T HER3 IGF1R_T HER3_2 IGF1R Fulvestrant **RTK** signaling PI3K pathway MAPK pathway AKT pathway HER2_3_2 HER2 3 HER2 IGF1R 2 ESR1 ESR1_2 FOXA1 Neratinib mTORC1 pathway ER signaling Apoptosis ER Trametini RAS **PI3K** Alpelisib Ipatasertib Proliferation Drugs PBX1 ER_transcription MAPK RAS_3 PI3K_2 PIP3 ER_transcription_2 PTEN MYC_2 MAPK_2 PIP3_2 mTORC2_pm KMT2D MYC RAS_2 mTORC2 PDK1 PIM PDK1_pm AKT Everolimus Palbociclib CDK46 SGK1_T SGK1 TSC p21_p27 p21_p27_T cyclinD FOXO3_Ub FOXO3 mTORC1 cycE_CDK2 cycE_CDK2_T cycD_CDK46 cycD_CDK46_2 PRAS40 BCL2_T BIM_T EIF4F S6K pRb pRb_3 cyclinD_2 pRb_2

Translation

 $e_{ji} \ge 0.2$

E2F

Proliferation

E2F_2

Proliferation 2

E2F_3

Proliferation_4

Proliferation_3

uncovering and characterizing control pathways for drug therapy

Gates, Correia, Wang & Rocha [2021]. PNAS. 118 (12): e2022598118.

BIM

BAD

BCL2

MCL1

Apoptosis_3

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uncovering and characterizing control pathways for drug therapy

causal (modular) dynamics via conditional effective connectivity



Manicka, Marques-Pita, & Rocha, [2022]. J. Royal Society Interface. 19(186):20210659. Rocha L.M. [2022]. Bioinformatics. btac360. Parmer, Rocha & Radicchi [2022]. Nature Communications. 13, 3457. Gates, Correia, Wang & Rocha [2021]. PNAS. 118 (12): e2022598118. Gates & Rocha [2016]. Scientific Reports 6, 24456.











effective modularity



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dynamically-decoupled modules

Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118. Manicka, Marques-Pita, & Rocha, [2022]. *J. Royal Society Interface*. **19**(186):20210659. Costa, Rozum, Marcus, & Rocha[2023]. *Entropy*. **25**(2):374. Park, Costa, Rocha, Albert, & Rozum [2023]. *PRX Life*. **1**, 023009.

canalization as a key mechanism for resilience

from evolutionary robustness to network and dynamical redundancy







Kauffman, S. A. (1984). *Phys. D Nonlinear Phen*.**10**,145–156.

Waddington CH (1942). Nature.**150** (3811):563–565

robustness of phenotypes is the result of a *buffering* of the developmental process.

dynamics of gene networks provides buffering (**selforganization**). But still easily chaotic.

Structure (*topological organization*), can provide larger stable or critical universe, but still easily chaotic.

canalized genetic **control** ignores some inputs (*redundancy*) to attain necessary resilience (tradeoff stability/evolvability)

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canalization as a key mechanism for resilience

from evolutionary robustness to network and dynamical redundancy



Alan Turing (1912-1954)

key contributions (most relevant to biocomplexity)

"The chemical basis of morphogenesis"

Turing, A. M. *Phil. Trans. R. Soc. Lond. B* 237, 37–72 (1952).
 Reaction-diffusion systems

"Computing machinery and intelligence"

Turing, A. M. *Mind* 49, 433–460 (1950).
 The "Turing Test"

On computable numbers with an application to the Entscheidungsproblem"

Turing, A. M. *Proc. Lond. Math. Soc.* s2–42, 230–265 (1936–37).
Turing machine, universal computation, decision problem



Brenner, Sydney. [2012]. "Life's code script." Nature 482 (7386): 461-461.

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Turing's tape

A fundamental principle of computation

- "On computable numbers with an application to the *Entscheidungsproblem*"
 - Turing, A. M. *Proc. Lond. Math. Soc.* s2–42, 230–265 (1936–37).
 Turing machine, universal computation, decision problem
 - Machine's state is controlled by a program, while data for program is on limitless external tape
 every machine can be described as a number that can be stored on the tape (for itself or another machine)
 - - Including a Universal machine
 - distinction between numbers that mean things (data) and numbers that do things (program)



A Turing Machine



imagine automata as agents

quorum sensing or what decision to take? (Density Classification)



random strategies

density classification task



local strategy: majority rule

density classification task



block expansion strategy

density classification task



emergent computation strategies

density classification task



 $P_{149}^{10^5} > 80 \%$



Integration and <u>transmission</u> of information across population

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best CA rules for emergent computation

for DST



Some other rules that are capable of collective information processing over time and space can solve this task with a range of performances where $P_{149}^{10^5} > 80 \%$

Rule	Hexadecimal Representation	$\mathcal{P}_{149}^{10^{5}}$	Produced by	Source	
Φ_{GKL}	5f005f005f005f005fff5f005fff5f	0.8143	HE	Gacs et al., 1978	
Φ_{Davis95}	2f035f001fcf1f002ffc5f001fff1f	0.8188	HE	Andre et al., 1996	
φ_{Das95}	70007ff0f0000fff0f00007ff0f310fff	0.8215	HE	Andre et al., 1996	
φ_{GP1995}	50055050500550555ff55ff55ff55ff	0.8212	GP	Andre et al., 1996	
Φ_{DMC}	504058705000f77037755837bffb77f	0.7784	GA	Das et al., 1994	
Φ_{COE1}	11430d7110f395705b4ff17f13df957	0.8498	CE	Juillè and Pollack, 1998	
Φ_{COE2}	1451305c0050ce5f1711ff5f0f53cf5f	0.8601	CE	Juillé and Pollack, 1998	
Φ_{GEP1}	50005ff050005ff05ff05ff05ff05ff05ff	0.8119	GEP	Ferreira, 2001	
Φ_{GEP2}	550077005500770f550f77ff55ff77	0.8250	GEP	Ferreira, 2001	

Integration and <u>transmission</u> of information across population

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Table I: Catalog of regular domains, particles and particle interactions for rule ϕ_{DMC}

Regular Domains	$\Lambda^0 = \{0+\}, \Lambda$	$\Lambda^{1} = \{1+\}, \Lambda^{2} = \{(01)+\}$	Hanson, J.E., Crutchfield, J.P., [199]			
Particles (velocities)	$\label{eq:gamma_linear} \begin{array}{l} \underline{\alpha} \ \sim \ \Lambda^0 \ \Lambda^1 \ (-) \\ \underline{\delta} \ \sim \ \Lambda^2 \ \Lambda^0 \ (-3) \end{array}$), $\beta \sim \Lambda^1 \Lambda^0$ (0), $\gamma \sim \Lambda^0 \Lambda^2$ (-1), $\mu \sim \Lambda^2 \Lambda^1$ (1),), $\eta \sim \Lambda^1 \Lambda^2$ (3)	Crutchfield, J.P., Hanson, J.E., [1993].			
	decay	α → <u>γ</u> + μ	1 hysica D. 07, 277-301.			
Observed Interactions	react	$\beta + \chi \rightarrow \eta, \mu + \beta \rightarrow \delta$, $\eta + \delta \rightarrow \beta$				
	annihilate	$\eta + \mu \rightarrow \Lambda^1, \chi + \delta \rightarrow \Lambda^0$	ocha@binghamton.edu asci.binghamton.edu/academics/i-bic			

how do best rules solve the problem?



comparison of different automata

how do best rules solve the problem?





Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046. Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118. Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.

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how do best rules solve the problem?







search in redescription (canalization) space

canalization (redundancy) improves evolutionary search

- Created much smoother search space
 - Allows more focused search of rules
 - Canalization, neutrality, robustness?
 - Second best rule in 1-D CA (best-known PS rule)
 - Best split-performance
 - Best rule in 2-D CA
- reason about emergent computation in new ways
 - Process-symmetry



Marques-Pita & Rocha. [2008]. ALIFE XI. MIT Press: 390-397.

						RULE	Generation	Annihilation
			RULE	Generation	Annihilation		{1, 0, 1, 0, #, #, #} {1, 0, #, 0, #, 1, 1} {1, 1, #, 0, 1, #, #} {1, #, 1, 0, 1, #, #}	{0, 0, 1, 1, 1, 1, #} {0, 0, #, 1, #, 1, 0} {0, 1, 0, 1, 1, #, #} {0, #, 0, 1, #, #, 0}
			ф _{мм2D320}	{#,#,#,#,0,#,#,1,1} {#,#,1,#,0,1,#,#,#} {#,1,#,#,0,1,#,#,#}	{0,0,#,#,1,#,#,#,#} {#,#,#,0,1,#,0,#,#} {#,#,#,0,1,#,#,0,#}	Ф _{ММ0802}	{1, #, 1, 0, #, 0, #} {1, #, #, 0, 1, 1, #} {1, #, #, 0, 1, #, 1} {#, 0, 0, 0, 0, 1, 1} {#, 1, 0, 0, 1, #, #} {#, 1, #, 0, 1, 0, #}	{1, #, 0, 1, #, 0, #} {#, 0, 0, 1, #, #, 0} {#, 1, 0, 1, #, 0, #} {#, 1, #, 1, 0, #, 0} {#, #, 0, 1, 0, #, 0} {#, #, 0, 1, 1, 0, #}
1=100	L=120	L=140	L=160	L=180			{#, 1, #, 0, 1, #, 0} {#, #, 0, 0, 1, 0, 1}	{#, #, 0, 1, #, 0, 0} {#, #, #, 1, 0, 1, 0}
Marques-Pita, Mitche	11 & Rocha. [2008]. <i>UC08</i> . LNCS. :	5146 -163. 204:			BINGHAMTO	N rocha@indiana. v casci.binghamte	edu on.edu/academics/i-bi

studying and explaining emergence

linking local and global/collective behavior

- Are emergent patterns good for explanation?
 - Do stripes or spots explain the "system"?
- Canalization (dynamical redundancy) is a powerful idea
 - Capture loci of control and building blocks of information transmission



Marques-Pita & Rocha, [2011]. IEEE Alife.

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realistic emergent/collective computation

Does canalization help?



realistic emergent/collective computation

Does canalization help?

• Studying the effect of noise on the density classification task

						1			
	Rule	Hexadecimal Representation	$\mathcal{P}_{149}^{10^5}$	Produced by	Source	INCORRECT	INCORRECT		INCORP
	Φ_{GKL}	510051005100510051115100511151	0.8143	HE	Gacs et al., 1978	100			
	Ф _{GP1995}	50055050500550555ff55ff55ff55ff	0.8212	GP	Andre et al., 1996		100	100	100
	Φ_{GEP2}	550077005500770155017711551177	0.8250	GEP	Ferreira, 2001	200	200	200	200
,		ra 100 140 1	50	100	149	300	300	300	300







Challa, Hao, Rozum, & Rocha.[2024]. *ALIFE 2024*. MIT Press. pp. 83. DOI: 10.1162/isal_a_00823. Marques-Pita & Rocha, [2011]. *IEEE Alife*.

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realistic emergent/collective computation

Does canalization help?



realistic emergent/collective computation

Does canalization help?



realistic emergent/collective computation

Does canalization help?



realistic emergent/collective computation

Does canalization help?



realistic emergent/collective computation

What about symmetry?

• Not so much, at least for existing (non-noise) CA rules....



Next lectures

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