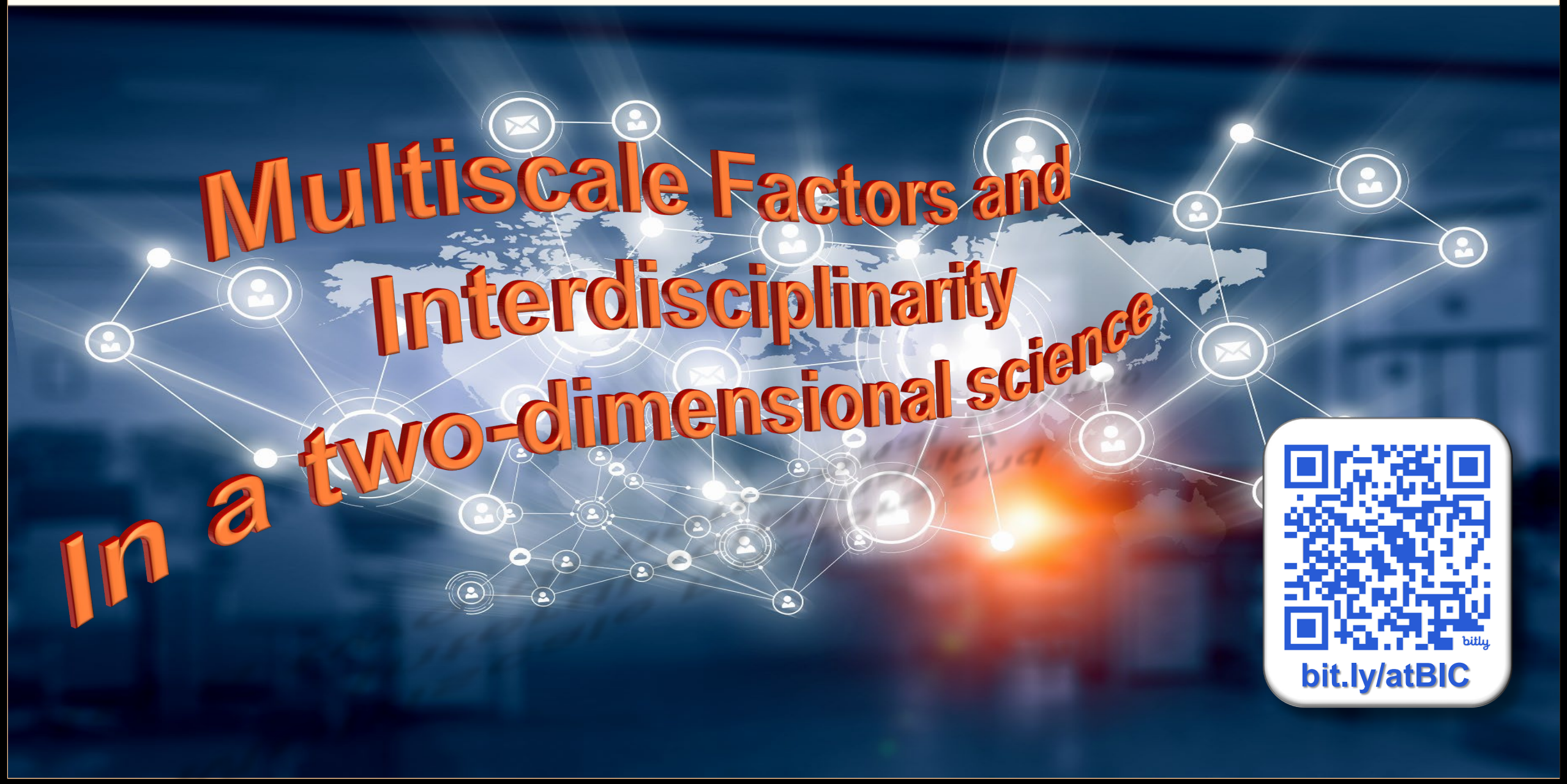
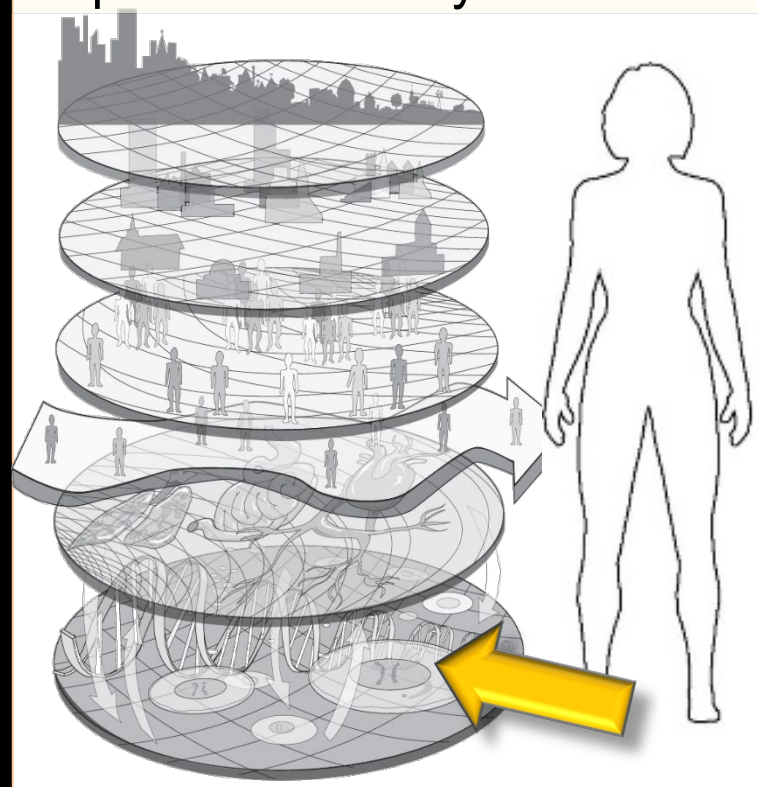
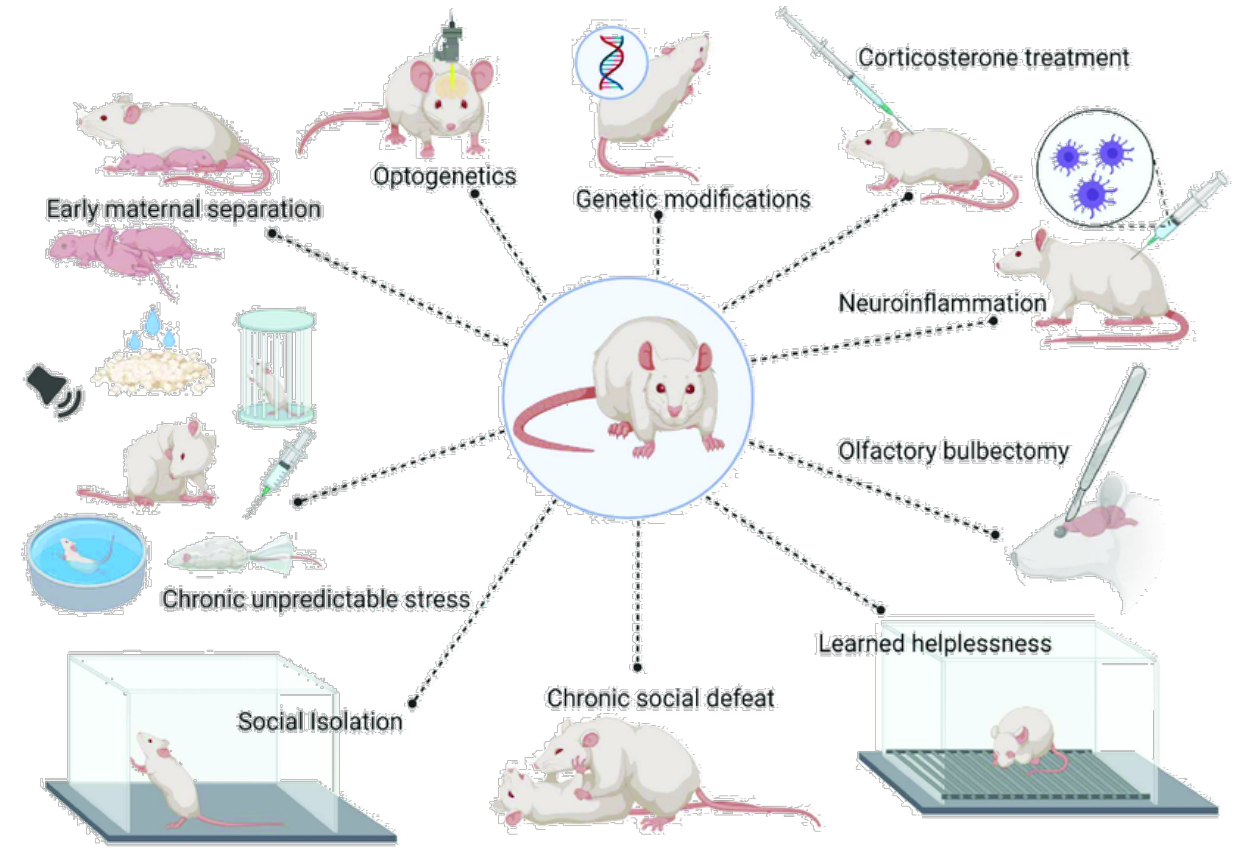

Multiscale Factors and
Interdisciplinarity
In a two-dimensional science
bitly
bit.ly/atBIC

depression/anxiety in mouse models





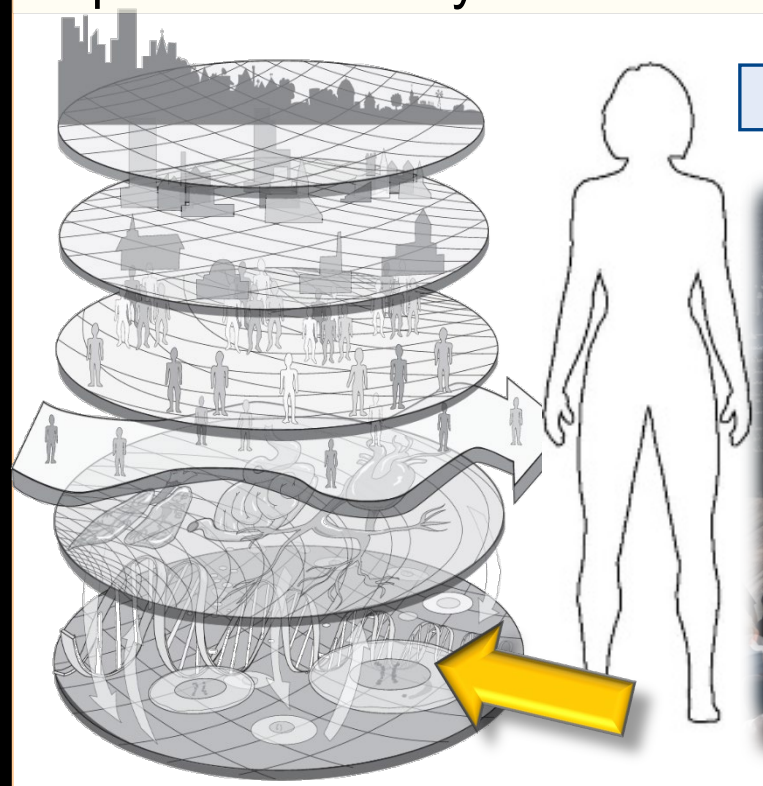
- **Mechanistic basis of complex multiscale disease**
  - assumed to reside in the genetic architecture of anxiety and depression
  - at most, in the architecture of the brain.
- **Emphasis on pharmaceuticals as the only interventions derived from "mechanistic understanding."**

Mir, F. R., & Rivarola, M. A. (2022). Sex differences in anxiety and depression: What can (and cannot) preclinical studies tell us? *Sexes*, **3**(1), 141-163.

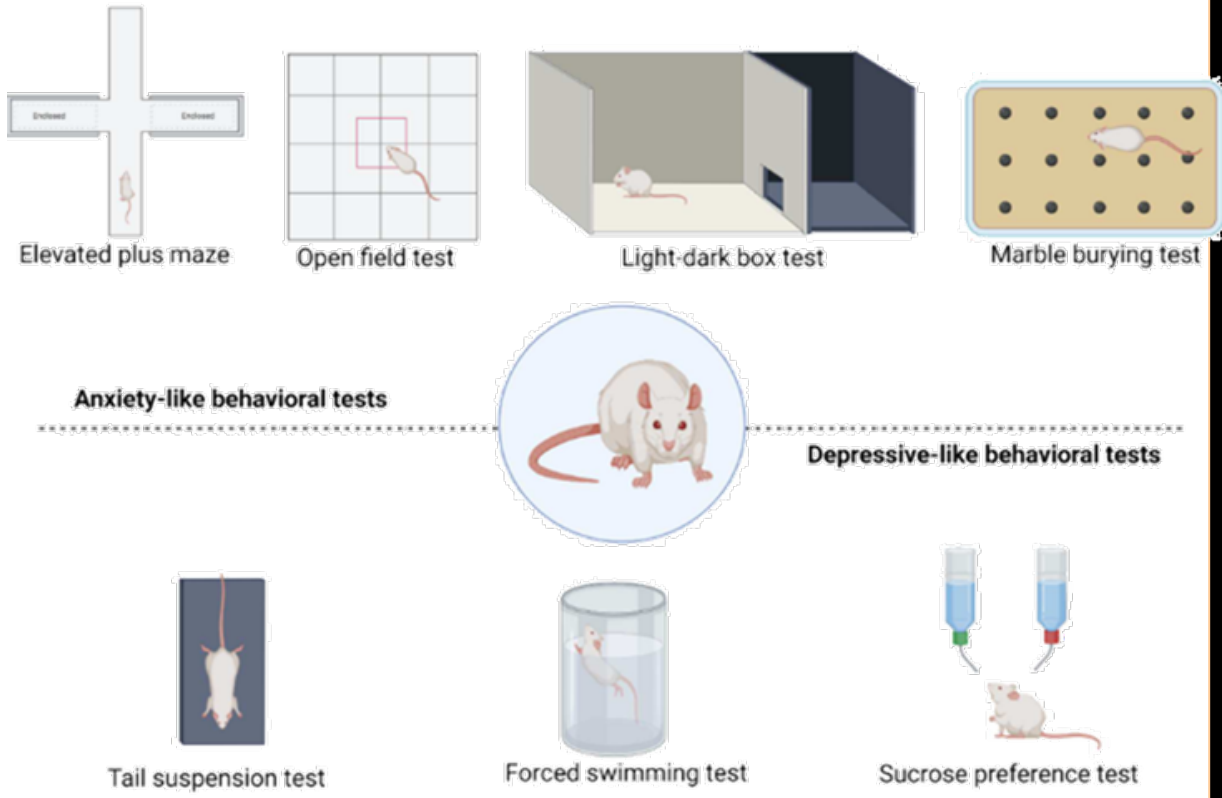
Pescosolido, B.A. 2006. Journal of Health and Social Behavior 47: 189-208.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

depression/anxiety in mouse models



where is language, society, policy?



- **Mechanistic basis of complex multiscale disease**
  - assumed to reside in the genetic architecture of anxiety and depression
  - at most, in the architecture of the brain.
- **Emphasis on pharmaceuticals as the only interventions derived from "mechanistic understanding."**

Pescosolido, B.A. 2006. Journal of Health and Social Behavior 47: 189-208.

Mir, F. R., & Rivarola, M. A. (2022). Sex differences in anxiety and depression: What can (and cannot) preclinical studies tell us? *Sexes*, **3**(1), 141-163.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

What is the best "mechanism" for intervention in psychopathology

depression/anxiety in a *multiscale* view of human disease

REVIEW ARTICLE CHILDREN'S HEALTH

HEALTH AFFAIRS > VOL. 43, NO. 10: CHILDREN, MEDICARE, PHARMACEUTICALS & MORE

REVIEW ARTICLE

Intended And Unintended Outcomes After FDA Pediatric Antidepressant Warnings: A Systematic Review

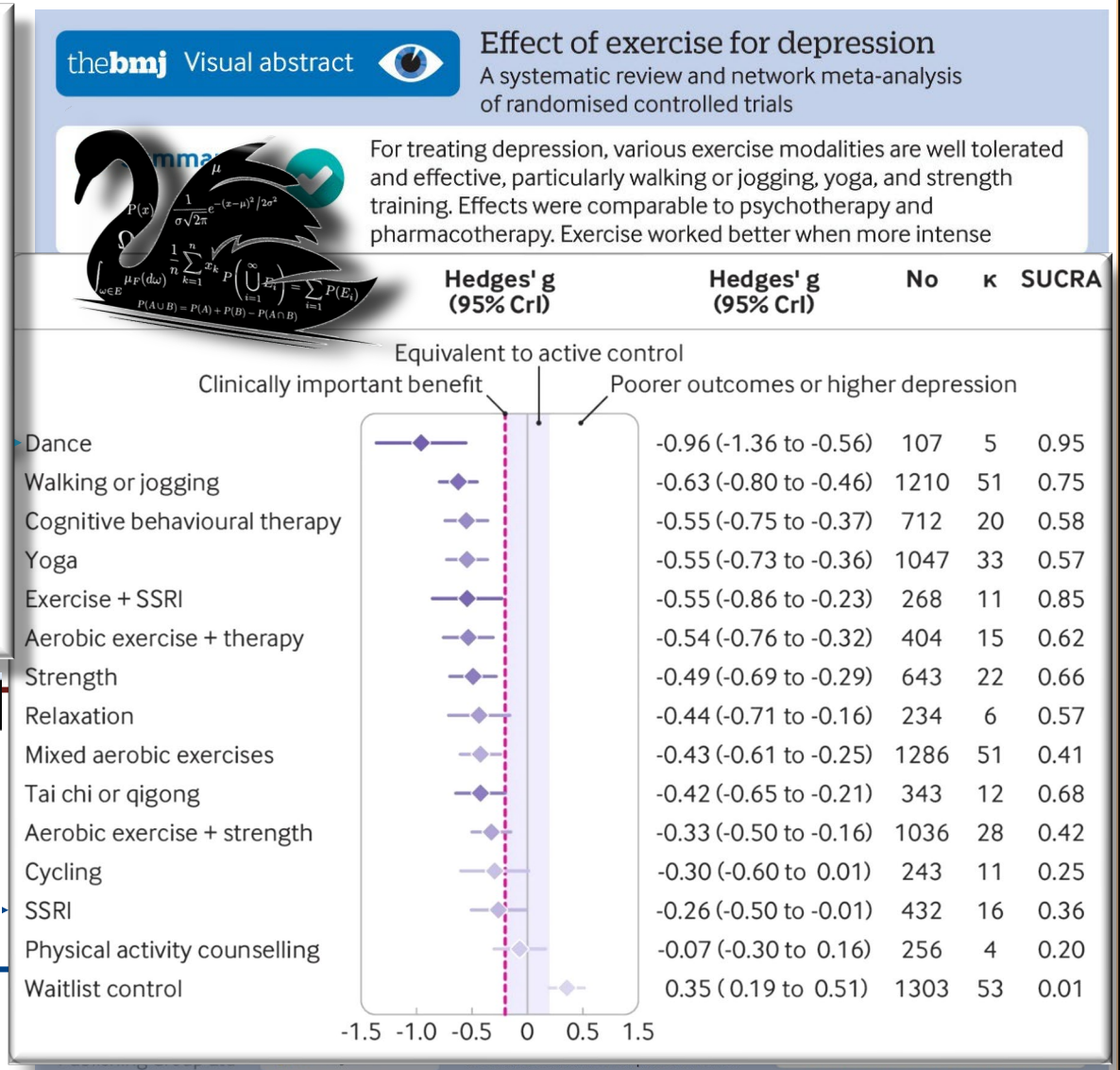
Stephen B. Soumerai, Ross Koppel, Huseyin Naci, Jeanne M. Madden, Andra Fry, Alyssa Halbisen, Jesenia Angeles, Jonah Koppel, Rachelle Rubin, and Christine Y. Lu

AFFILIATIONS

PUBLISHED: OCTOBER 2024 Open Access https://doi.org/10.1377/hlthaff.2023.00263

CNN Health | Life, But Better | Fitness | Food | Sleep | Mindfulness | More | Watch

FDA antidepressant warnings of suicide risk among kids may have the opposite effect, study finds



Noetel, Michael, et al. "Effect of exercise for depression: systematic review and network meta-analysis of randomised controlled trials." *bmj* **384** (2024).

Soumerai, Stephen B., et al [2024] *Health Affairs* **43**.10: 1360-1369.

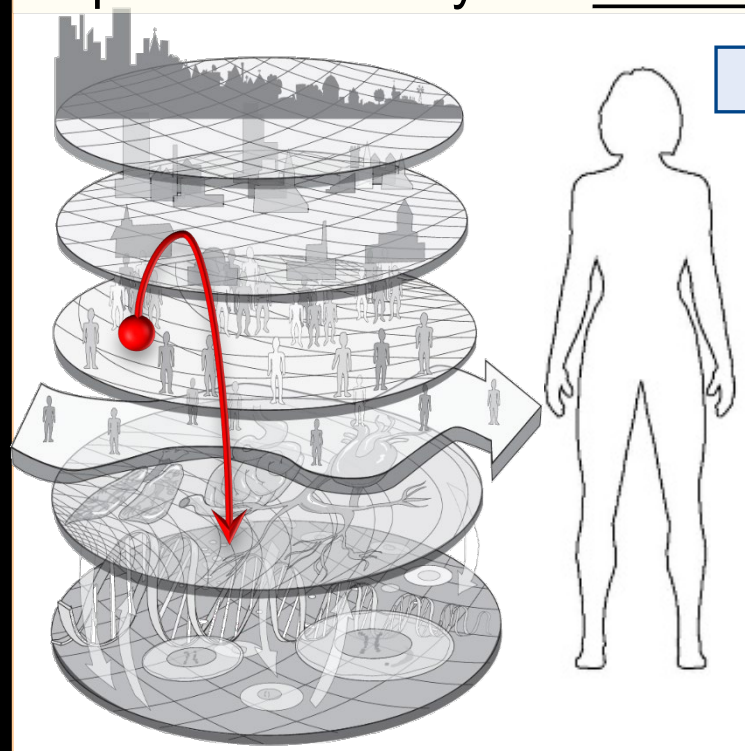
Pescosolido, B.A. 2006. Journal of Health and Social Behavior 47: 189-208.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

What is the best "mechanism" for intervention in psychopathology

depression/anxiety in a *multiscale* view of human disease



where is language, society, policy?

"**Mechanism**" in complex multiscale disease assumed to reside in **molecular architecture**.
Interventions: pharmaceutical, molecular, cellular…

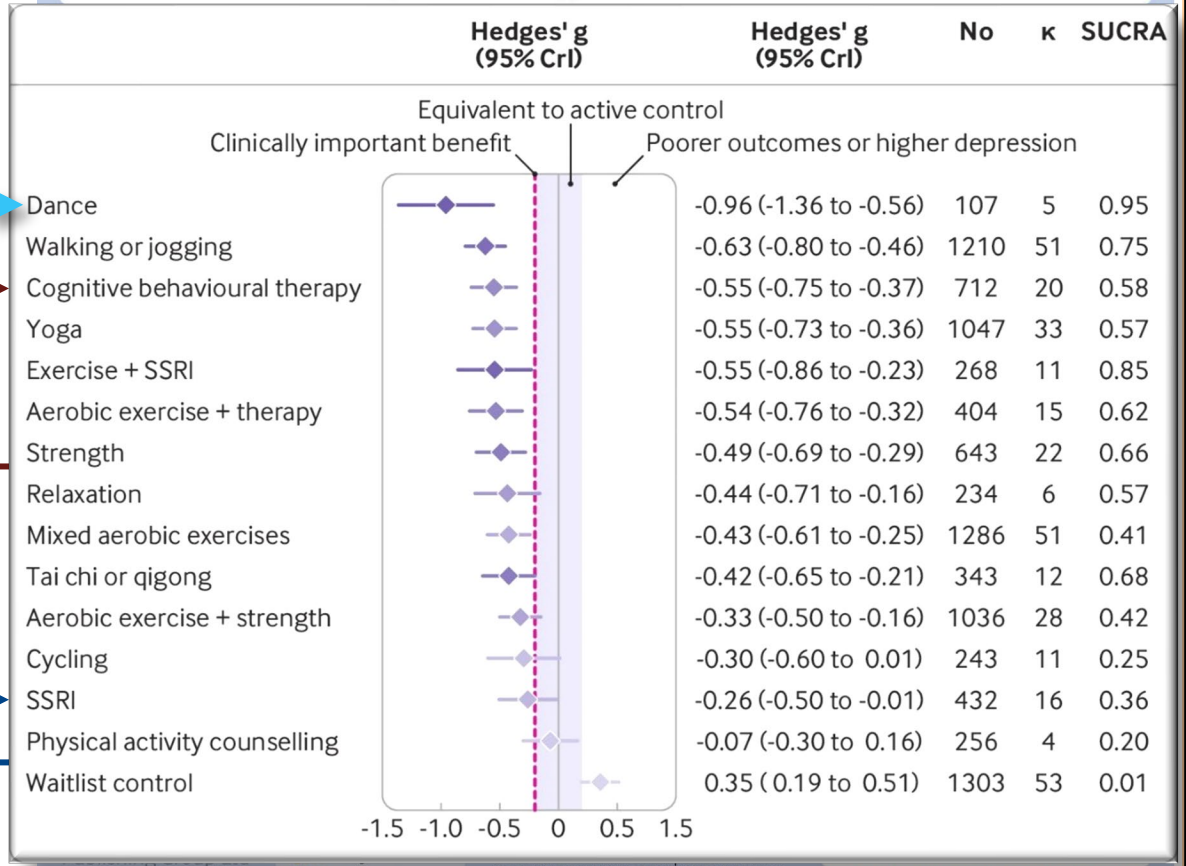
thebmj Visual abstract

Effect of exercise for depression

A systematic review and network meta-analysis of randomised controlled trials

Summary

For treating depression, various exercise modalities are well tolerated and effective, particularly walking or jogging, yoga, and strength training. Effects were comparable to psychotherapy and pharmacotherapy. Exercise worked better when more intense



Noetel, Michael, et al. "Effect of exercise for depression: systematic review and network meta-analysis of randomised controlled trials." *bmj* **384** (2024).

Soumerai, Stephen B., et al [2024] *Health Affairs* **43**.10: 1360-1369.

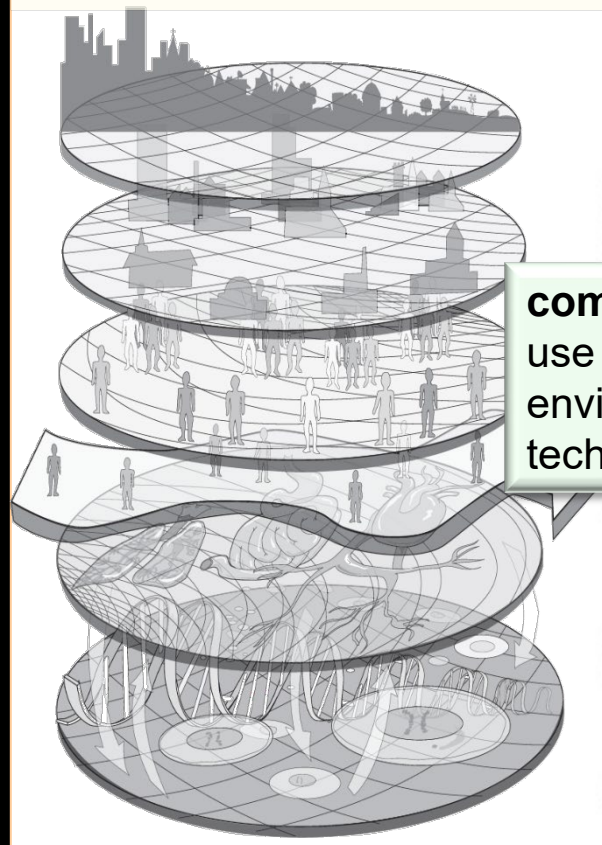
Pescosolido, B.A. 2006. Journal of Health and Social Behavior 47: 189-208.

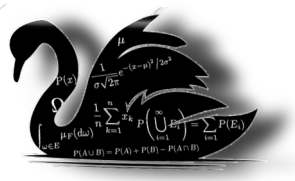
BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

What is the best “mechanism” for intervention in disease?

multiscale view of disease, including human data

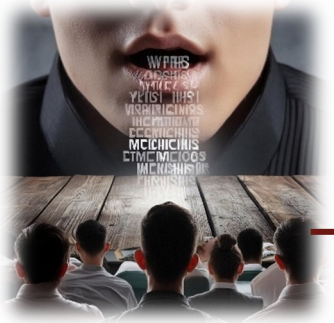




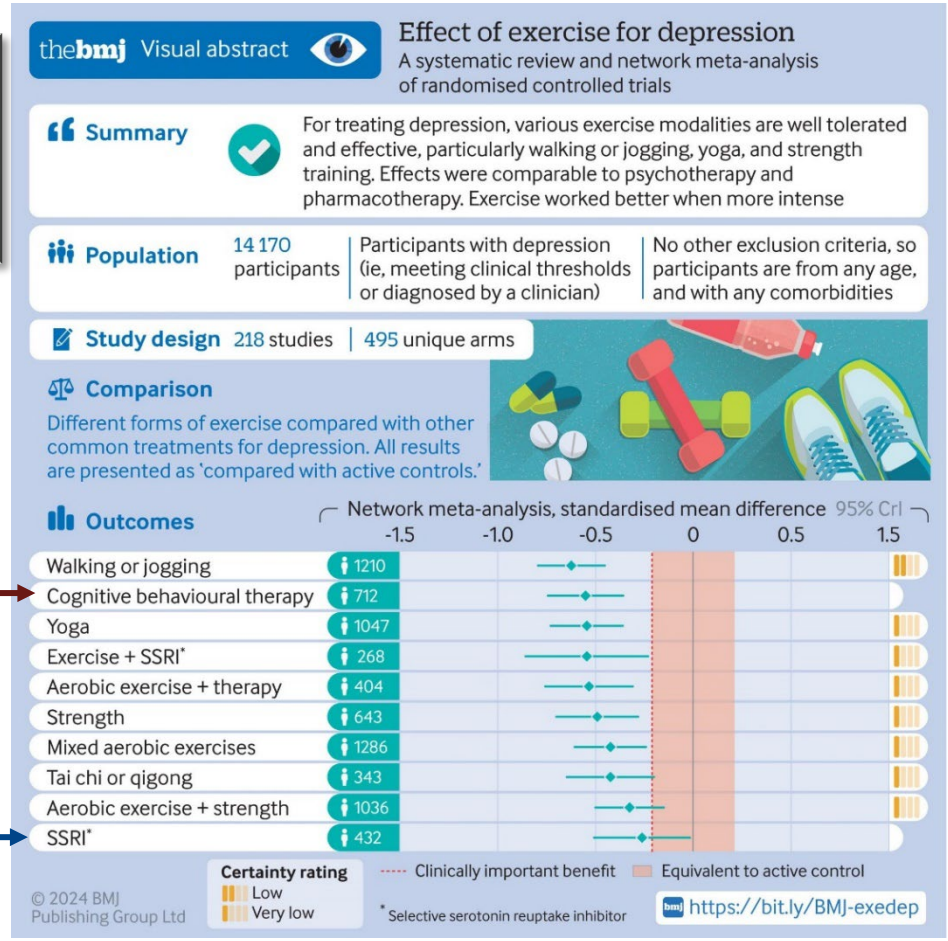
“**Mechanism**” in complex multiscale disease assumed to reside in **molecular architecture**.
Interventions: pharmaceutical, molecular, cellular…

complex systems, multiscale approach: agnostic use of all *multiomics* levels, as well as medical history, environmental, psychological, linguistic, social, technological, and political layers (*exposome*).

interventions: whatever **mechanism** works best, from pharmaceuticals to policy.



Mechanism is pragmatic: levels of explanation should not be assumed, but experimentally established to maximize *intervention*, prediction, and explainability

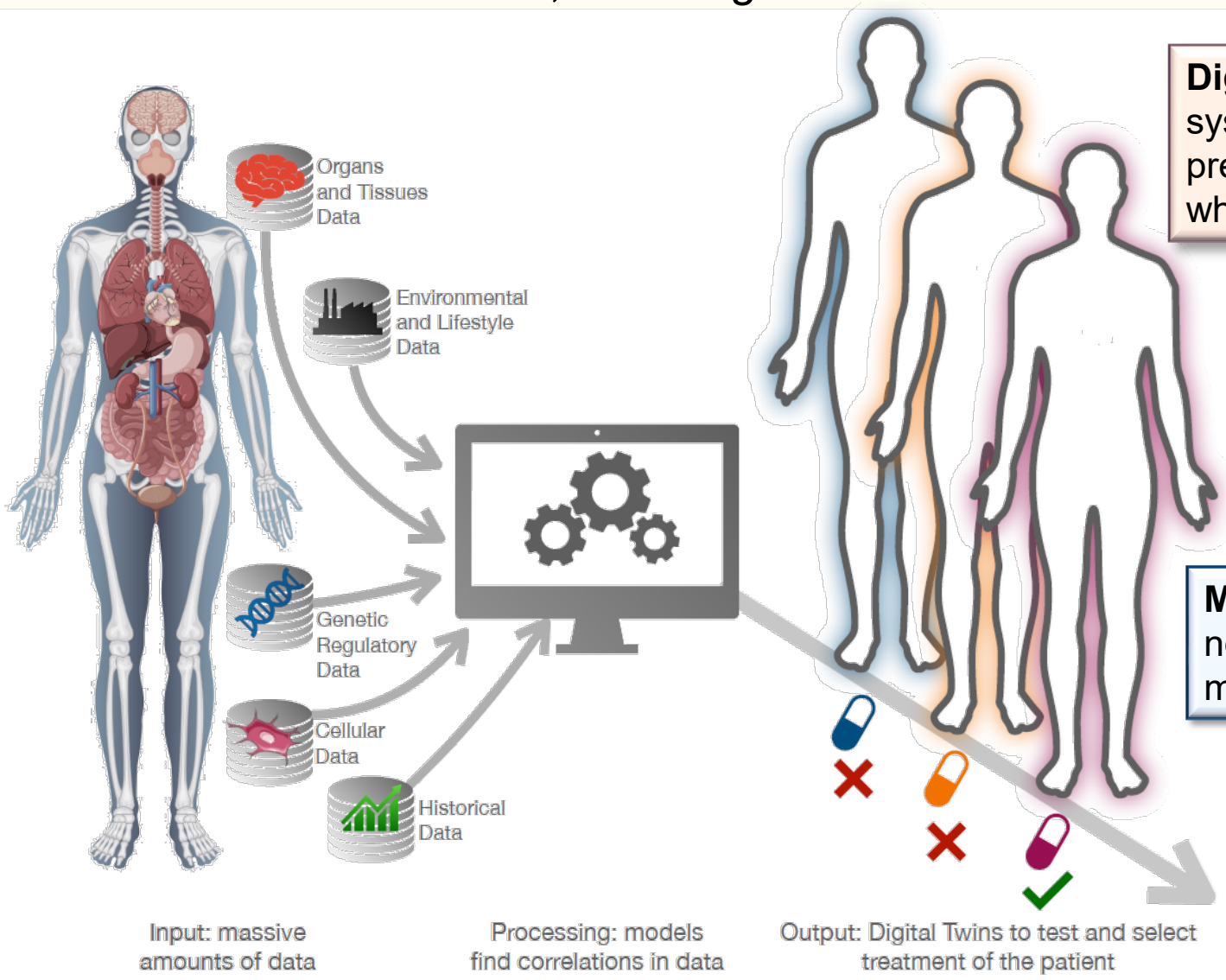


Noetel, Michael, et al. "Effect of exercise for depression: systematic review and network meta-analysis of randomised controlled trials." *bmj* **384** (2024).

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

Pescosolido, B.A. 2006. Journal of Health and Social Behavior 47: 189-208.

multiscale view of disease, including human data from all levels



Digital twin: in-silico *replication* of a biological cell, sub-system, organ or a whole organism with a transparent predictive model of their relevant ***causal mechanisms*** which responds in the same manner to ***interventions***.

complex systems, multiscale approach: agnostic use of all *multiomics* levels, as well as medical history, environmental, psychological, linguistic, social, technological, and political layers (*exposome*).

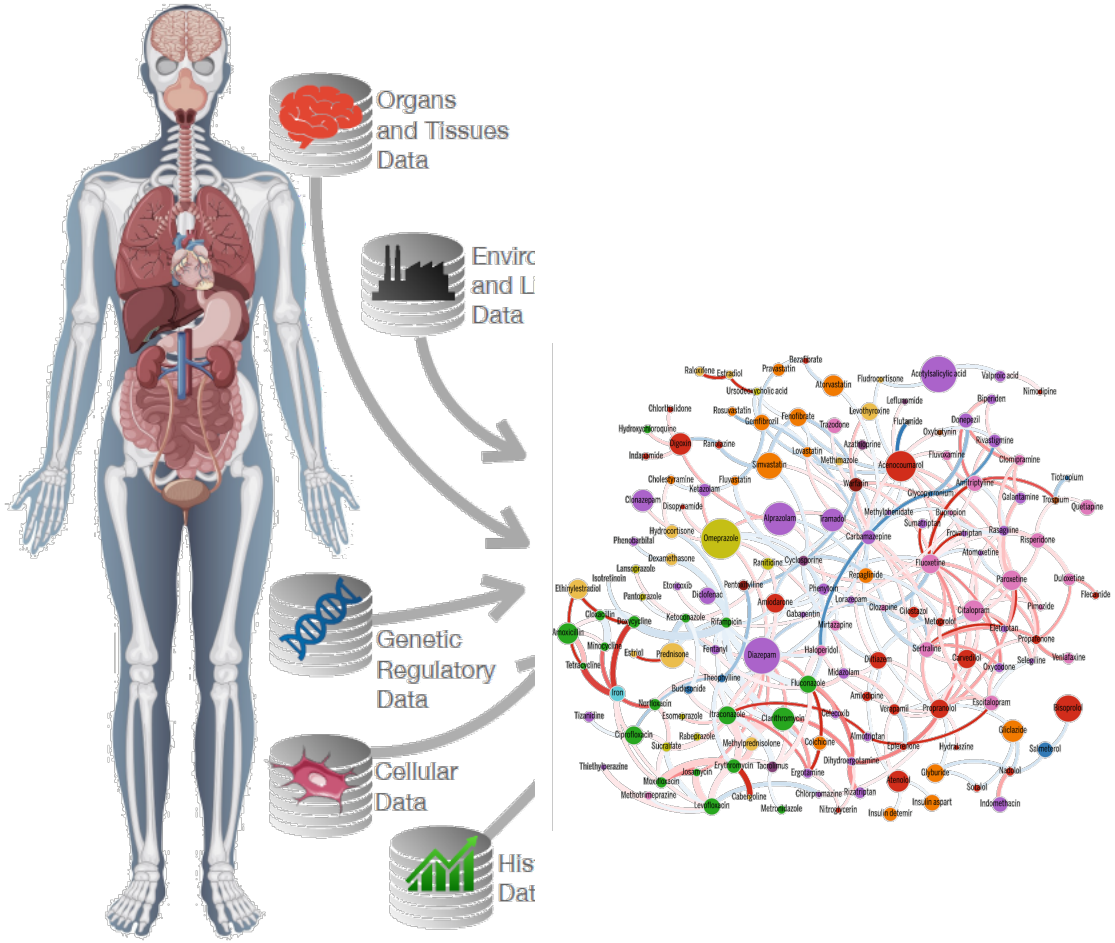
Mechanism is pragmatic: levels of explanation should not be assumed, but experimentally established to maximize *intervention*, prediction, and *explainability*

interventions: whatever **mechanism** works best, from pharmaceuticals to policy.

De Domenico, et al [2024]. "Challenges and opportunities for digital twins in precision medicine: a complex systems perspective". *NPJ Digital Medicine*. In press. *arXiv*:2405.09649.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

multiomics

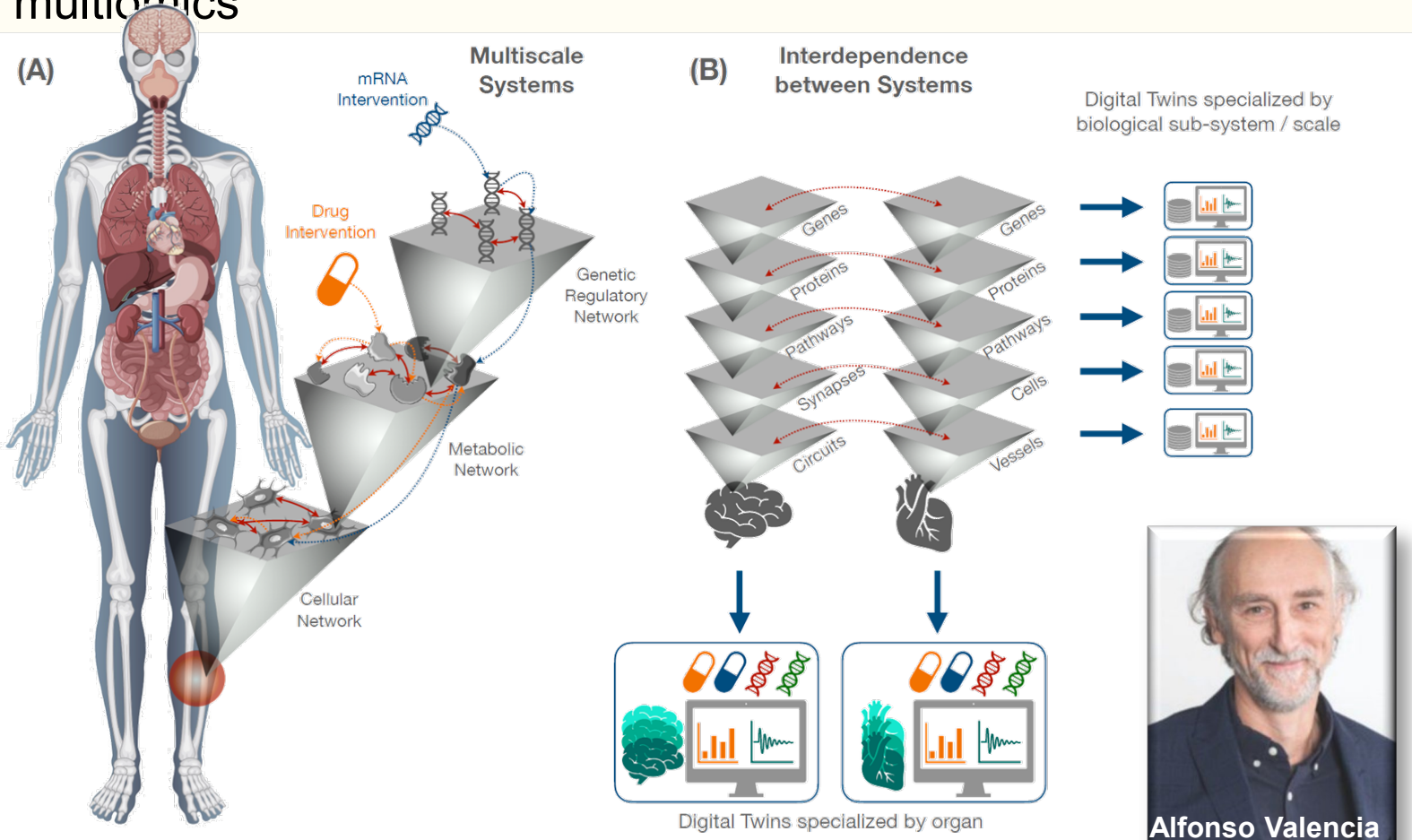


complex systems, multiscale approach: agnostic use of all *multiomics* levels, as well as medical history, environmental, psychological, linguistic, social, technological, and political layers (*exposome*).

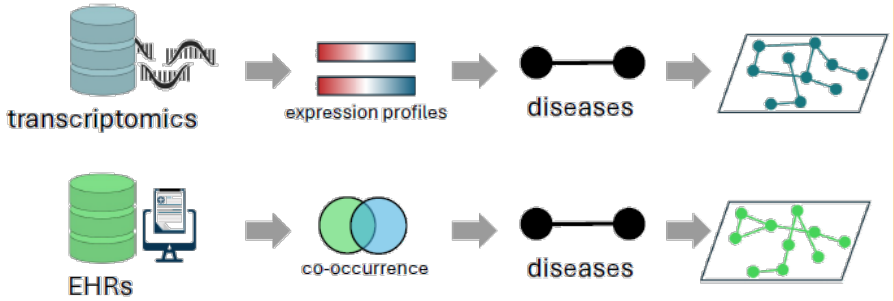
De Domenico, et al [2024]. *NPJ Digital Medicine*. In press. *arXiv*:2405.09649.

BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

multiomics



Layer	Source
Transcriptomics	GEO
EHRs	Danish population
genes	DisGeNET
miRNAs	HMDD
drugs	CTD
symptoms	HSDN
metabolome	HMDB
microbiome	DISBIOME



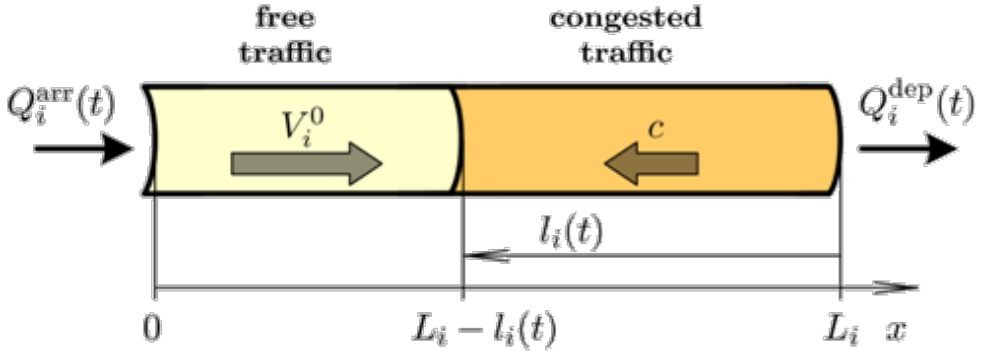
complex systems, multiscale approach: agnostic use of all *multiomics* levels, as well as medical history, environmental, psychological, linguistic, social, technological, and political layers (*exposome*).

Sanchez-Valle et al [2020]. *Nature communications*, **11**: 2854.
Núñez-Carpintero et al [2024]. *Nature communications*, **15**:1227.
De Domenico, et al [2024]. *NPJ Digital Medicine*. In press. *arXiv*:2405.09649.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

Dirk Helbing's Modeling traffic and human group behavior

- Vehicles and people modeled as particles in a fluid medium
  - Free traffic: behaves as a gas
    - Particles move freely
  - Congested traffic: behaves as a liquid
    - movement of particles strongly depends on surrounding dynamics
  - Shock waves
    - emerge from density variations
    - Example in congested traffic
      - The velocity change of a vehicle propagates (with a homogenous time delay) in the opposite direction of traffic as downstream vehicle respond to changes in upstream vehicles
      - propagation speed aprox. -15 km/h (In free traffic = free vehicle velocity).



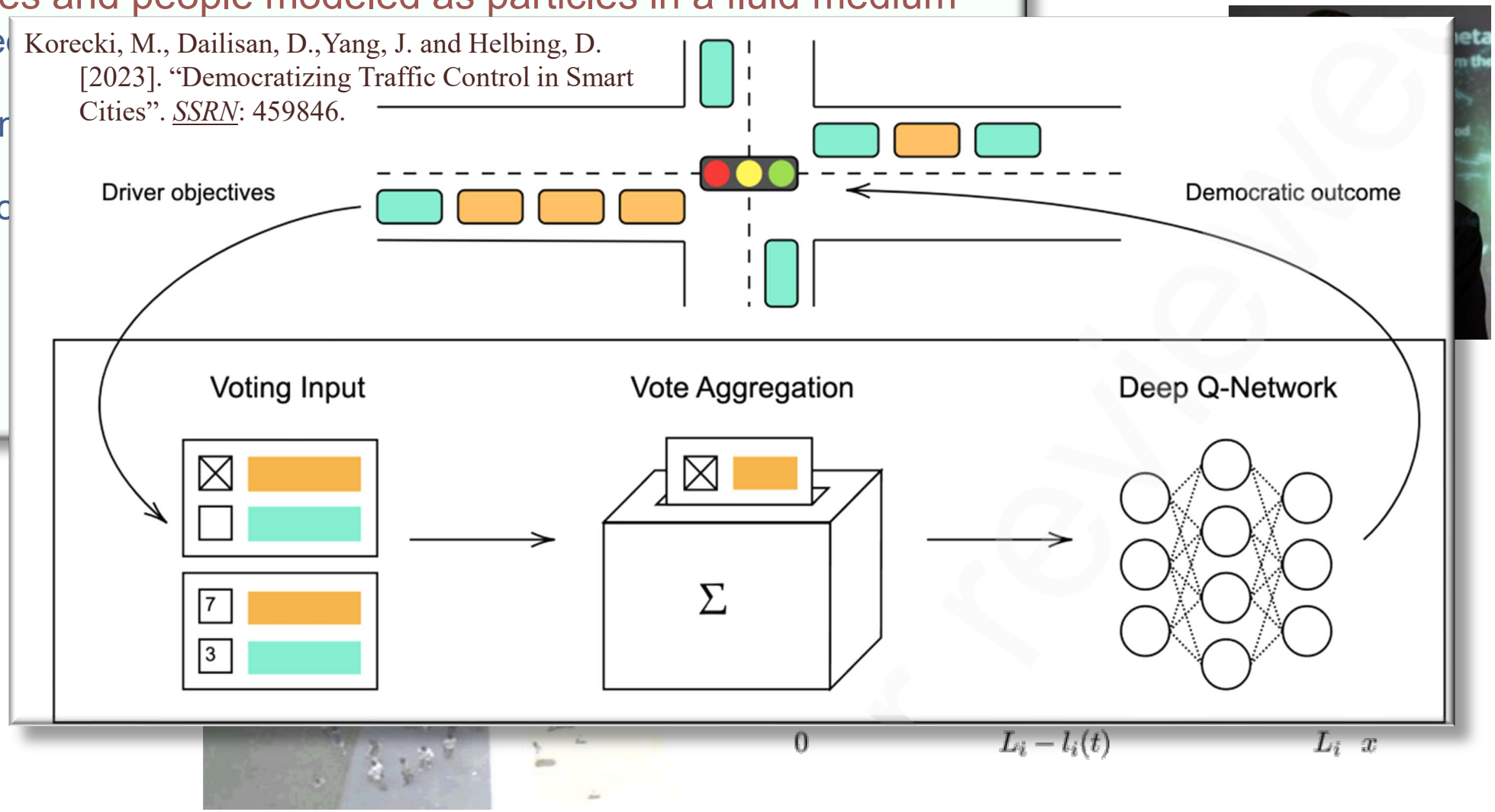
D. Helbing: Traffic and related self-driven many-particle systems.
Reviews of Modern Physics **73**, 1067-1141 (2003).

BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

Dirk Helbing's Modeling traffic and human group behavior

- Vehicles and people modeled as particles in a fluid medium
  - Fre
    -
  - Cor
    -
  - Sho
    -
    -

Korecki, M., Dailisan, D.,Yang, J. and Helbing, D. [2023]. "Democratizing Traffic Control in Smart Cities". *SSRN*: 459846.

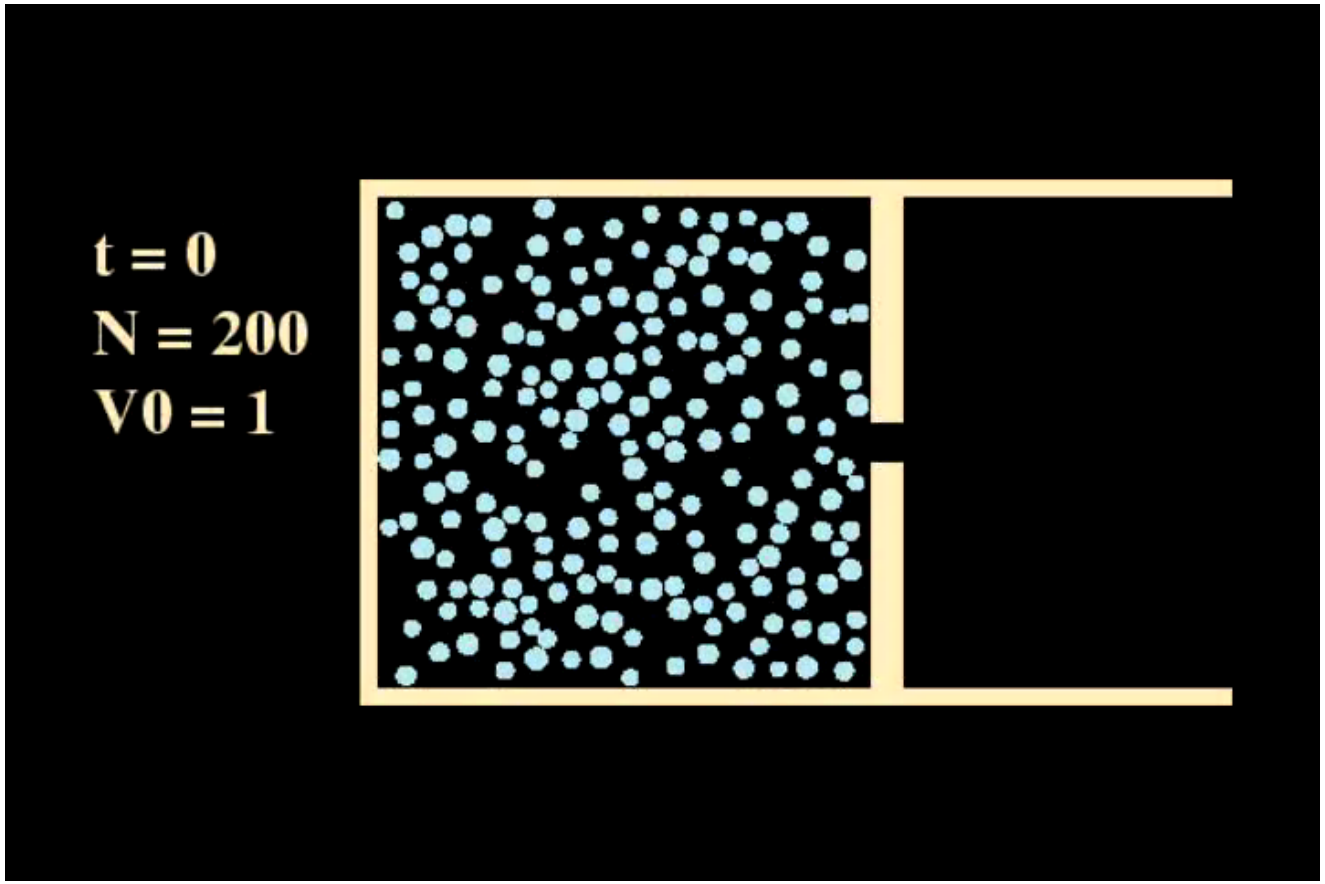


D. Helbing: Traffic and related self-driven many-particle systems. *Reviews of Modern Physics* **73**, 1067-1141 (2003).

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

modeling crowd disasters

- People modeled as self-driven many-particle systems
- Testing individualistic vs herding behavior as well as environmental solutions

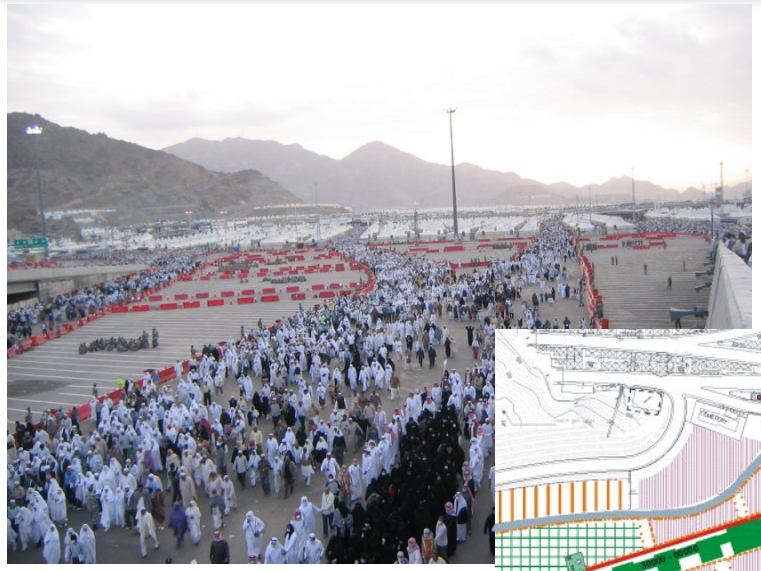


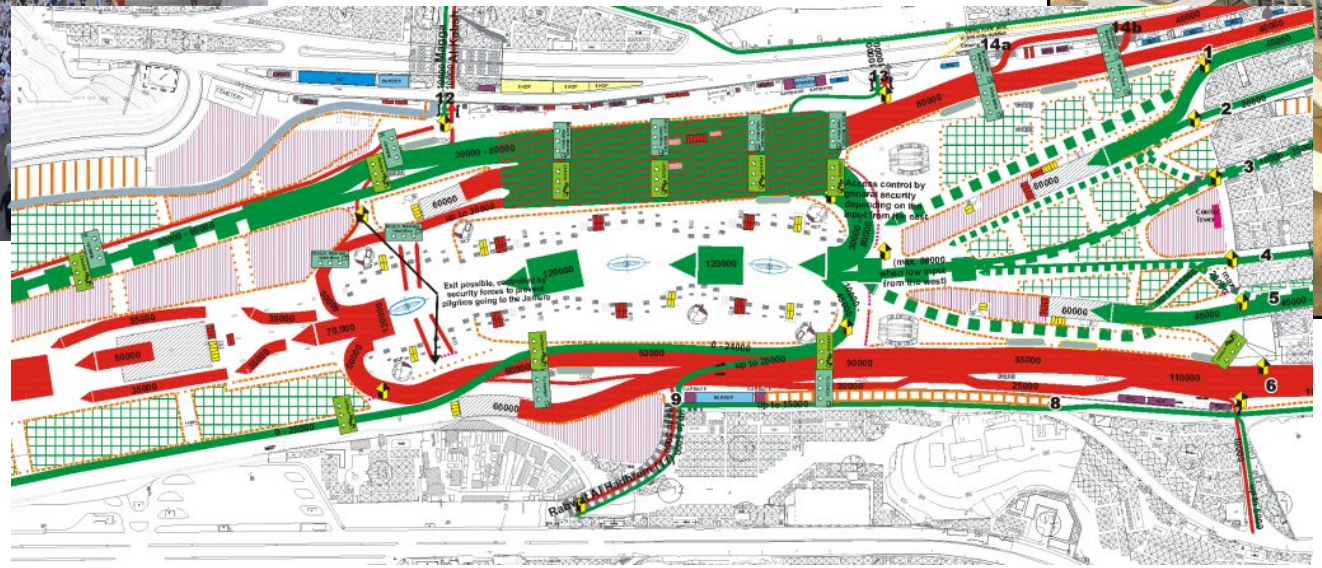
D. Helbing, A. Johansson and H. Z. Al-Abideen (2007) The Dynamics of Crowd Disasters: An Empirical Study. *Physical Review E* 75, 046109.

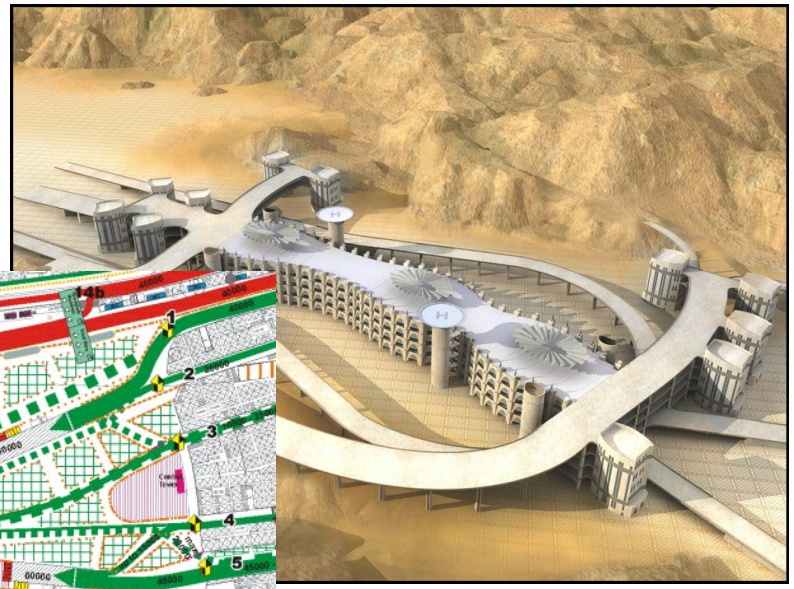
BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

modeling crowd disasters

- People modeled as self-driven many-particle systems
- Testing individualistic vs herding behavior as well as environmental solutions







D. Helbing, A. Johansson and H. Z. Al-Abideen (2007) The Dynamics of Crowd Disasters: An Empirical Study. *Physical Review E* 75, 046109.

BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

Inductive and deductive actionable models

may work in complex interrelated domain (with rare control events)

Melanie Mitchell: Current AI systems seem to be lacking a crucial aspect of human intelligence: rich internal models of the world. A tenet of modern cognitive science is that humans are not simply conditioned-reflex machines; instead, we have inside our heads *abstracted models* of the physical and social worlds that reflect the causes of events rather than merely correlations among them

AI's challenge of understanding the world". *Science* **382**,eadm8175(2023)

examples

unobserved scenarios

Parameter estimation

Initial conditions

General Rule

Formal, explainable, actionable model/theory

Logical consequences

????

observations

Symbols

Encoding

Measure

Measure

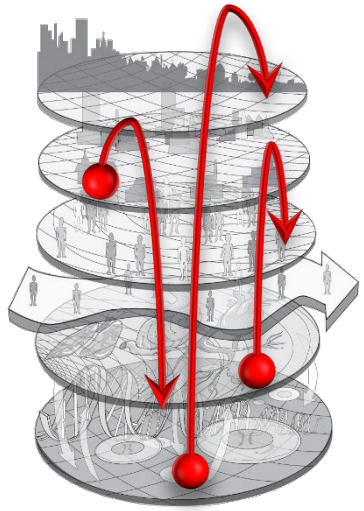
$World_0$

$World_1$

$World_2$

Howard Pattee

Robert Rosen



Nassim Nicholas Taleb

"predictions of events **depend** more and more **on theories** when their probability is small and system is **complex**"

Complex Physical Laws

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

mechanistic models, estimated parameters

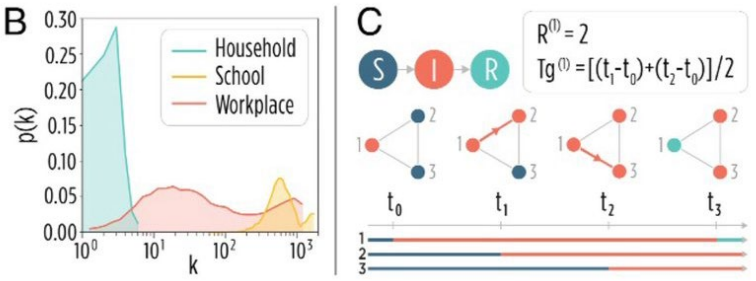
PNAS

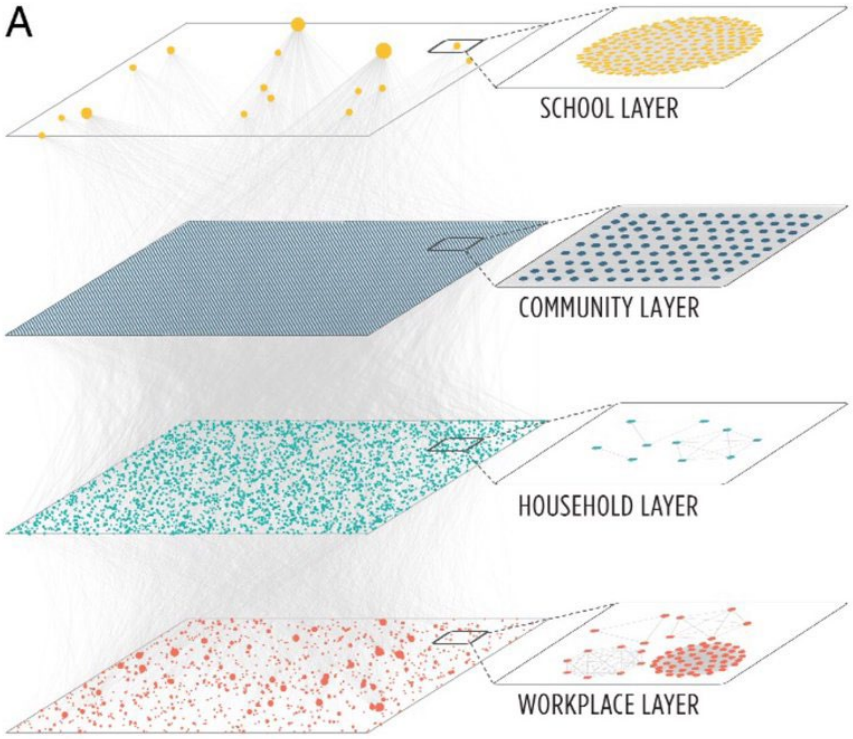
Measurability of the epidemic reproduction number in data-driven contact networks

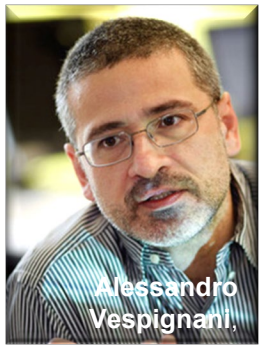
Quan-Hui Liu[a,b,c], Marco Ajelli[c,d], Alberto Aleta[e,f], Stefano Merler[d], Yamir Moreno[e,f,g], and Alessandro Vespignani[c,g,1]

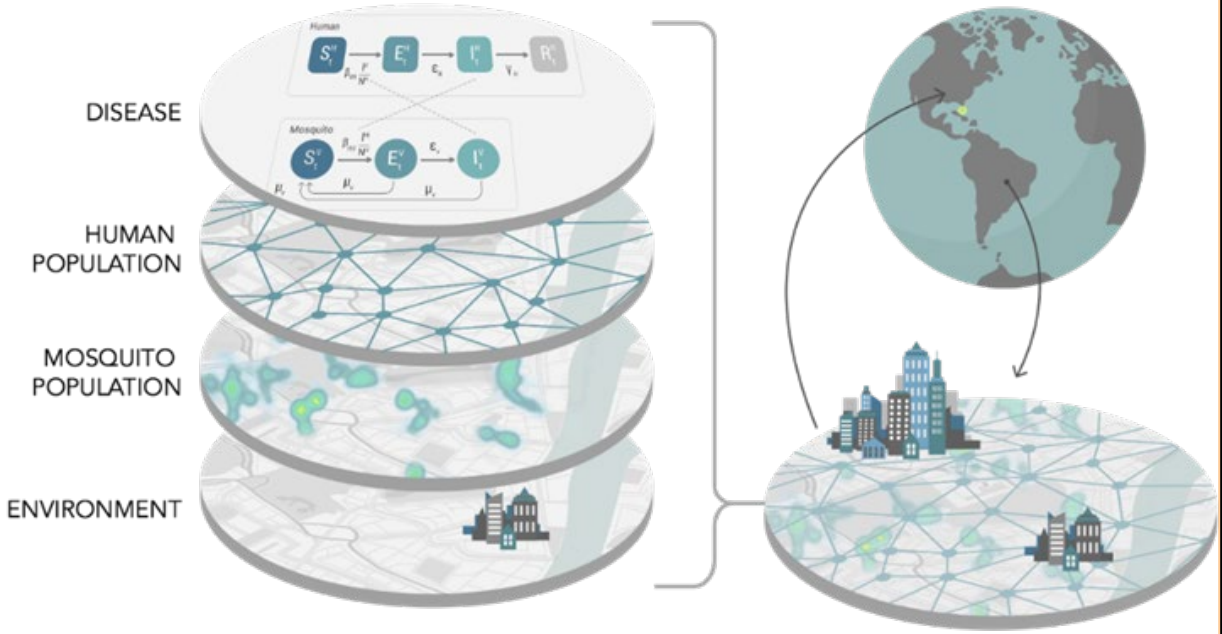
[a]Web Sciences Center, University of Electronic Science and Technology of China, Chengdu 611731, Sichuan, People's Republic of China; [b]Big Data Research Center, University of Electronic Science and Technology of China, Chengdu 611731, Sichuan, People's Republic of China; [c]Laboratory for the Modeling of Biological and Socio-Technical Systems, Northeastern University, Boston, MA 02115; [d]Bruno Kessler Foundation, 38123 Trento, Italy; [e]Institute for Biocomputation and Physics of Complex Systems, University of Zaragoza, 50018 Zaragoza, Spain; [f]Department of Theoretical Physics, University of Zaragoza, 50009 Zaragoza, Spain; and [g]ISI Foundation, 10126 Turin, Italy

Edited by Simon A. Levin, Princeton University, Princeton, NJ, and approved October 16, 2018 (received for review June 27, 2018)





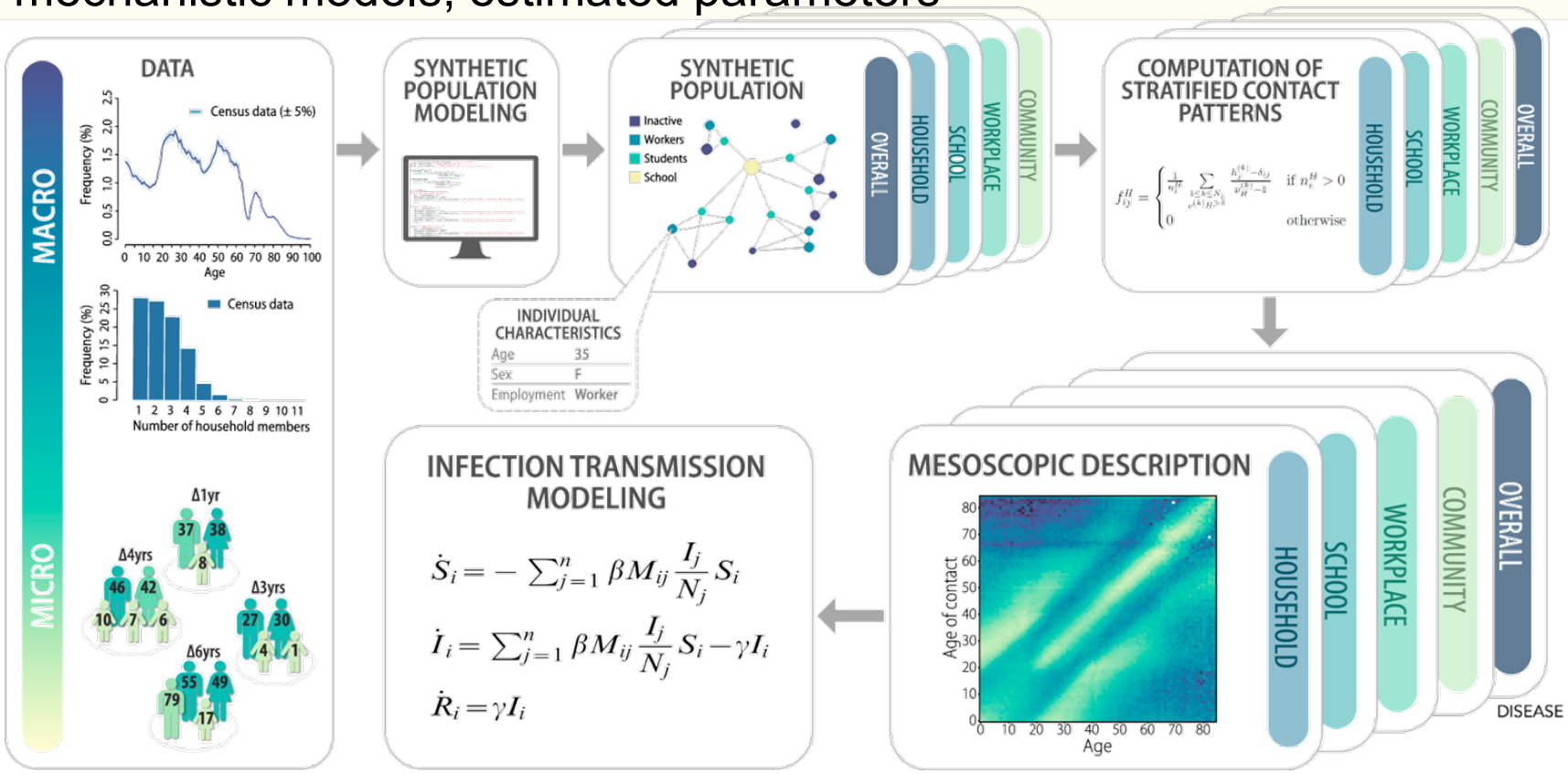


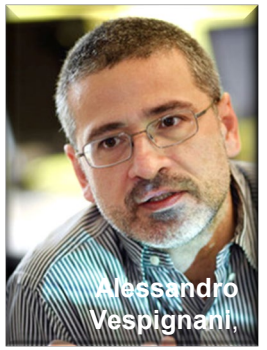


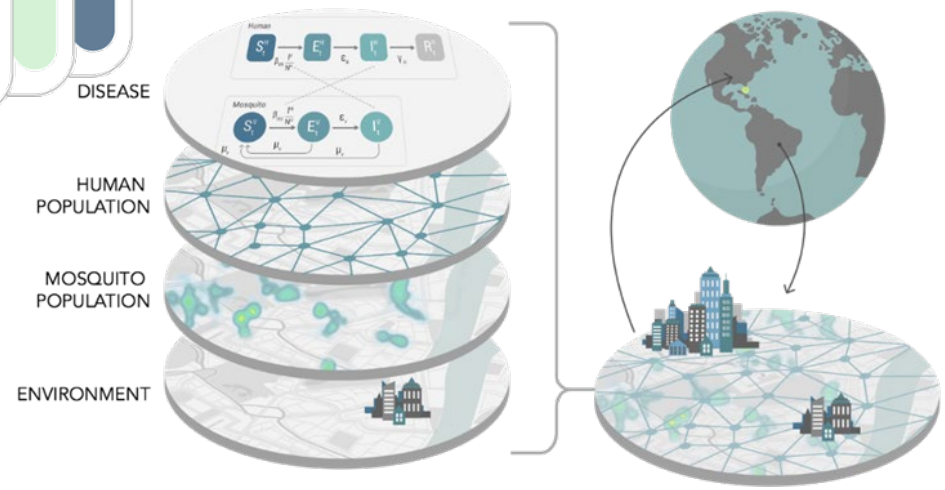
BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

mechanistic models, estimated parameters







nature COMMUNICATIONS

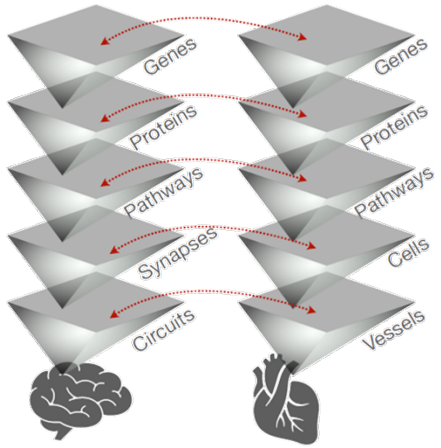
Inferring high-resolution human mixing patterns for disease modeling

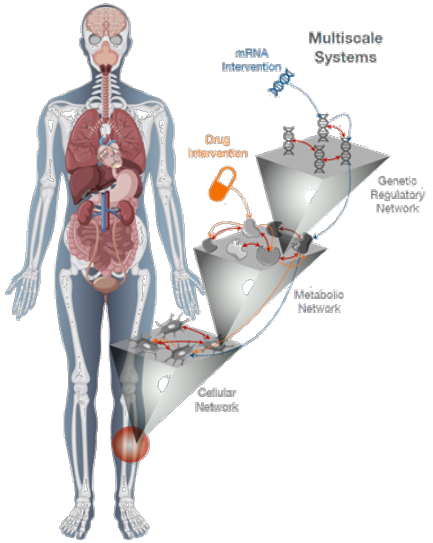
Dina Mistry[1,2], Maria Litvinova[2,3,4], Ana Pastore y Piontti[2], Matteo Chinazzi[2], Laura Fumanelli[5], Marcelo F. C. Gomes[6], Syed A. Haque[2], Quan-Hui Liu[7], Kunpeng Mu[2], Xinyue Xiong[2], M. Elizabeth Halloran[8,9], Ira M. Longini Jr.[10], Stefano Merler[5], Marco Ajelli[2,4]✉ & Alessandro Vespignani[2,3]✉

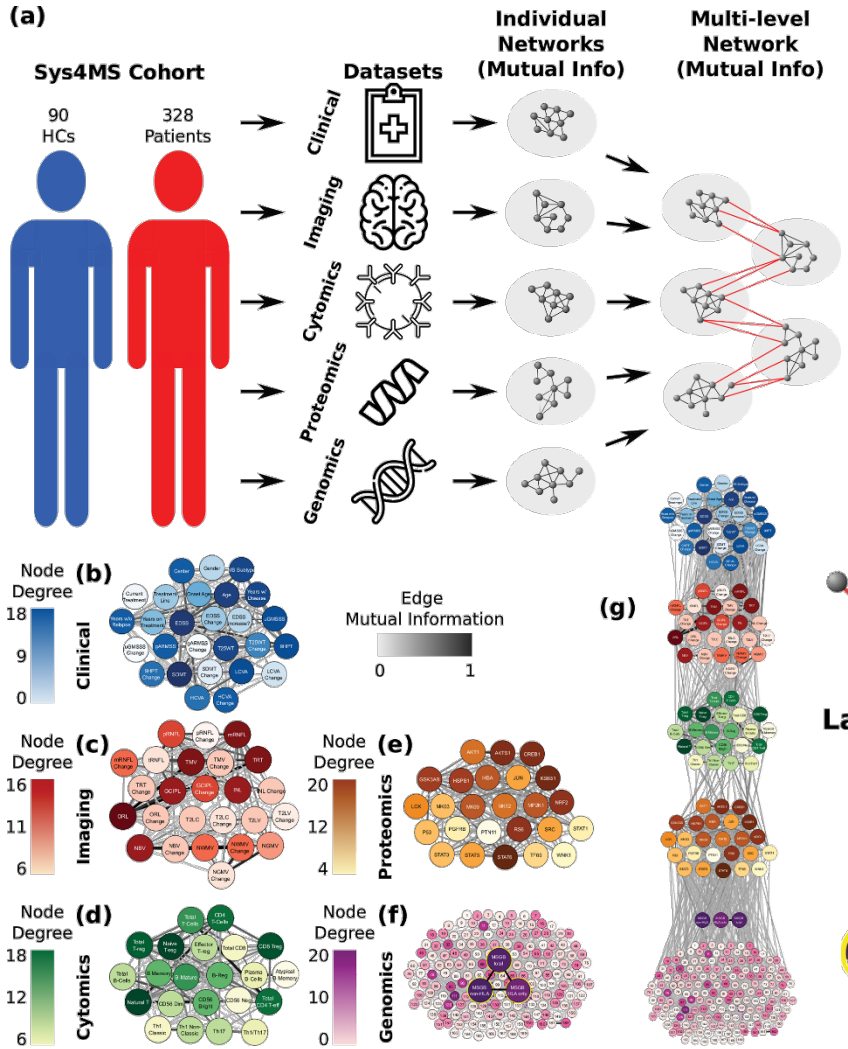
BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

multilayer network models of multiscale interdependence in disease







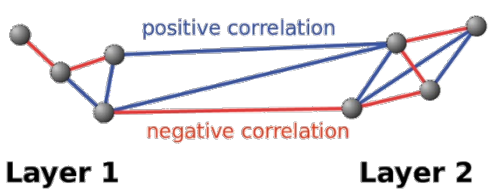
PLOS COMPUTATIONAL BIOLOGY

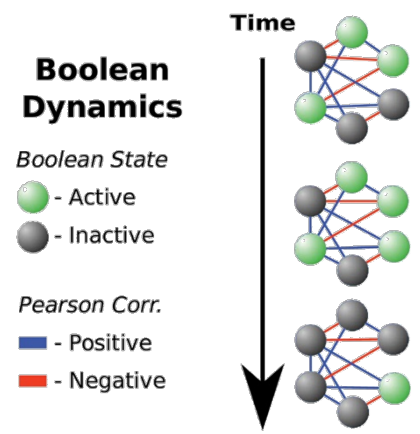
OPEN ACCESS PEER-REVIEWED

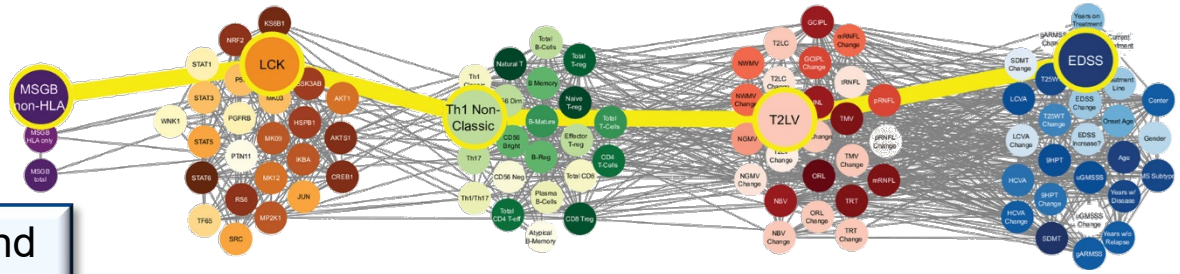
RESEARCH ARTICLE

Multiscale networks in multiple sclerosis

Keith E. Kennedy, Nicole Kerlero de Rosbo, Antonio Uccelli, Maria Cellerino, Federico Ivaldi, Paola Contini, Raffaele De Palma, Hanne F. Harbo, Tone Berge, Steffan D. Bos, Einar A. Høgestøl, Synne Brune-Ingebretsen, Sigrid A. de Rodez Benavent, [...], Pablo Villoslada [view all]







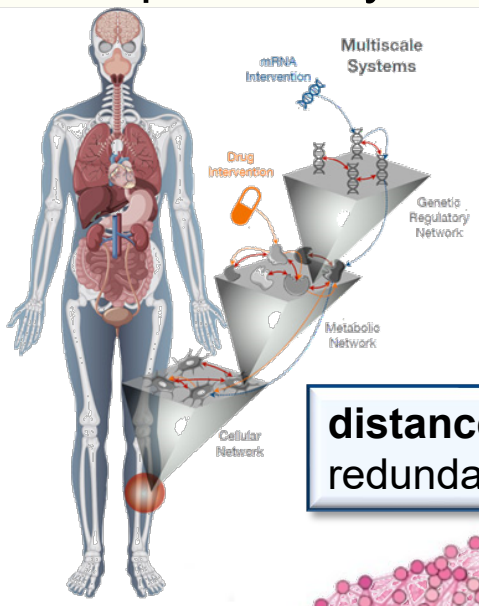
network pathways for identification and validation of correlations and **explainable** putative causal mechanism: “lines of argumentation”

De Domenico, et al [2024]. *NPJ Digital Medicine*. In press. *arXiv*:2405.09649.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

for explainability and computability

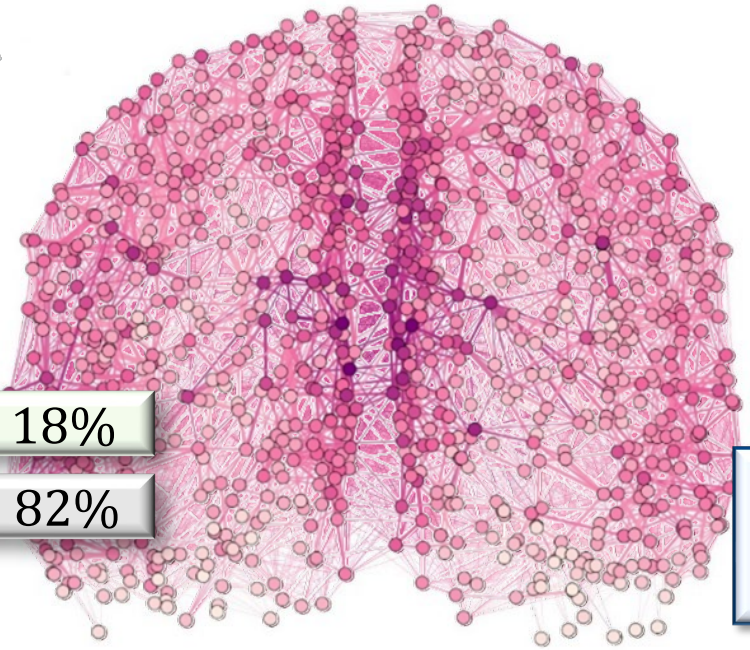


functional (control) hierarchies (especially symbolic codes) establish a “selective loss of detail”.

handles for interventions: If there is emergence of new levels, there must be ***redundancy*** for control to work.

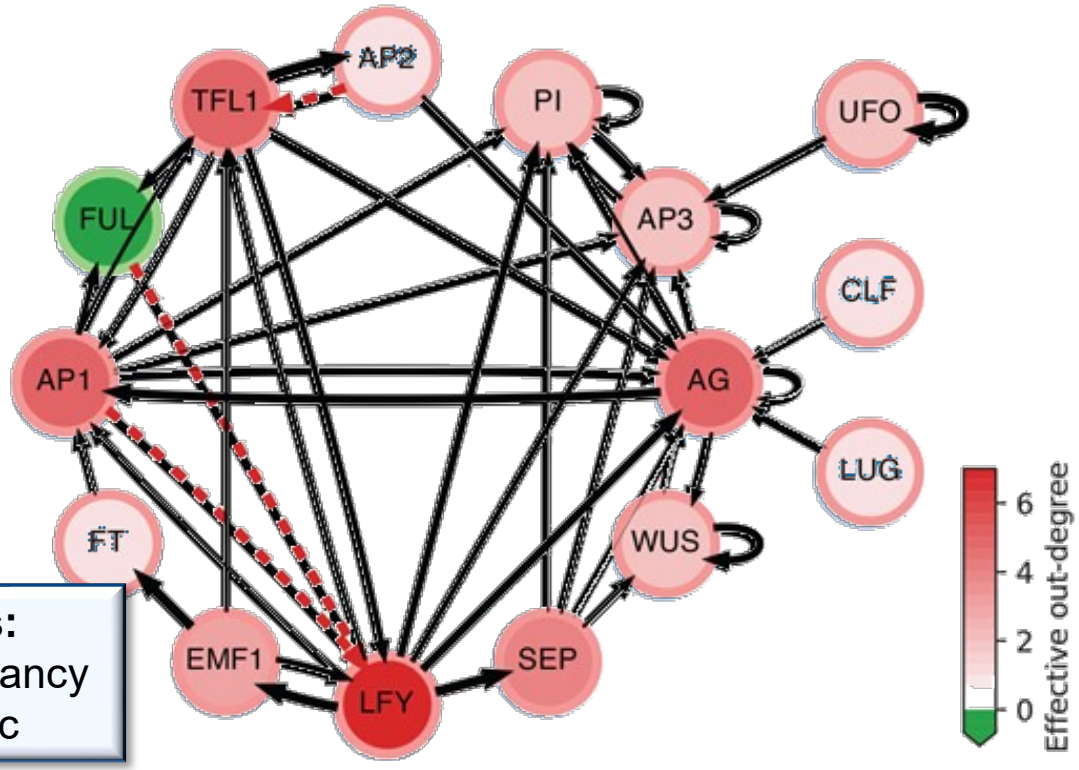
Howard Pattee

distance backbones of networks: removing redundancy from (shortest) pathways



$\tau^m \approx 18\%$

$\sigma^m \approx 82\%$

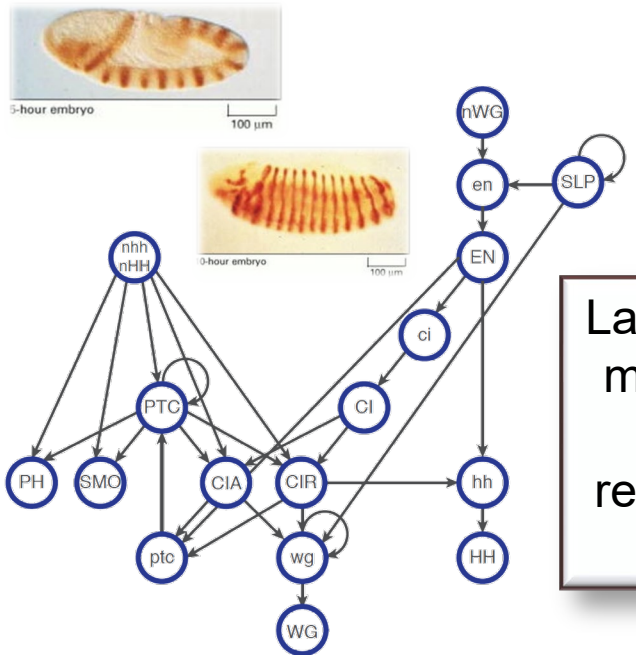


Effective causal pathways: removing dynamical redundancy from causal (multilayer) logic

Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Simas, Correia & Rocha [2021]. *J Complex Networks*. **9** (6), cnab021.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

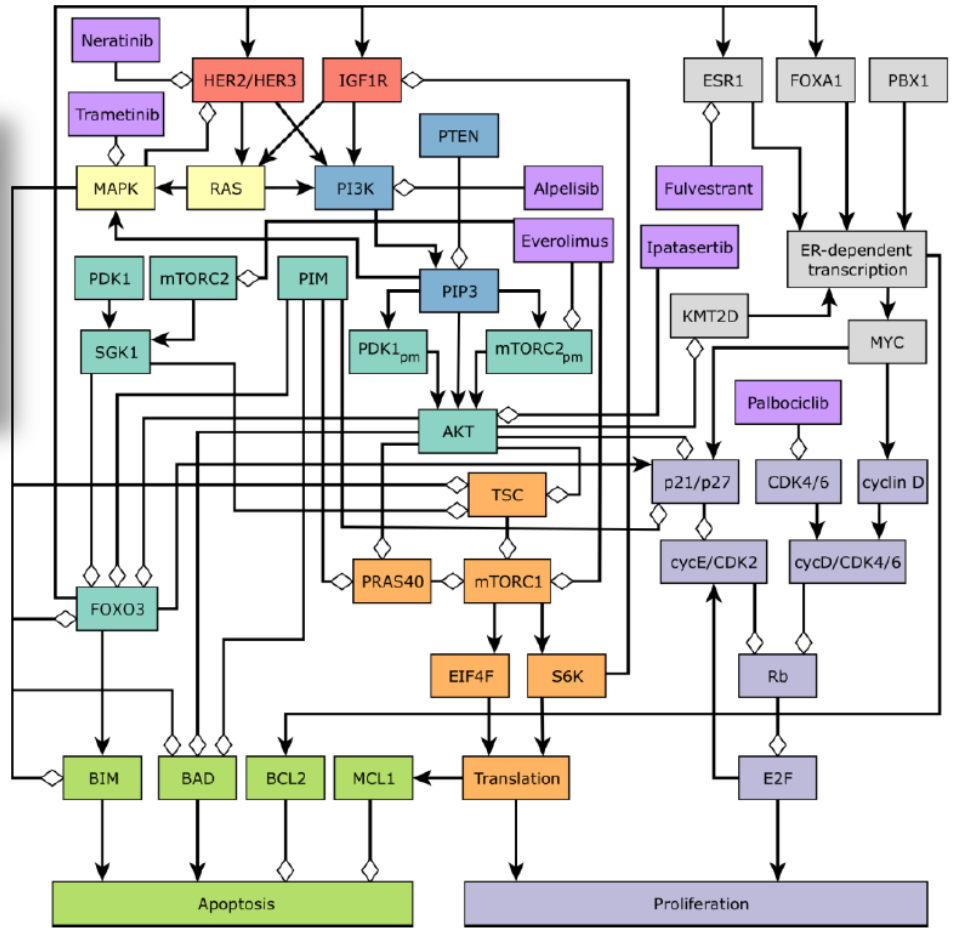
biochemical dynamics from synthesis of experimental data



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,&]

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



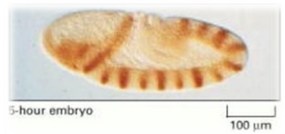
Node	*State − TransitionFunction*
SLP_i^{t+1}	$\leftarrow 0$ if $i=1 \vee i=2$; 1 if $i=3 \vee i=4$;
wg_i^{t+1}	$\leftarrow (CIA_i^t \wedge SLP_i^t \wedge \neg CIR_i^t) \vee (wg_i^t \wedge (CIA_i^t \vee SLP_i^t) \wedge \neg CIR_i^t)$
WG_i^{t+1}	$\leftarrow wg_i^t$
en_i^{t+1}	$\leftarrow (WG_{i-1}^t \vee WG_{i+1}^t) \wedge \neg SLP_i^t$
EN_i^{t+1}	$\leftarrow en_i^t$
hh_i^{t+1}	$\leftarrow EN_i^t \wedge \neg CIR_i^t$
HH_i^{t+1}	$\leftarrow hh_i^t$
ptc_i^{t+1}	$\leftarrow CIA_i^t \wedge \neg EN_i^t \wedge \neg CIR_i^t$
PTC_i^{t+1}	$\leftarrow ptc_i^t \vee (PTC_i^t \wedge \neg HH_{i-1}^t \wedge \neg HH_{i-1}^t)$

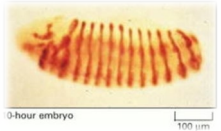
Helikar et al. [2012] *BMC Syst. Biol.* **6**, 96.
Zañudo, Scaltriti, & Albert. *Cancer convergence* **1**.1 (2017): 1-25.
Albert & Othmer [2003]. *J. Theor. Bio.* **223**: 1-18.

Cell Collective

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

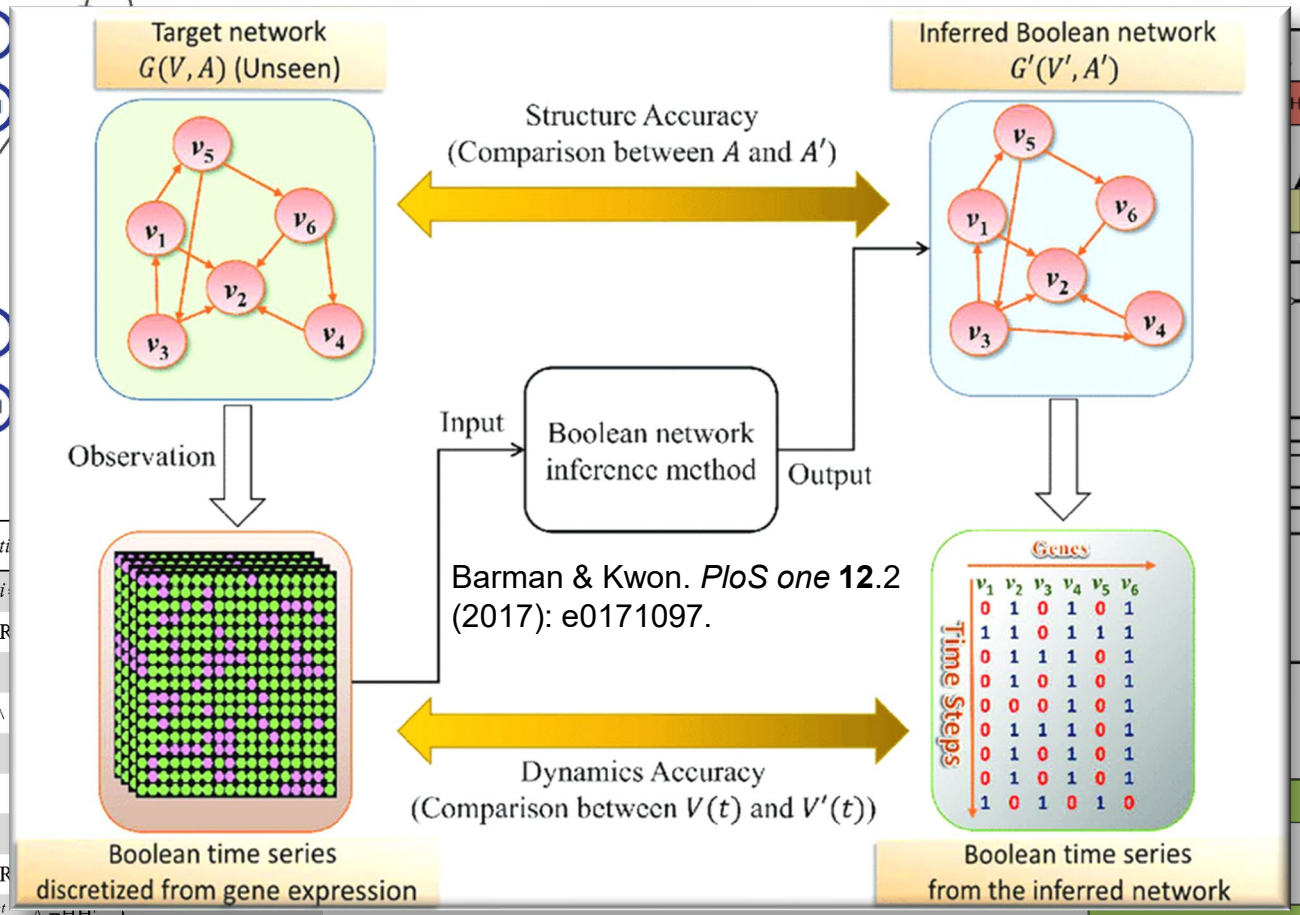
biochemical dynamics from synthesis of experimental data

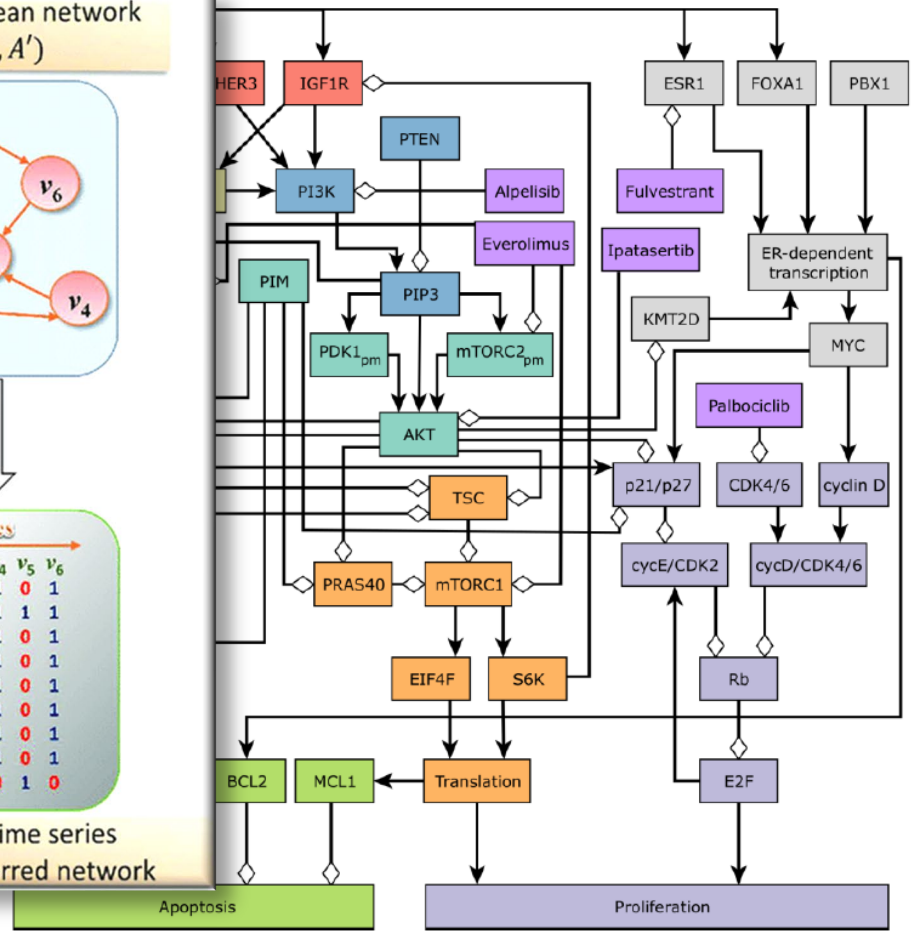




Node	*State − TransitionFuncti*
SLP_i^{t+1}	$\leftarrow 0$ if $i=1 \vee i=2$; 1 if i
wg_i^{t+1}	$\leftarrow (CIA_i^t \wedge SLP_i^t \wedge \neg CIR$
WG_i^{t+1}	$\leftarrow wg_i^t$
en_i^{t+1}	$\leftarrow (WG_{i-1}^t \vee WG_{i+1}^t) \wedge$
EN_i^{t+1}	$\leftarrow en_i^t$
hh_i^{t+1}	$\leftarrow EN_i^t \wedge \neg CIR_i^t$
HH_i^{t+1}	$\leftarrow hh_i^t$
ptc_i^{t+1}	$\leftarrow CIA_i^t \wedge \neg EN_i^t \wedge \neg CIR$
PTC_i^{t+1}	$\leftarrow ptc_i^t \vee (PTC_i^t \wedge \neg HH_{i-1}^t \wedge \neg HH_{i-1}^t)$

A network modeling approach to elucidate drug resistance mechanisms and predict combinatorial drug treatments in breast cancer





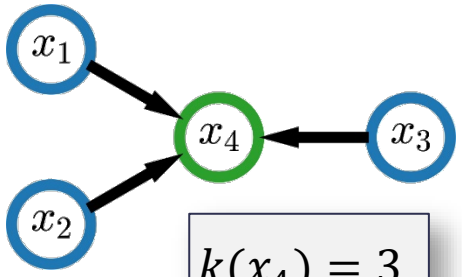
Helikar et al. [2012] *BMC Syst. Biol.* **6**, 96.
Zañudo, Scaltriti, & Albert. *Cancer convergence* **1**.1 (2017): 1-25.
Albert & Othmer [2003]. *J. Theor. Bio.* **223**: 1-18.

Cell Collective

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

quantifying redundancy in automata networks

with the effective graph (nonlinear collective measure of effective control)



$x_4 = x_1 \wedge x_2$

look-up-table (LUT)

$F(x_4)$

	x_1	x_2	x_3		x_4
f_1	0	0	0	:	0
f_2	0	0	1	:	0
f_3	0	1	0	:	0
f_4	0	1	1	:	0
f_5	1	0	0	:	0
f_6	1	0	1	:	0
f_7	1	1	0	:	1
f_8	1	1	1	:	1

LUT entry/input condition → f_7

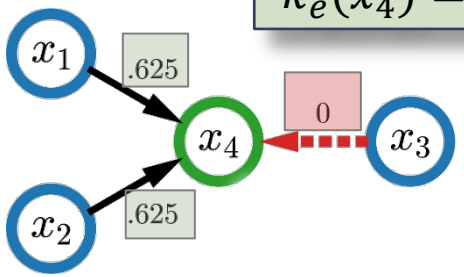
on/off state variable

$F'(x_4)$

	x_1	x_2	x_3		x_4
f_1'	#	0	#	:	0
f_2'	0	#	#	:	0
f_3'	1	1	#	:	1

prime implicant → f_3'

wildcard symbol



$k_e(x_4) = 1.25$

Prime Implicants (Quine-McCluskey)

minimal transition control: set of wildcard schemata is **DNF** of prime implicants (Blake Canonical Form)

Measuring ***redundancy*** and its dual ***effectiveness***

input redundancy:

$k_r(x)$ = mean number of "#" in LUT

$$k_r(x_4) = \frac{1 \times 2 + 2 \times 6}{8} = 1.75$$

effective connectivity:

$$k_e(x) = k(x) - k_r(x)$$

$$k_e(x_i) = \sum_{j=1}^{k} e_{ji}$$

edge effectiveness

$$r_{ji} = \frac{\sum_{f_\alpha \in F_i} \operatorname{avg}_{\upsilon : f_\alpha \in \Upsilon_\upsilon^i} (j \rightarrowtail \#)_\upsilon}{|F_i|},$$

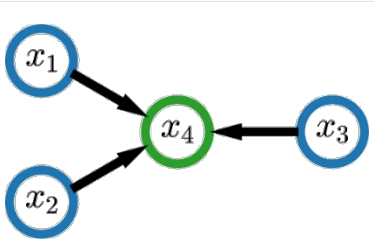
$$e_{ji} = 1 - r_{ji}.$$

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

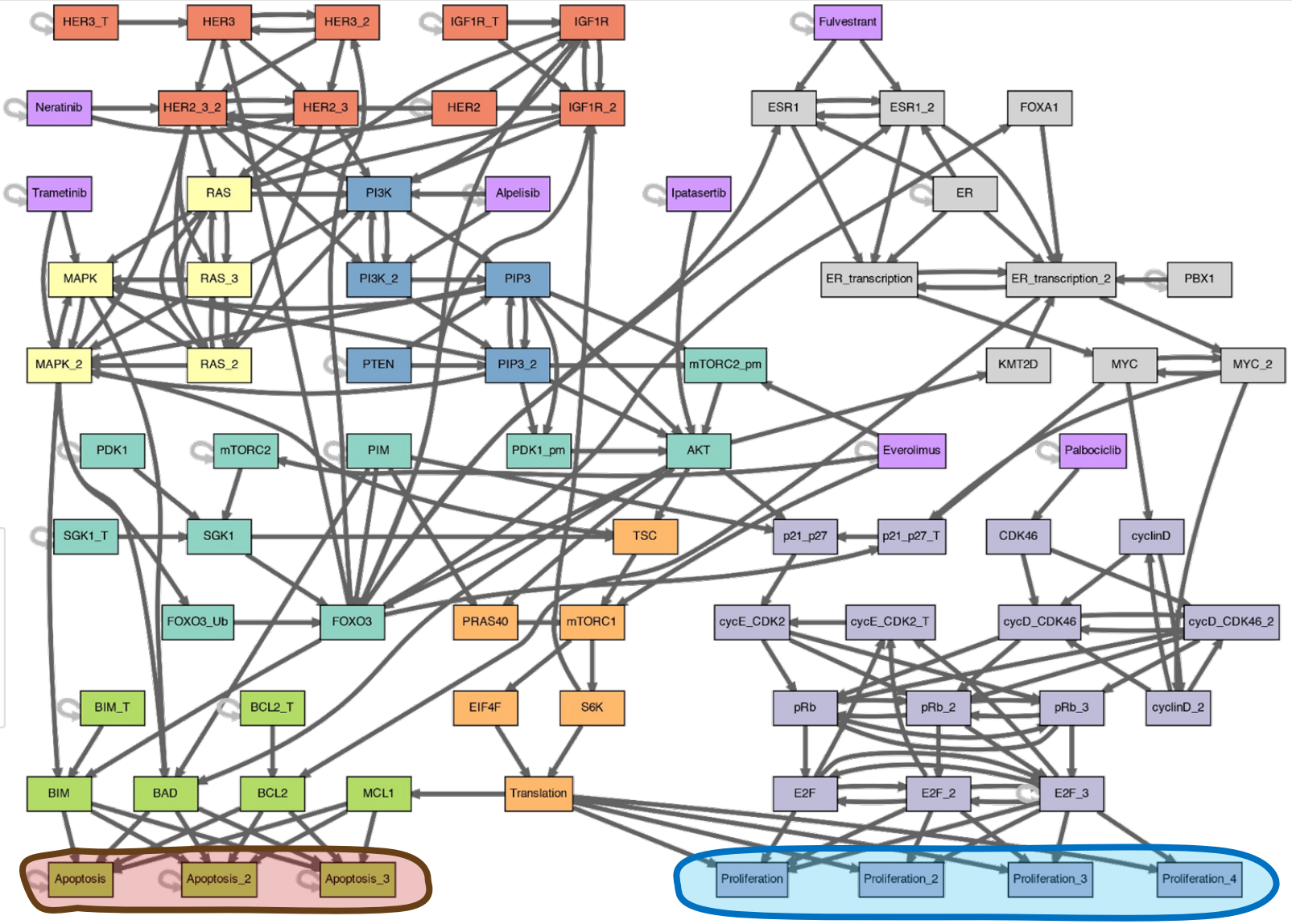
BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

effective graph: redundancy and control in biochemical regulation

(actionable) model of pharmachology in ER+ breast cancer



0	0	0	0
0	0	1	0
0	1	0	0
0	1	1	0
1	0	0	0
1	0	1	0
1	1	0	1
1	1	1	1



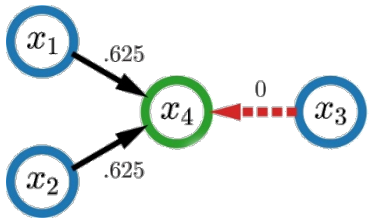
Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.
Gates & Rocha [2016]. *Scientific Reports* **6**, 24456.
Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046.
Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Parmer, Rocha & Radicchi [2022]. *Nature Communications*. **13**, 3457.

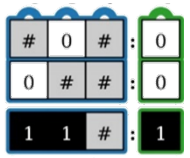
pypi.python.org/pypi/cana

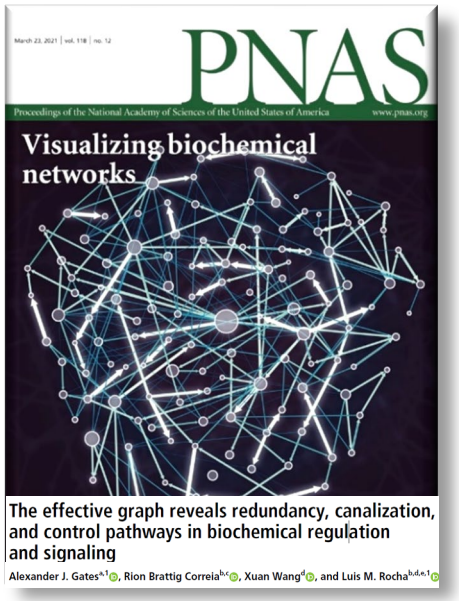
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

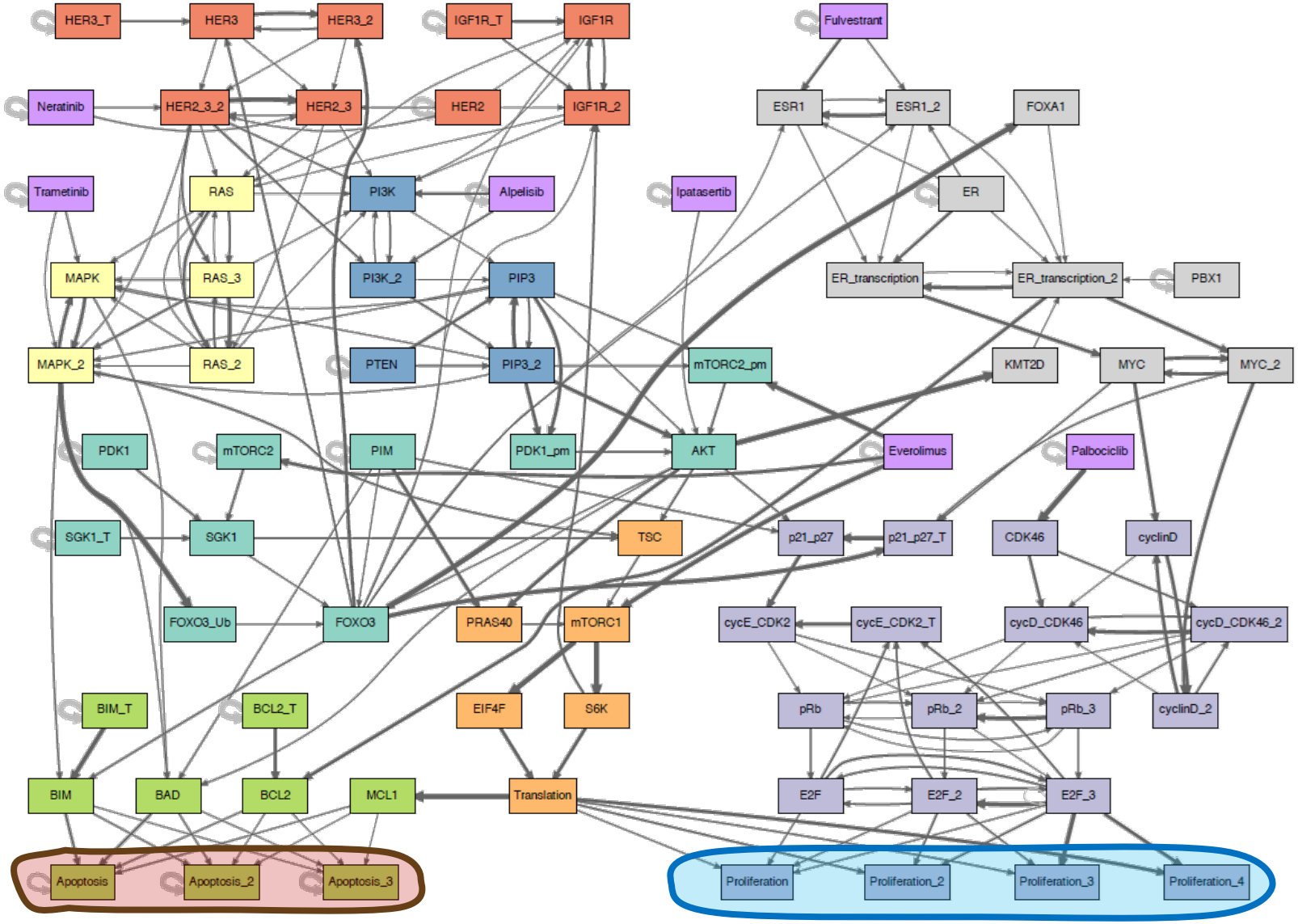
effective graph: redundancy and control in biochemical regulation

(actionable) model of pharmachology in ER+ breast cancer









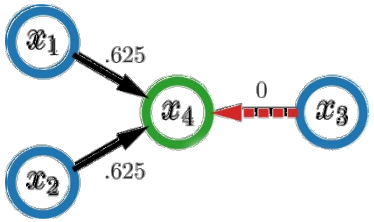
Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.
Gates & Rocha [2016]. *Scientific Reports* **6**, 24456.
Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046.
Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Parmer, Rocha & Radicchi [2022]. *Nature Communications*. **13**, 3457.

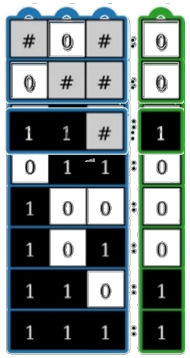
pypi.python.org/pypi/cana

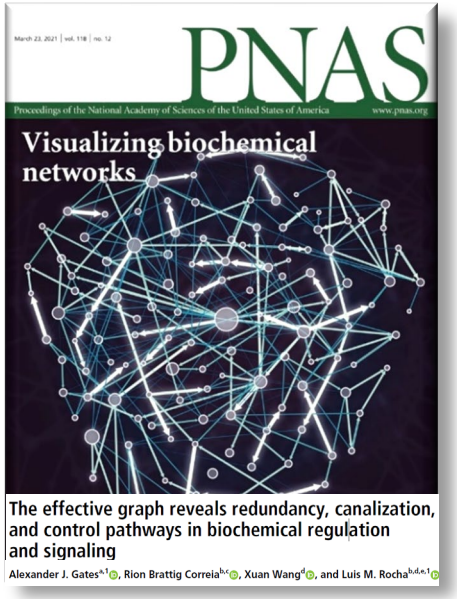
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

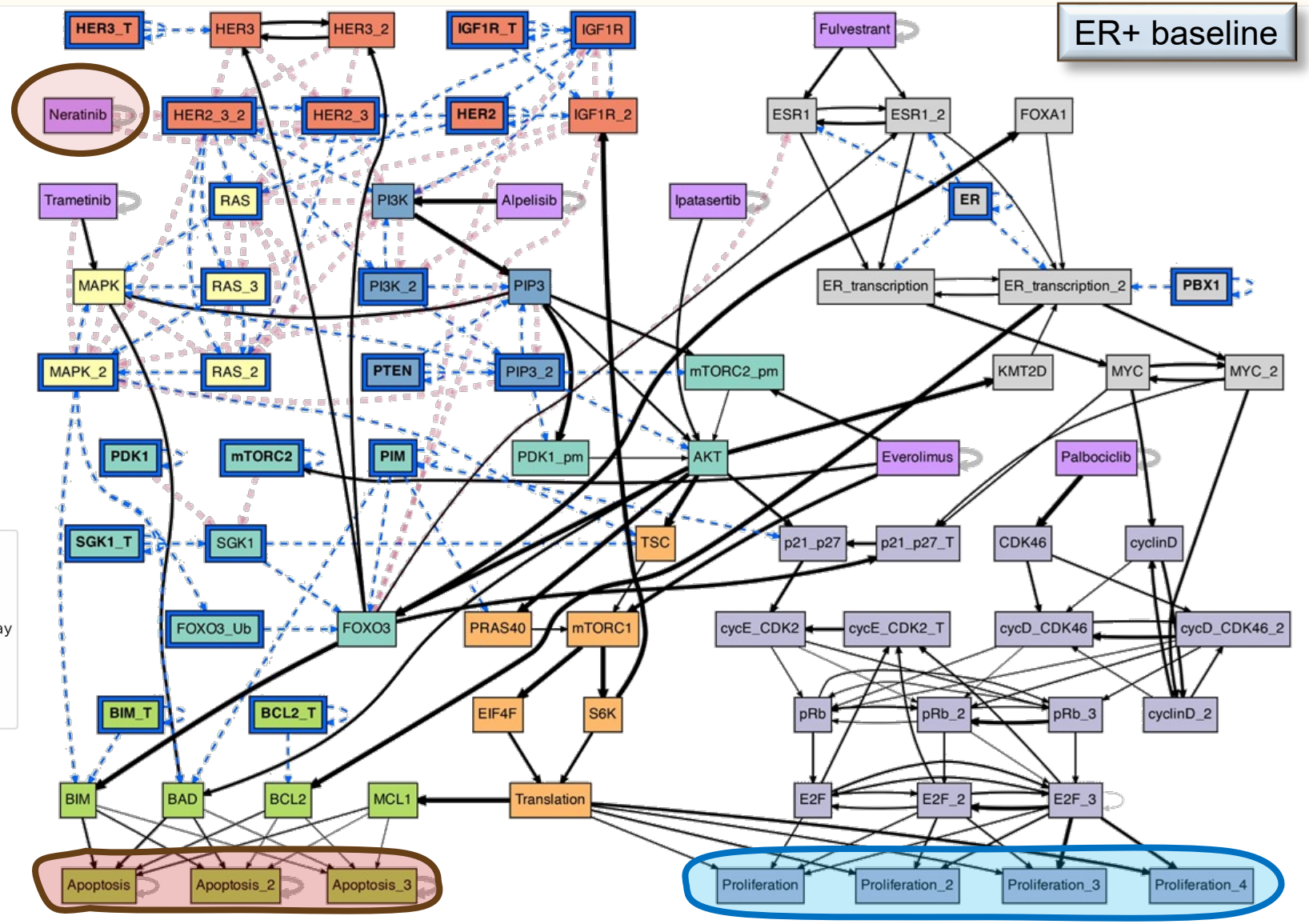
effective graph: redundancy and control in biochemical regulation

(actionable) model of pharmachology in ER+ breast cancer









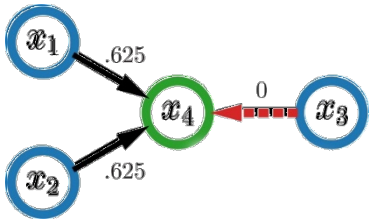
Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.
Gates & Rocha [2016]. *Scientific Reports* **6**, 24456.
Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046.
Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Parmer, Rocha & Radicchi [2022]. *Nature Communications*. **13**, 3457.

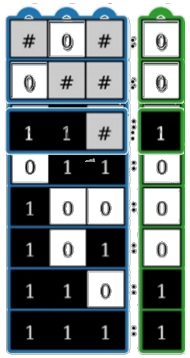
pypi.python.org/pypi/cana

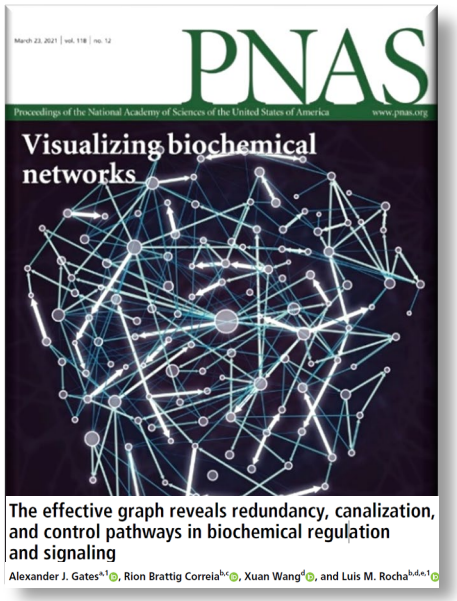
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

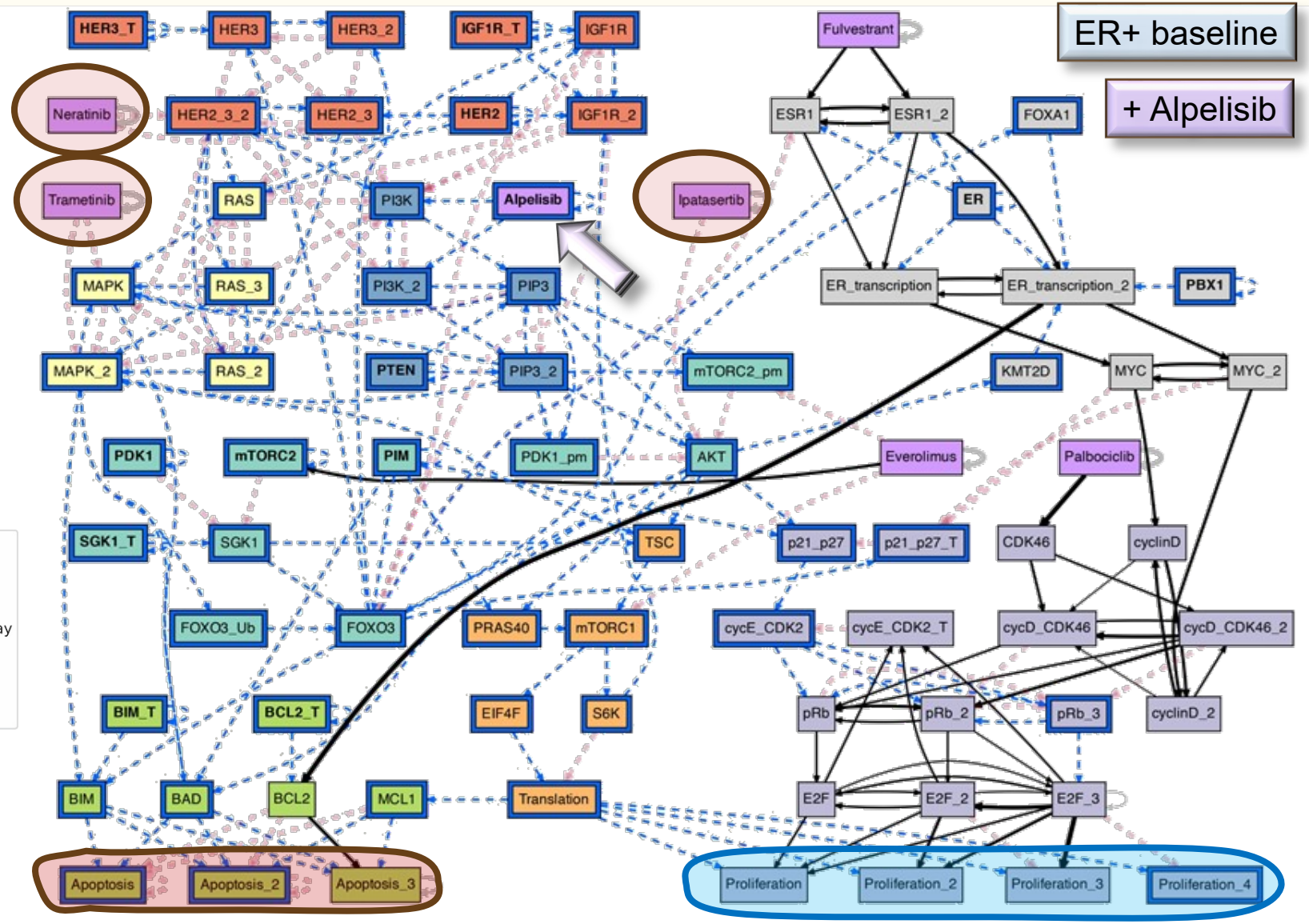
effective graph: redundancy and control in biochemical regulation

(actionable) model of pharmachology in ER+ breast cancer









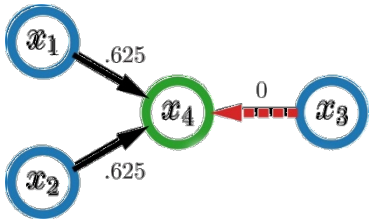
Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.
Gates & Rocha [2016]. *Scientific Reports* **6**, 24456.
Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046.
Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Parmer, Rocha & Radicchi [2022]. *Nature Communications*. **13**, 3457.

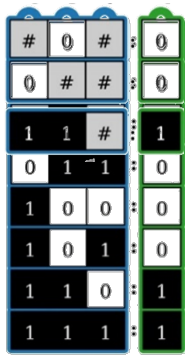
pypi.python.org/pypi/cana

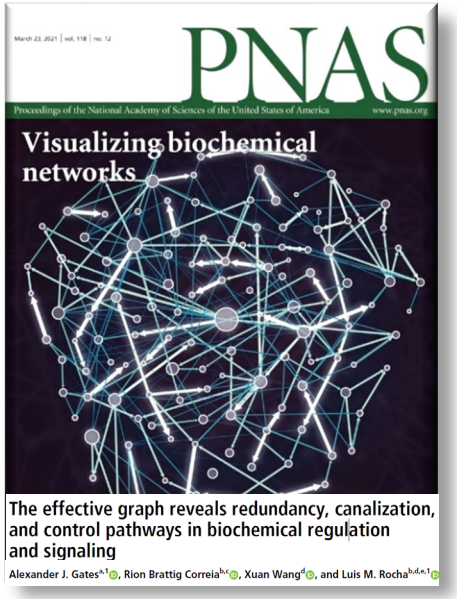
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

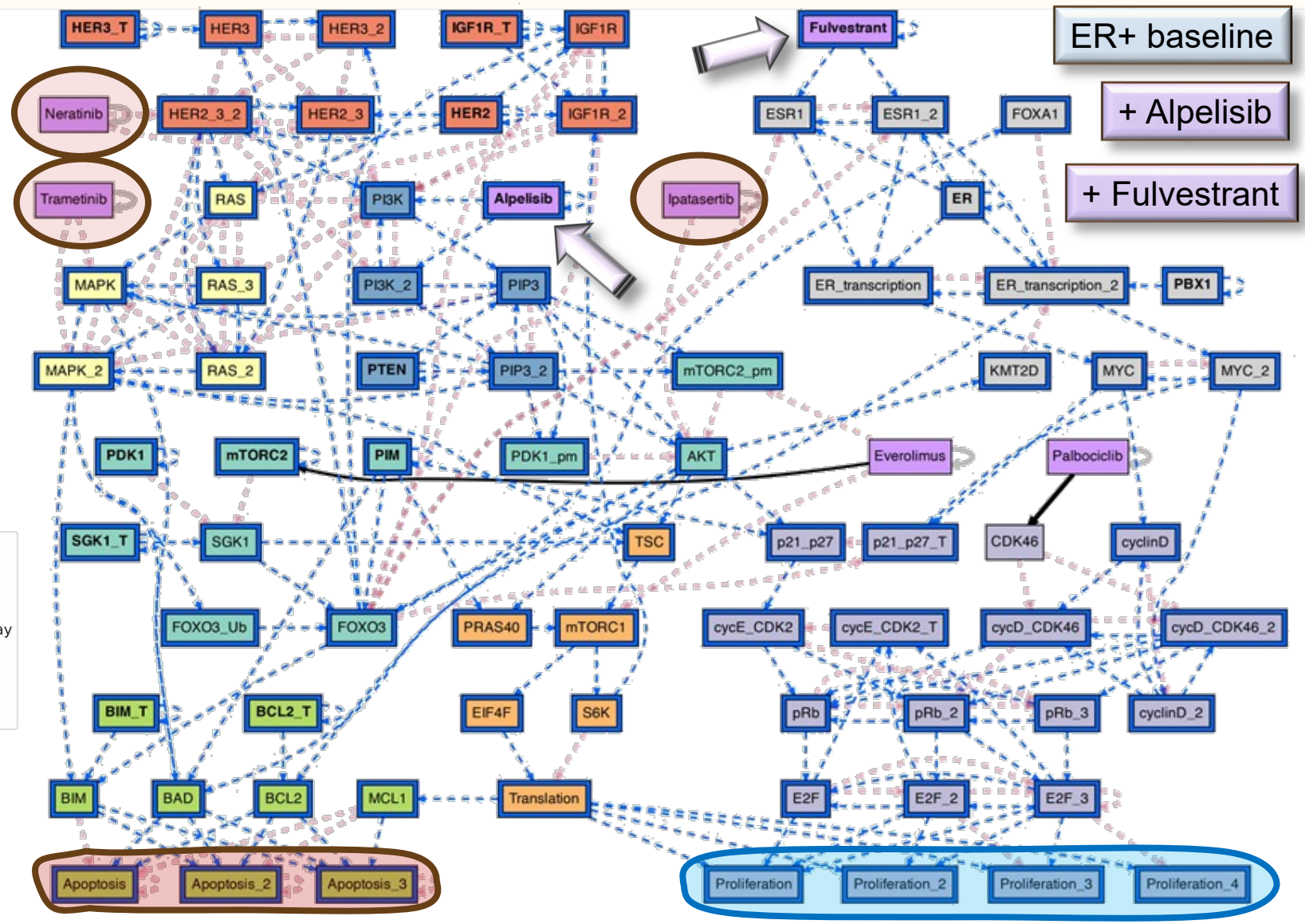
effective graph: redundancy and control in biochemical regulation

(actionable) model of pharmachology in ER+ breast cancer









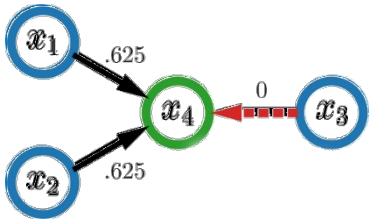
Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.
Gates & Rocha [2016]. *Scientific Reports* **6**, 24456.
Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046.
Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Parmer, Rocha & Radicchi [2022]. *Nature Communications*. **13**, 3457.

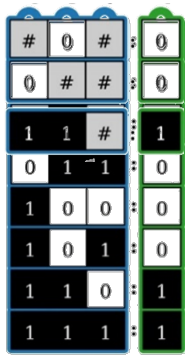
pypi.python.org/pypi/cana

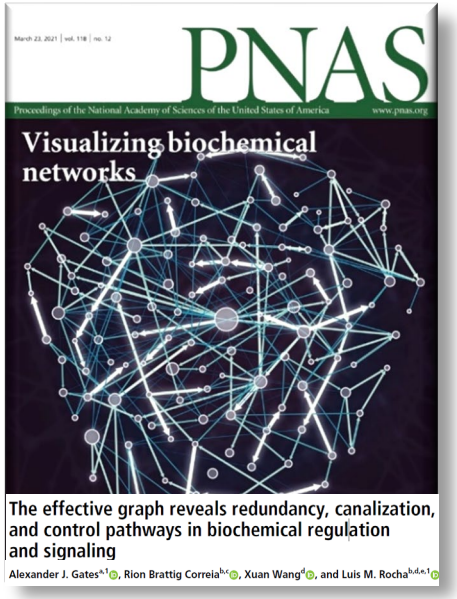
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

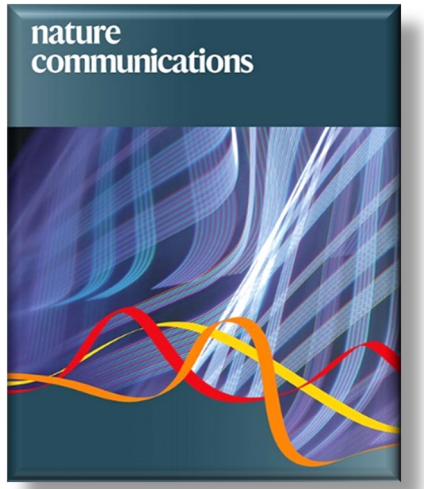
effective graph: redundancy and control in biochemical regulation

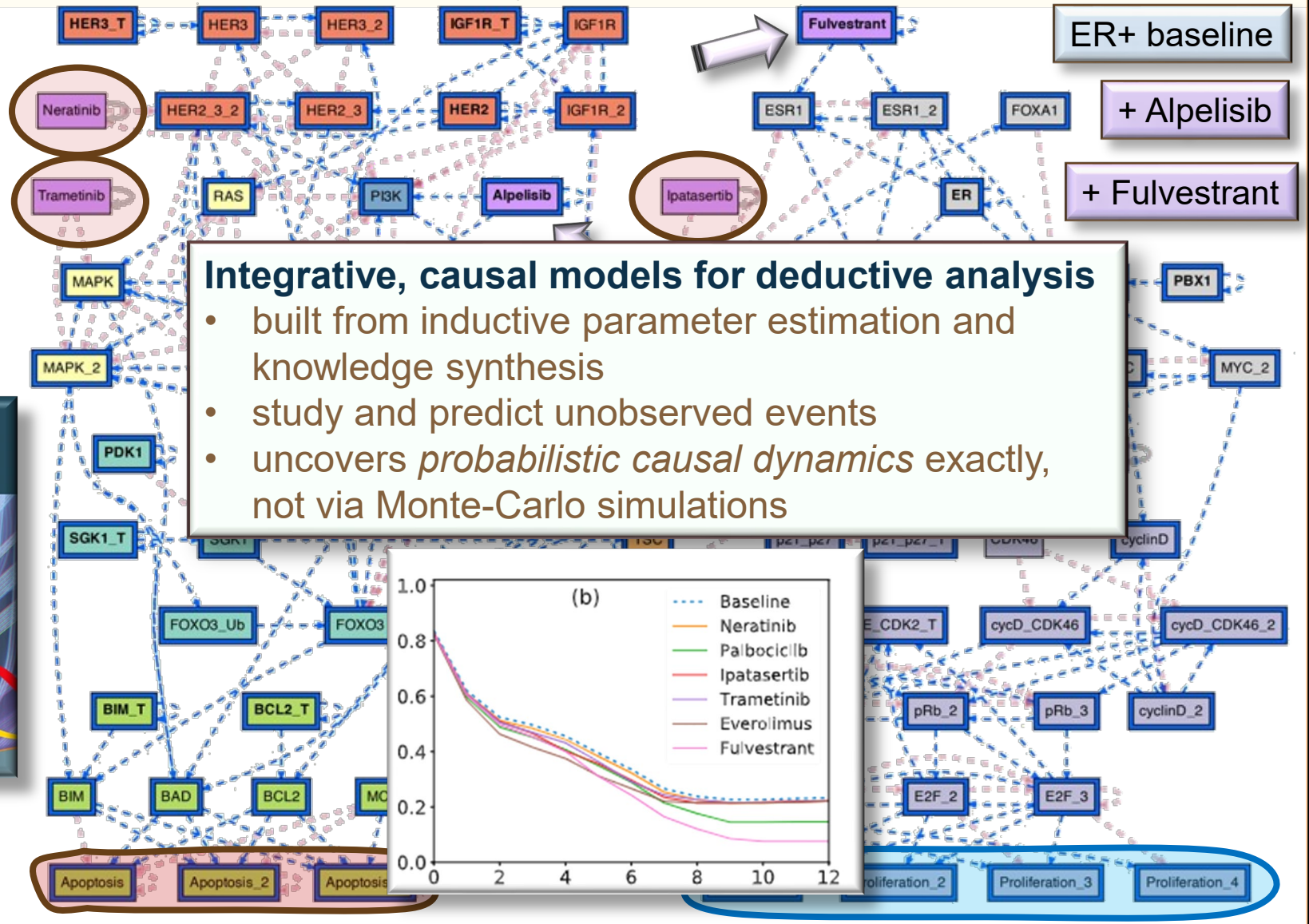
(actionable) model of pharmachology in ER+ breast cancer











Integrative, causal models for deductive analysis

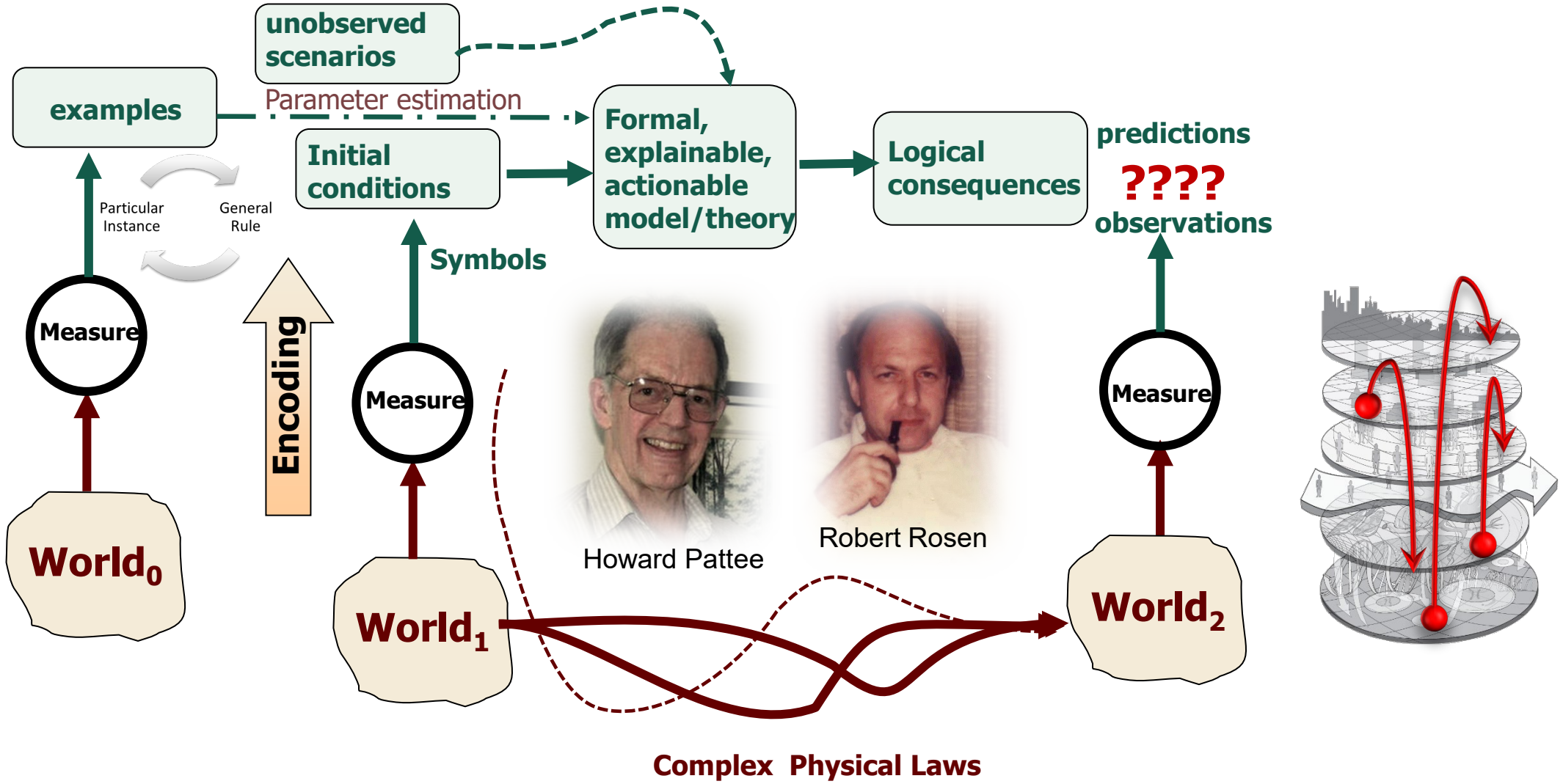
- built from inductive parameter estimation and knowledge synthesis
- study and predict unobserved events
- uncovers *probabilistic causal dynamics* exactly, not via Monte-Carlo simulations

Marques-Pita & Rocha, [2013]. *PLoS ONE*, **8**(3): e55946.
Gates & Rocha [2016]. *Scientific Reports* **6**, 24456.
Correia, Gates, Wang & Rocha [2018]. *Frontiers in Physyology* **9:** 1046.
Gates, Correia, Wang & Rocha [2021]. *PNAS*. **118** (12): e2022598118.
Parmer, Rocha & Radicchi [2022]. *Nature Communications*. **13**, 3457.

pypi.python.org/pypi/cana

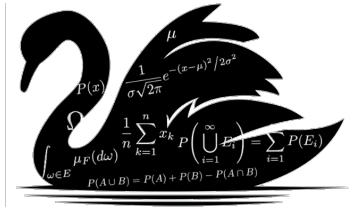
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

may work in complex interrelated domain (with rare control events)



BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

may work in complex interrelated domain (with rare control events)



unobserved scenarios

examples

Parameter estimation

Initial conditions

Simplified, Formal, explainable, actionable model/theory

Logical consequences

predictions

????

observations

Particular Instance

General Rule

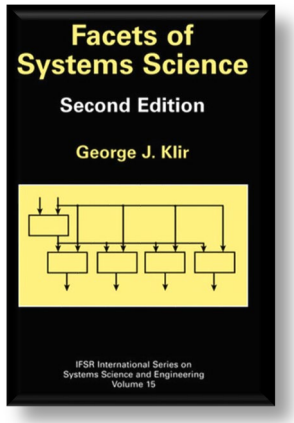
Symbols

Encoding

Measure

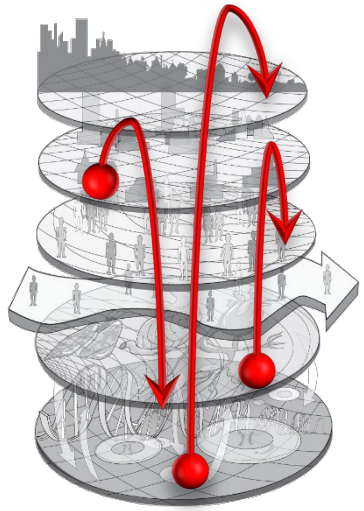
Measure

Measure



Howard Pattee

Robert Rosen



$World_0$

$World_1$

$World_2$

George Klir

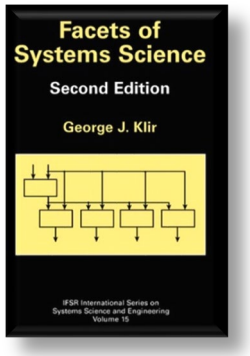
Complex Physical Laws

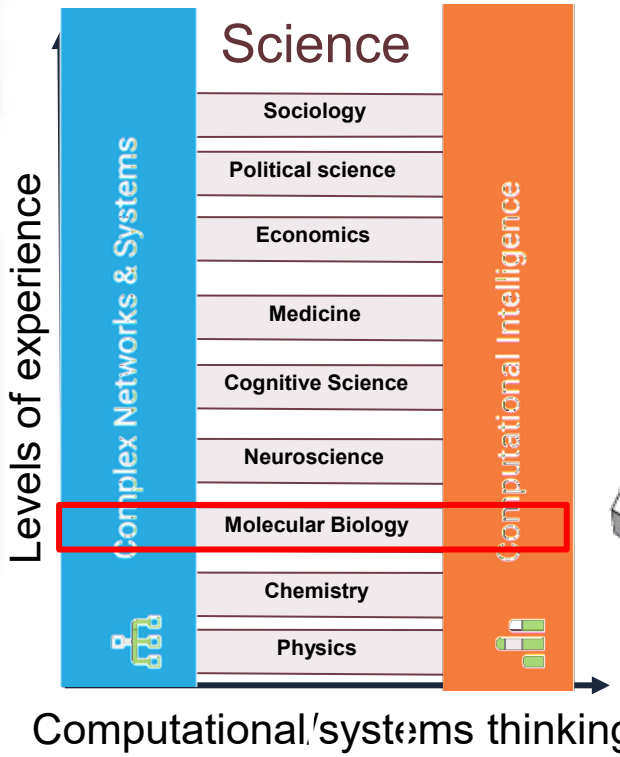
Model and data simplification is key for feasibility and explainability.

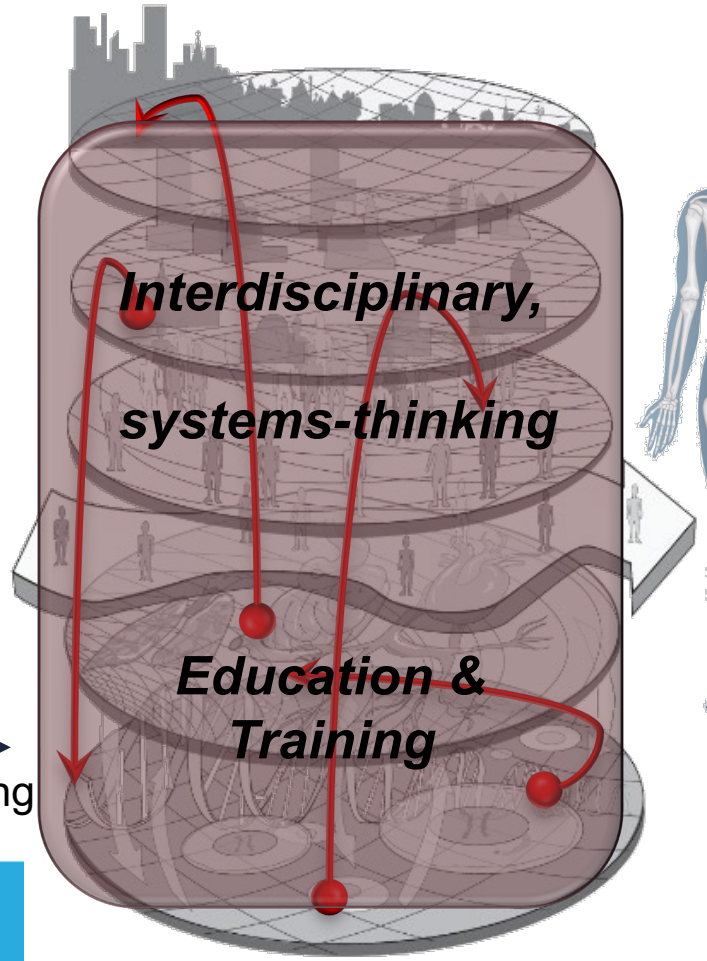
BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

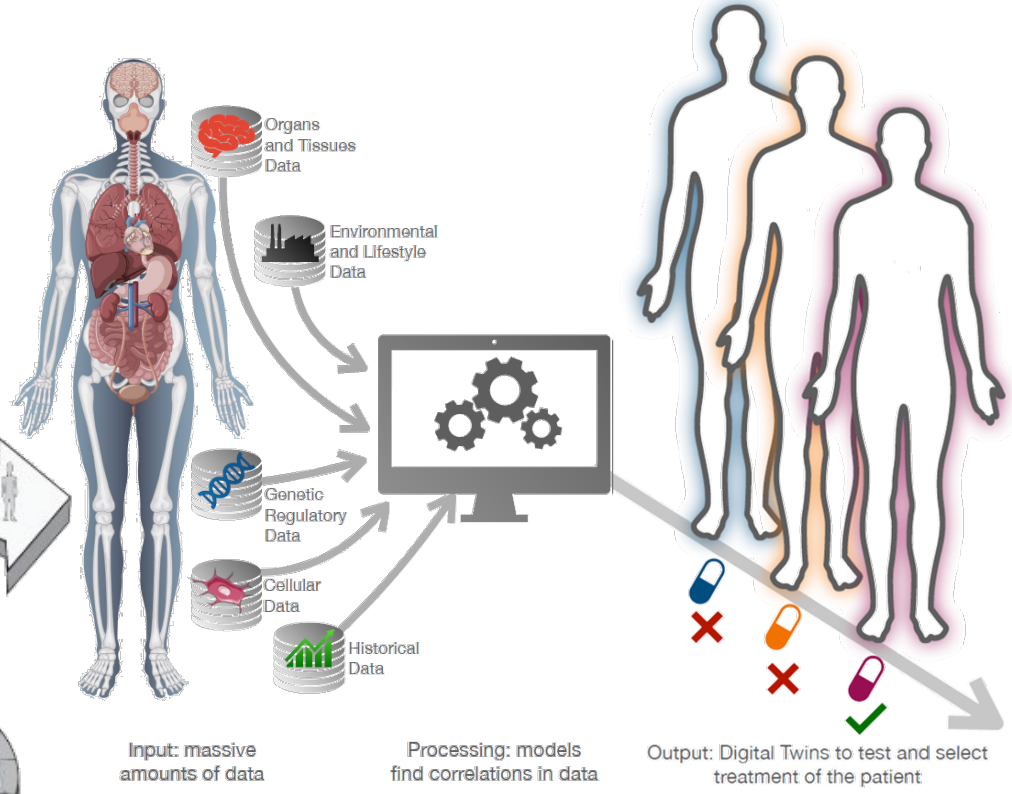
multiscale factors in social, technological and biomedical problems



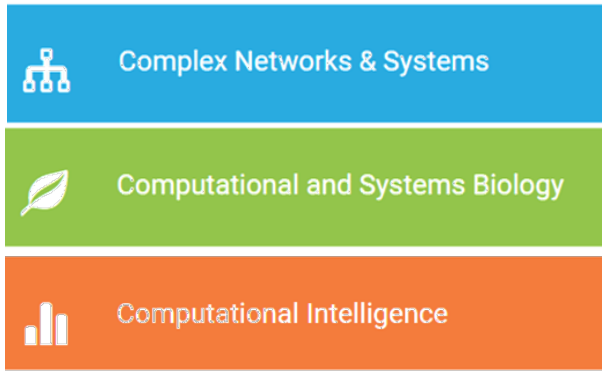




Pescosolido, B.A. 2006. Journal of Health and Social Behavior 47: 189-208.

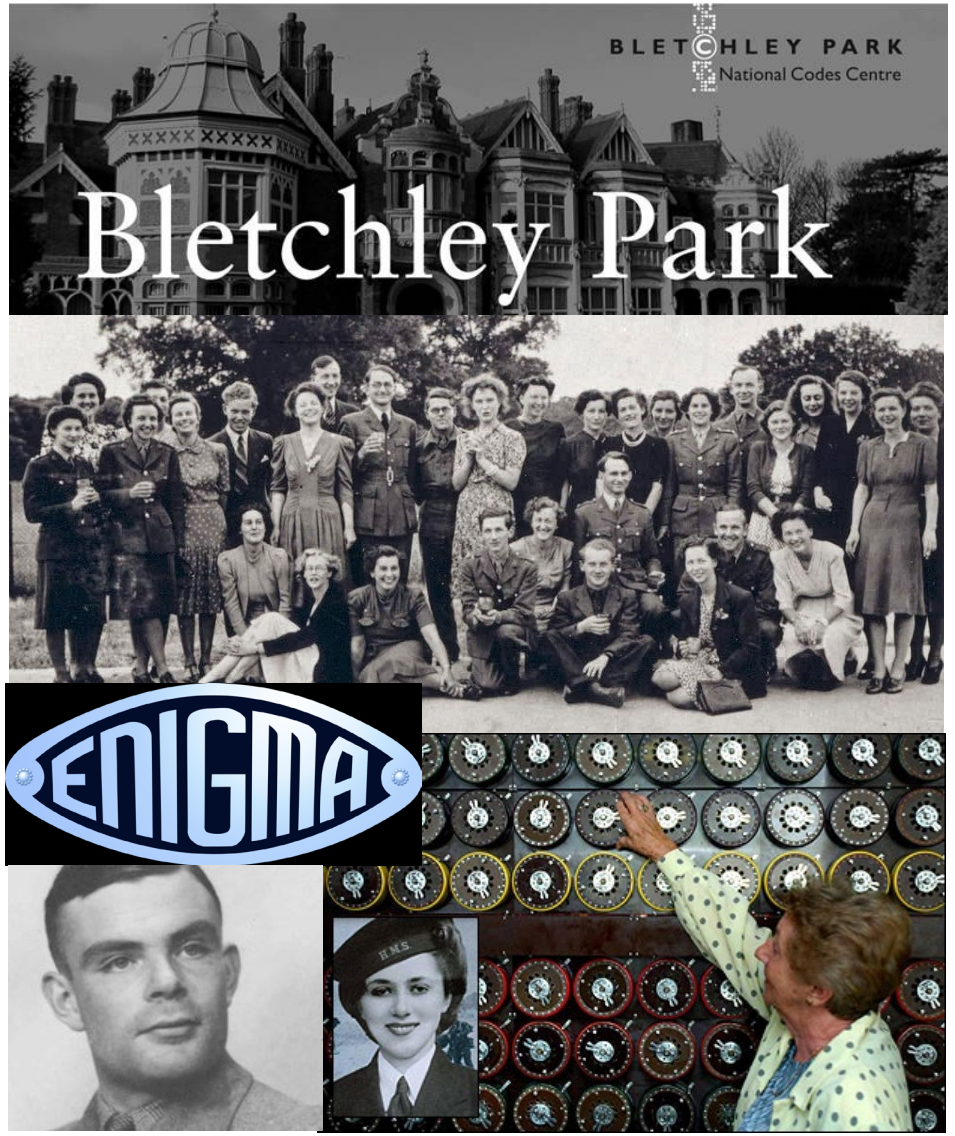


De Domenico, et al [2024]. *NPJ Digital Medicine*. In press. *arXiv*:2405.09649.



BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

Necessity is the mother of invention



BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

necessary to tackle 21st century problems

Nature, **525**(7569):289–90.

Van Noorden, R. [2015]. "Interdisciplinary research by the numbers". *Nature*, **525**(7569):306–7.

Ledford, H. [2015]. *Nature,* **525**(7569):308–11.

nature International weekly journal of science

NATURE | NEWS FEATURE

عربي

How to solve the world's biggest problems

Interdisciplinarity has become all the rage as scientists tackle climate change and other intractable issues. But there is still strong resistance to crossing borders.

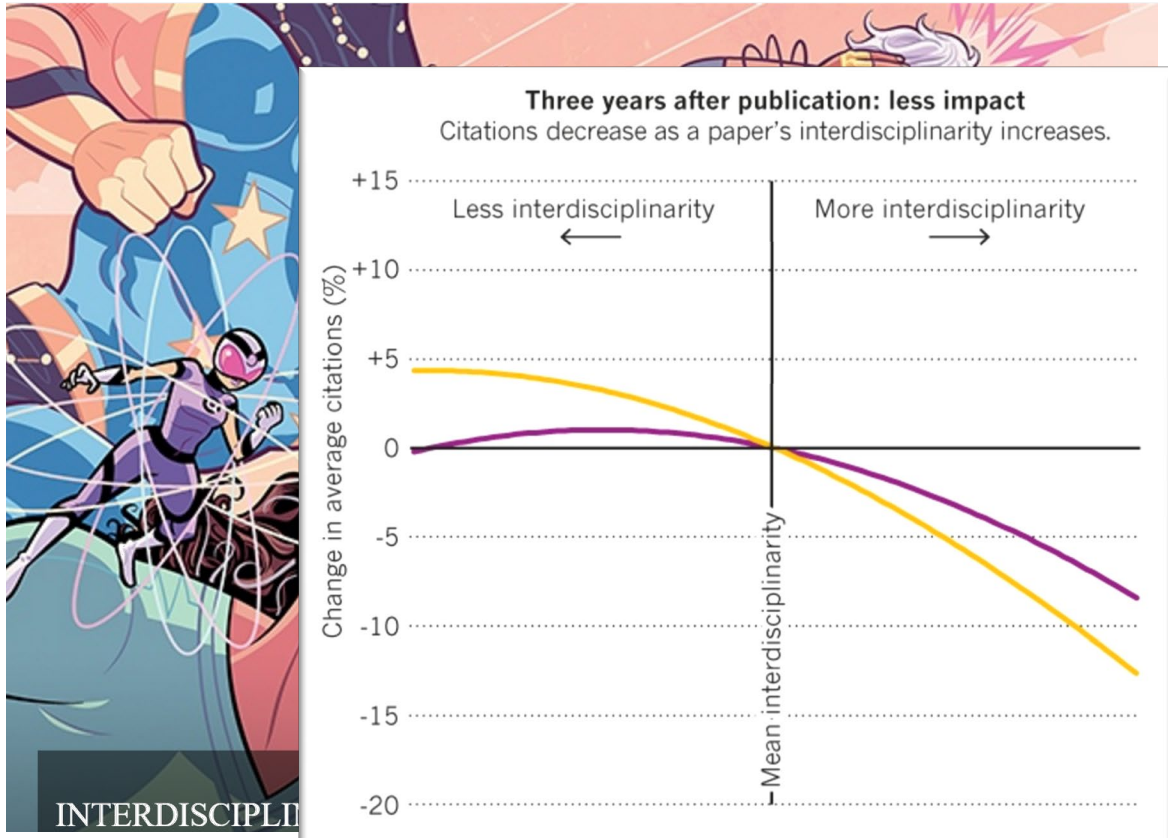
Heidi Ledford

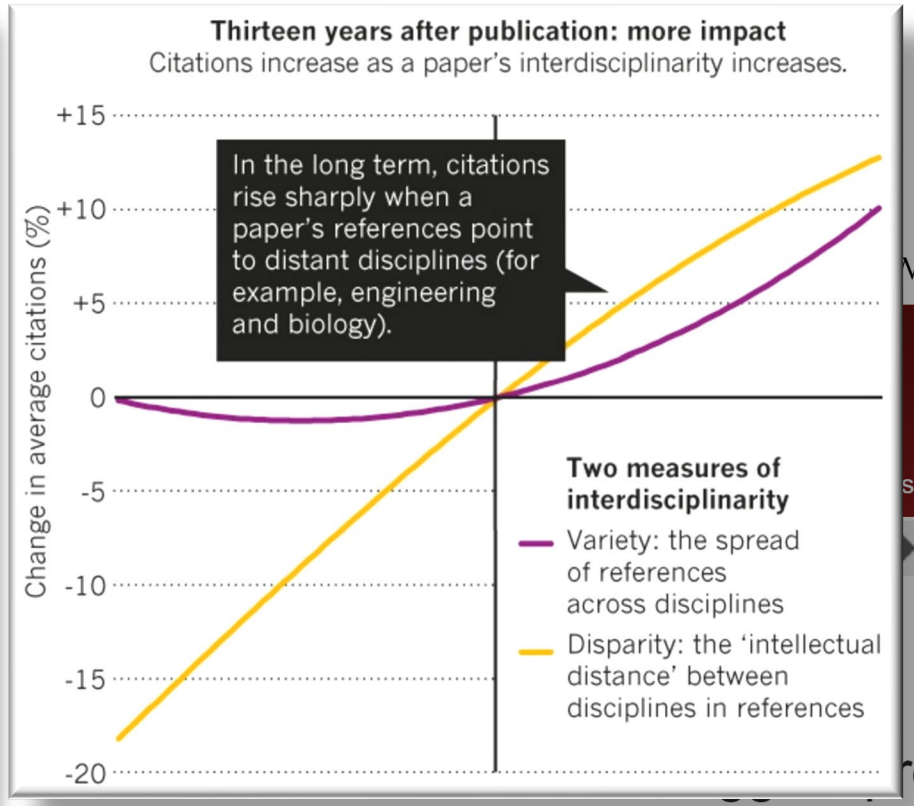
16 September 2015 | Corrected: 21 September 2015

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK

rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

necessary to tackle 21st century problems





Nature, **525**(7569):308–11.

sue | Archive | Audio & Video

roblems

Interdisciplinarity has become all the rage as scientists tackle climate change and other intractable issues. But there is still strong resistance to crossing borders.

Heidi Ledford

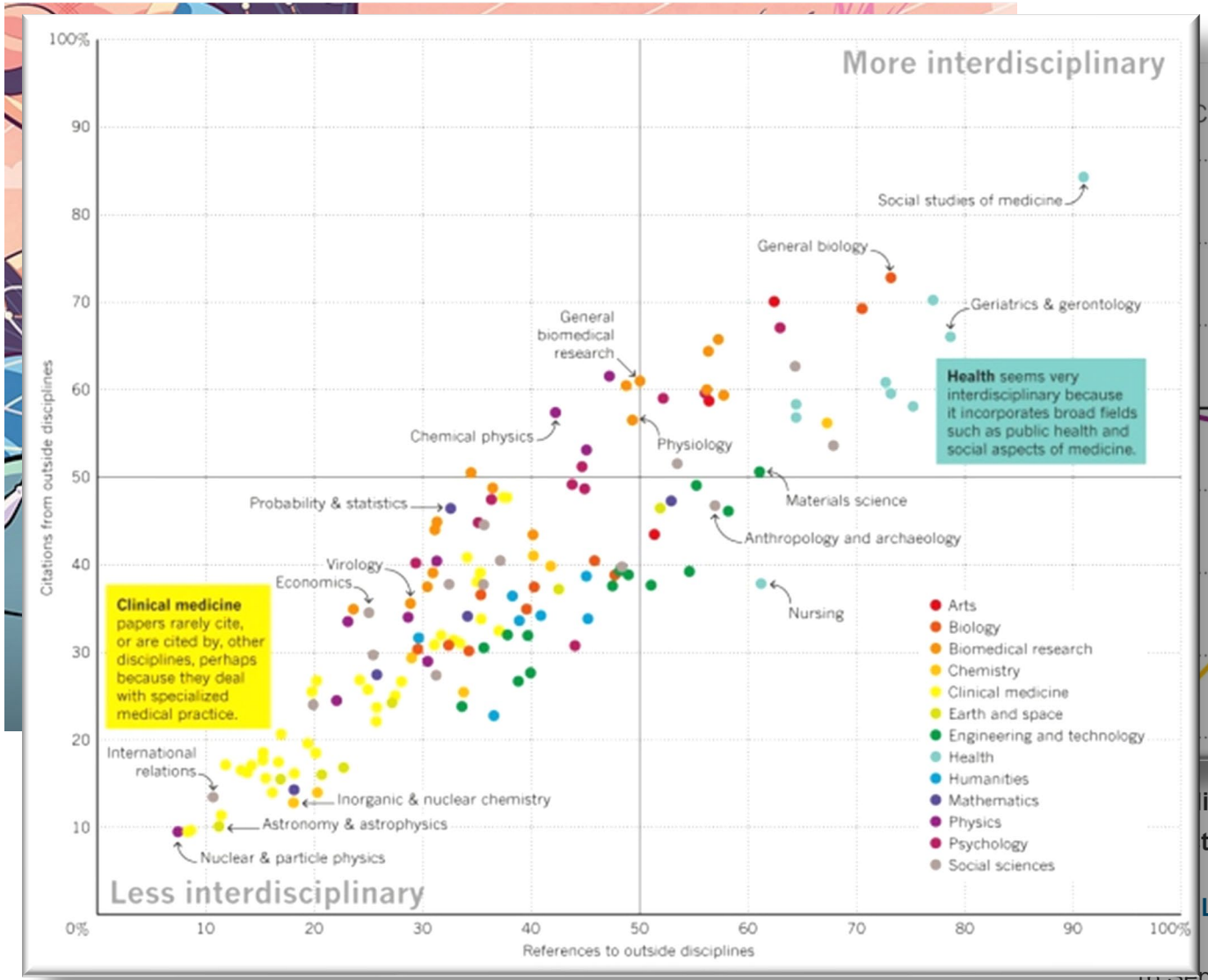
16 September 2015 | Corrected: 21 September 2015

Nature, **525**(7569):289–90.

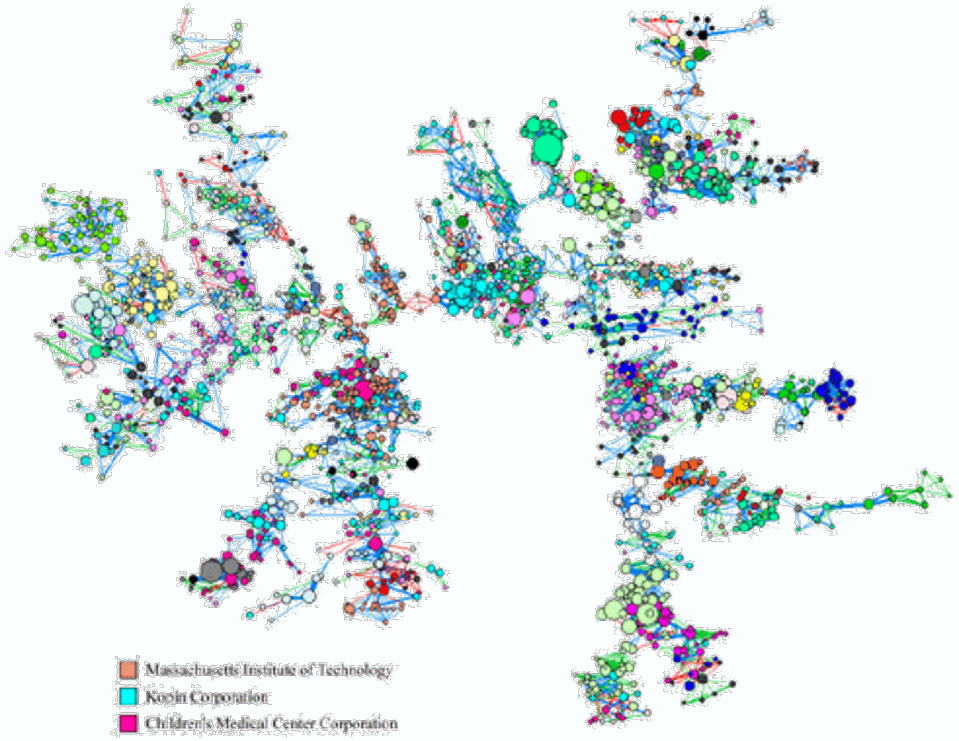
Van Noorden, R. [2015]. "Interdisciplinary research by the numbers". *Nature*, **525**(7569):306–7.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

necessary to tackle 21st century problems



Biotech Invention Network



Fleming, Lee. "Perfecting Cross-Pollination." *Harvard Business Review* **82** (9) : 22-24.

Fleming, Lee, and Adam Juda. "A Network of Invention." *Harvard Business Review* **82** (4).

Van Noorden, R. [2015]. "Interdisciplinary research by the numbers". *Nature*, **525**(7569):306–7.

BINGHAMTON UNIVERSITY STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501

siloed academic, research, and career incentives

S. Baker. “Interdisciplinary research ‘struggles to bridge academic silos’”. *Times Higher Education*. June 7, 2019.

- Frozen department structure
  - university departments built within disciplinary walls hinder collaboration and team building
  - difficult for a single-PI group to develop interdisciplinary competence
  - promotion of Faculty/PIs based on short-term rewards
  - incentives for teaching and training to move within walls (e.g. tuition revenue, faculty lines)
  - academic inbreeding

BINGHAMTON UNIVERSITY
STATE UNIVERSITY OF NEW YORK
rocha@binghamton.edu
casci.binghamton.edu/academics/ssie501