Spreading dynamics: From neural networks to COVID-19

Viola Priesemann

Max-Planck-Institut für Dynamik und Selbstorganisation

Göttingen

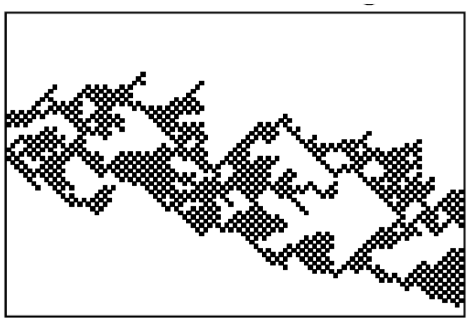
Overview

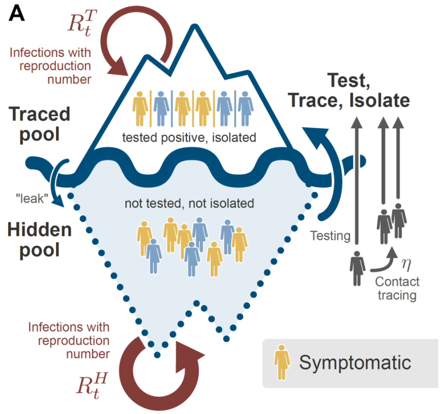
- **Subsampling Theory:** Inferring collective properties even under sparse spatial sampling
  Levina & VP, Nat Commun, 2017
  Wilting & VP, Nat Commun, 2018

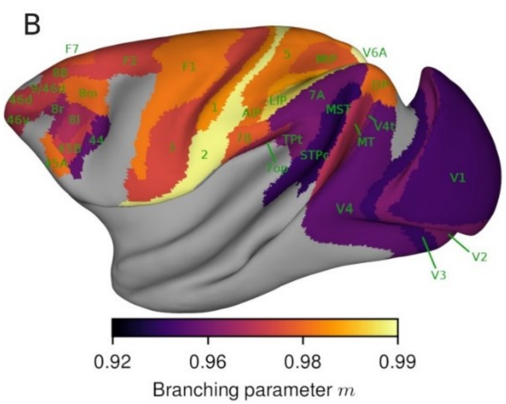
- **COVID-19 Pandemic:** Predicting future scenarios & developing mitigation strategies
  Bauer et int., Priesemann, Plos Comp Biol, 2021
  Contreras et int., VP, Nat Commun, 2021
  Contreras et int., VP, Science Adv, 2021
  Dehning et int., VP, Science, 2020
  Iftekhar, VP et al., The Lancet Reg. Health Eur., 2021
  VP et al., The Lancet, 2021a,b,c

- **Collective Computation in Living Neural Networks:** Critical phenomena, fine-tuning of computation, and clinical implications
  Cramer et int., VP. Nat Commun, 2020
  Hagemann et int., VP, Plos Comp Biol., 2021
  Zierenberg, Wilting & Priesemann, PRX, 2018

- **Outlook**

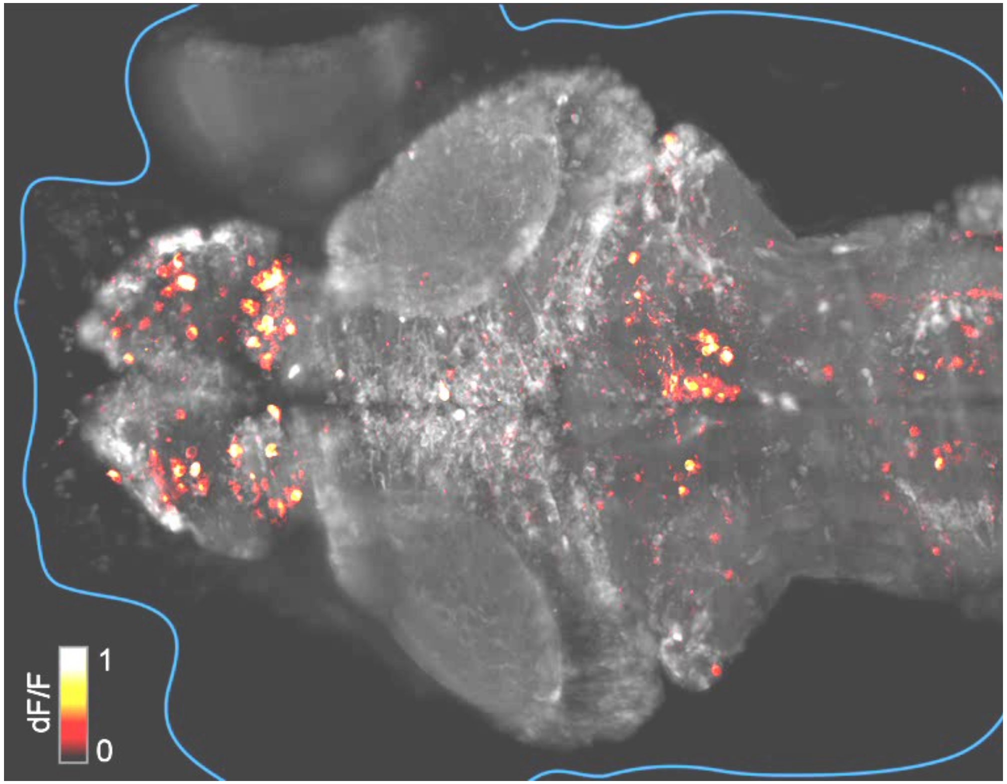






Collective Dynamics

Light sheet fluorescence imaging in a zebra fish larva



100.000 neurons (80bn in human)
10 – 10.000 connections/neuron

Interactions:

- pulse-like (“spikes“)
- directed
- time-delayed
- plastic (learning!)

High-dimensional topology
→ difficult to characterize collective properties

[Ahrens, Orger, Robson, Li, Keller; *Nat. Meth.*, 2013]

Subsampling Can Bias Inference

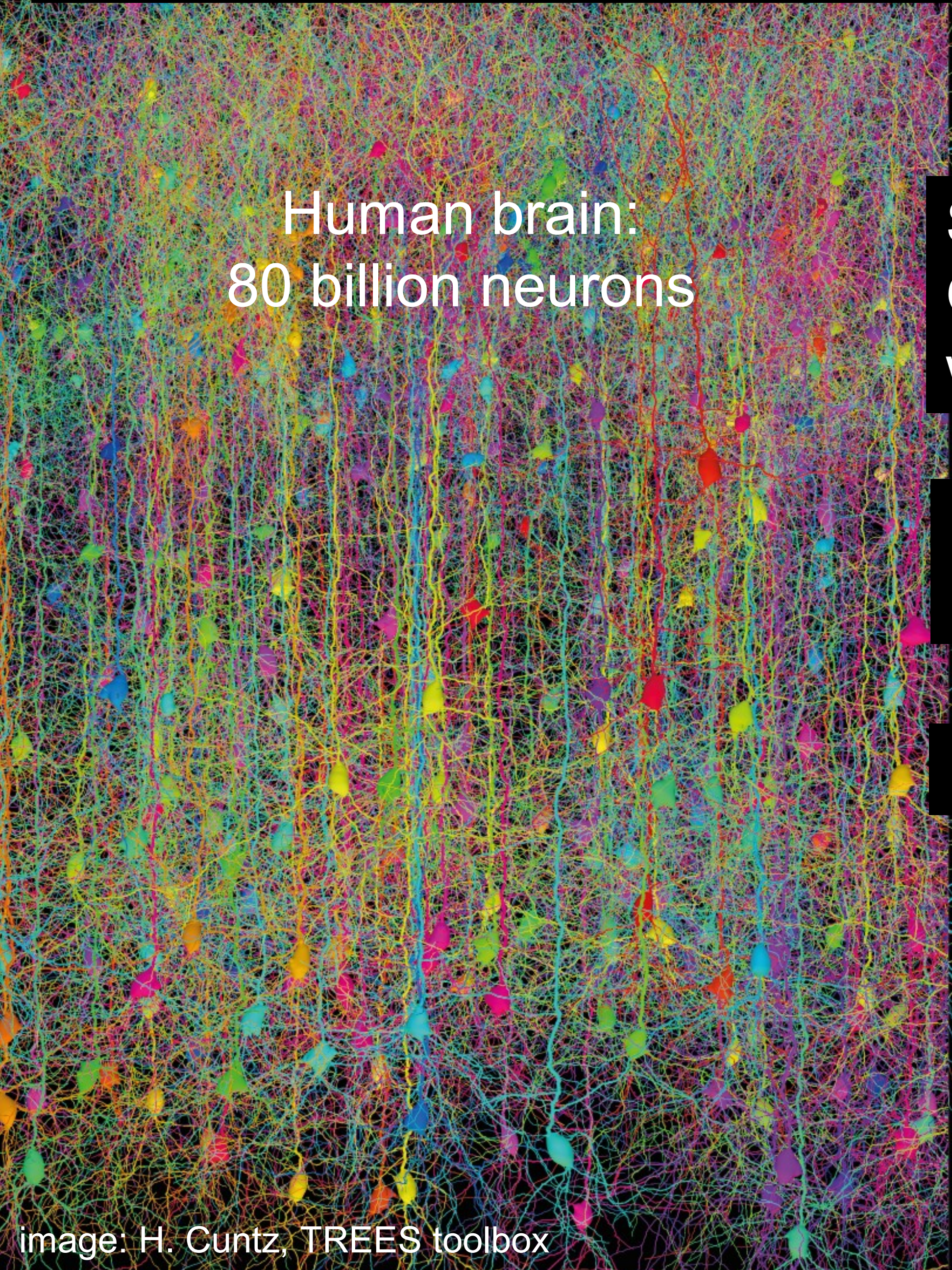


image: H. Cuntz, TREES toolbox

Sampling (experiment):
Only 100-1000 neurons with sufficient precision

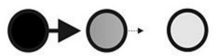
Subsampling bias leads to misestimations

→ Bias-free inference

Neto, Spitzner & VP, arxiv
Spitzner et al., Plos One, 2021
Wilting & VP, Cerebral Cortex, 2019
Wilting & VP, Nature Communications, 2018
Levina & VP, Nature Communications, 2017

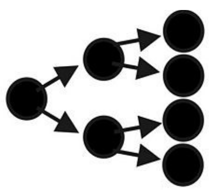
Propagating Activity as a Branching Process

control parameter *R*
expected number of "children"



$R < 1$ subcritical

$R = R_c = 1$ critical



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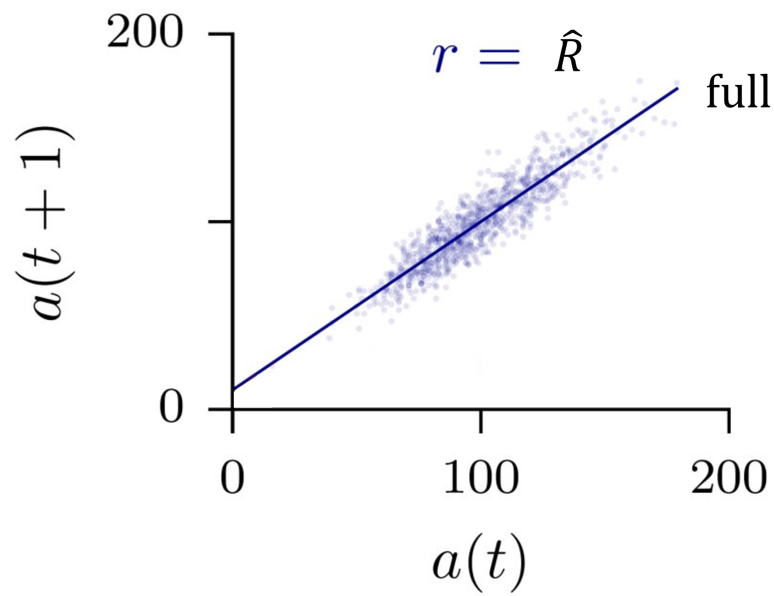
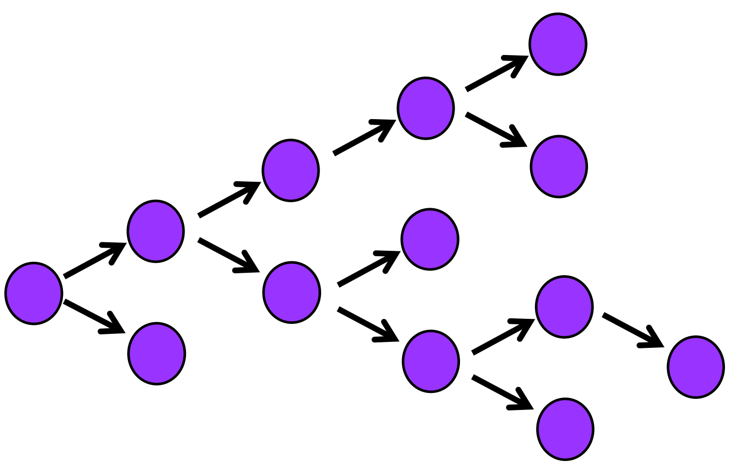


sampled activity



Branching process

activity $A(t)$ in system: $A(t) = \sum_{i=1}^{A(t-1)} Y_{i,t} + h_t$

h_t	external input (random variable)
Y	# activated units per active unit (r.v.)
$R = E[Y]$	mean # "children" per unit or eff. coupling strength

[Galton & Watson, 1875]
[Wilting & VP, Nature Communications, 2018]
[Levina & VP, Nature Communications, 2017]

Propagating Activity as a Branching Process

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expected number of "children"

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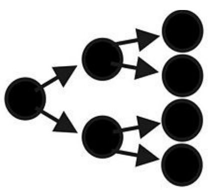
subcritical

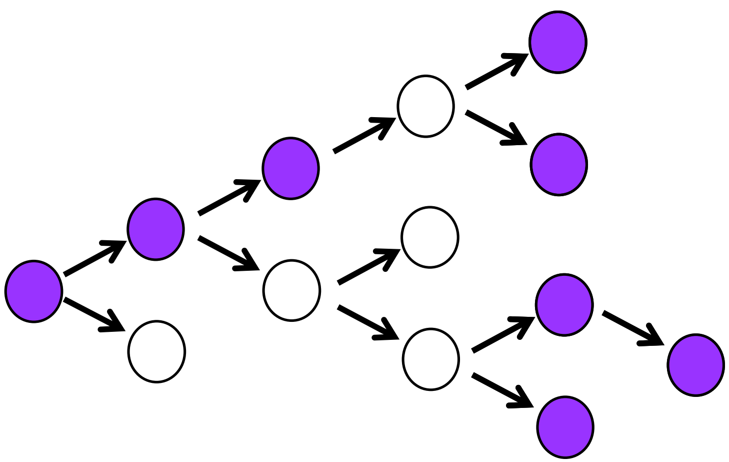
$R = R_c = 1$

critical

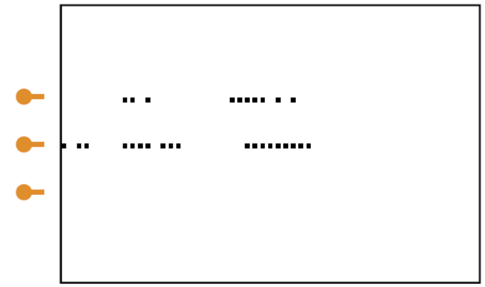


$R > 1$

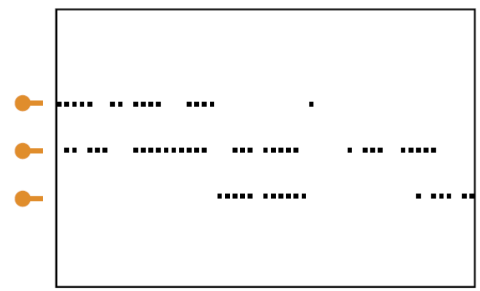
supercritical



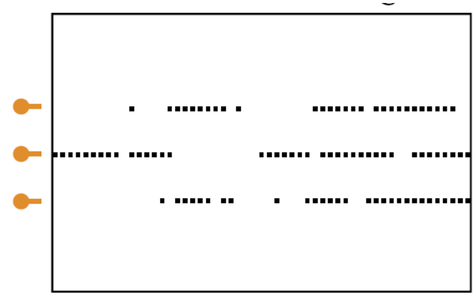
$R < 1$



$R = 1$



$R > 1$



Propagating Activity as a Branching Process

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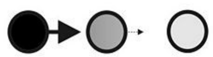

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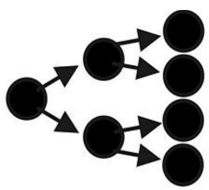

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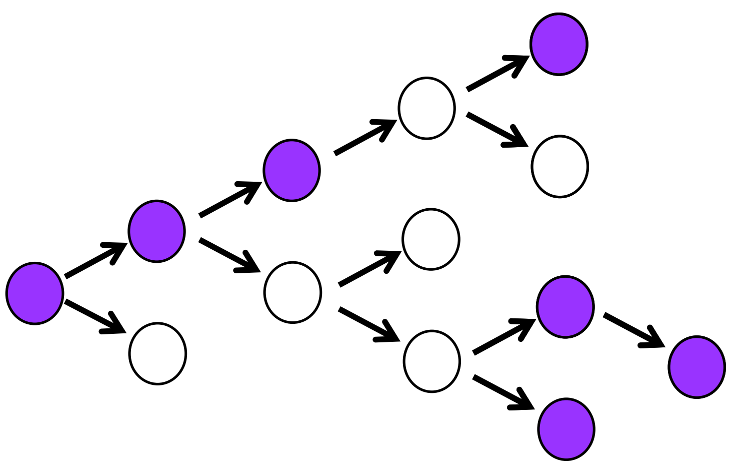
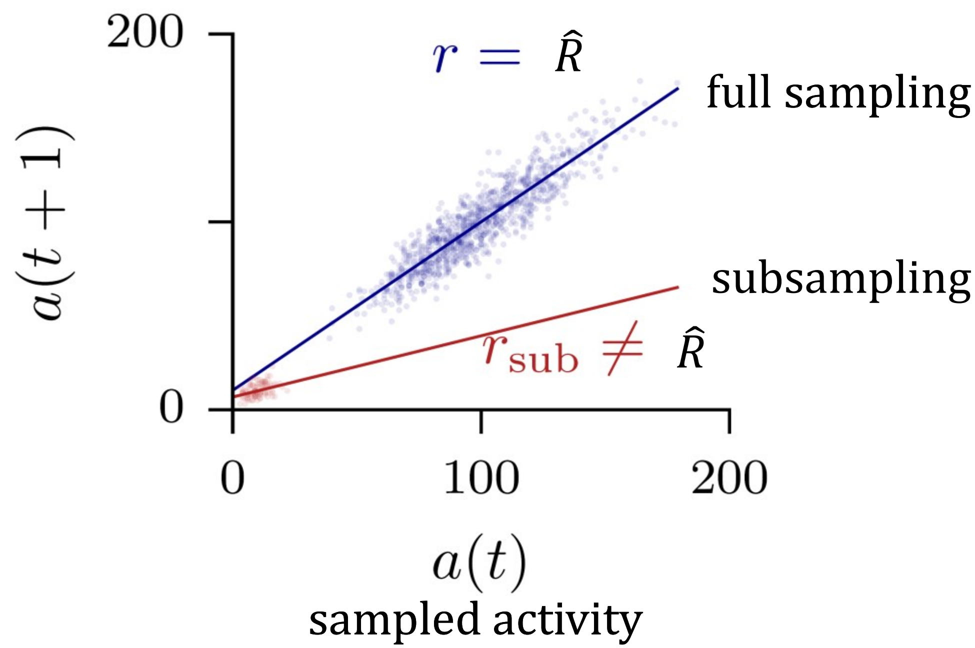




→ Correlation strength r
is biased under subsampling!

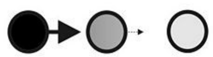
Ansatz:

- ➢ Generalizing estimator to any Δt:
  $r(a(t), a(t + \Delta t))$.
  Thereby we can partial out the bias

[Wilting & VP, Nature Communications, 2018]

Inferring Spreading Dynamics

control parameter *R*
expected number of "children"



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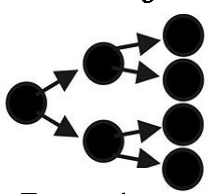

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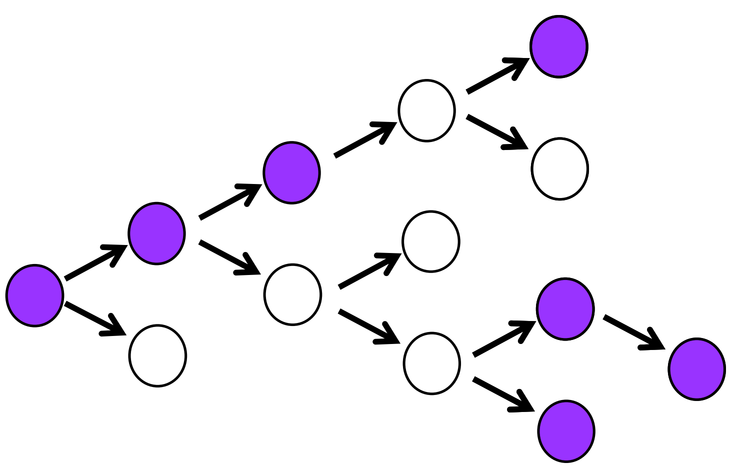


- returns the control parameter *R*, instead of a binary test for or against criticality

Efficient, precise, easily applicable:

- It only requires knowing a(t), i.e. the *sampled* activity at each time step
- It does not require knowing the system size N, the number of sampled units n, or any of the moments of the process.
- Ideal conditions: Estimation of control parameter from a single unit!

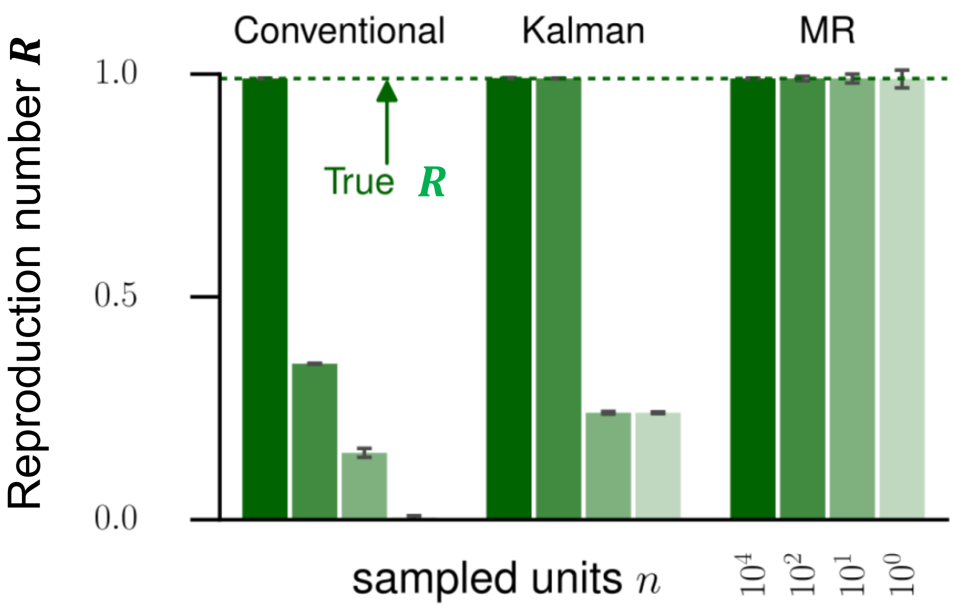
Adopted by: J.Beggs, K.Hengen, C.Butfering; e.g. Ma et al., Neuron, 2019

Python Toolbox: github.com/Priesemann-Group

[Spitzner et al., Plos One, 2021]
[Dehning et int. VP, Science, 2020]
[Wilting & VP, Nature Communications, 2018]
[Levina & VP, Nature Communications, 2017]

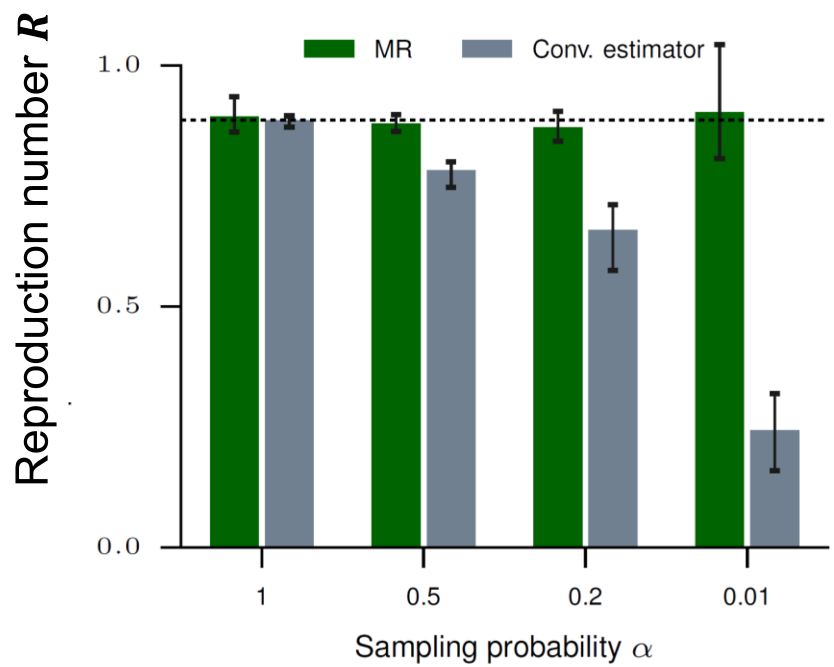
Overcoming the Subsampling Problem – to Assess Disease Spreading

Estimation of the reproduction number $\boldsymbol{R}$ in a model of 10.000 neurons



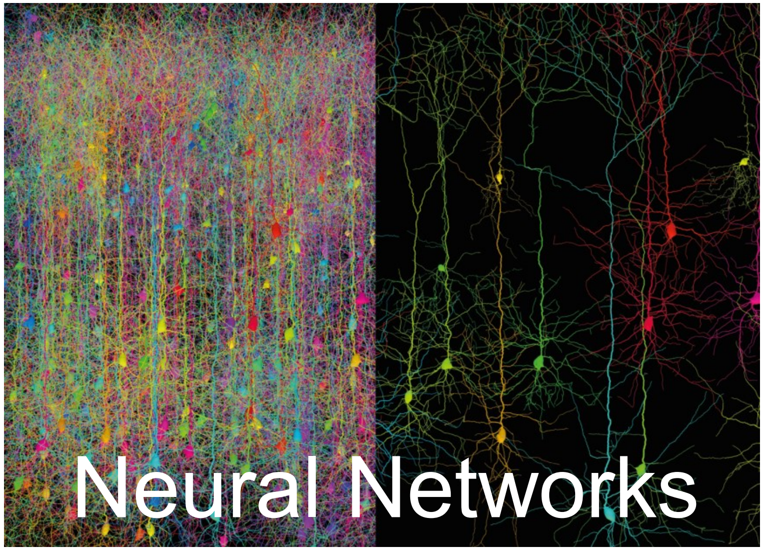
[Wilting & VP, Nature Communications, 2018]

Estimation of the reproduction number $\boldsymbol{R}$ from measles case numbers



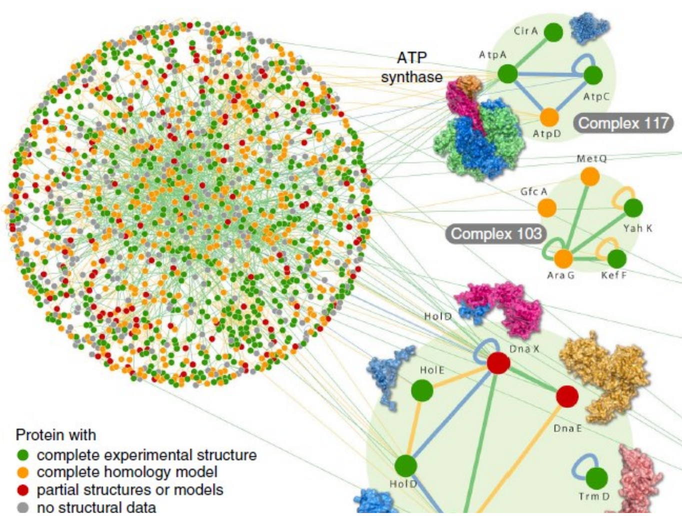
COVID-19:
[VP et al., The Lancet, 2021a,b,c]
[Bauer et int., VP, Plos CB, 2021]
[Contreras et int., VP, Nat Commun, 2021]
[Linden et int., VP, Dtsch. Arzteblt Int. 2020]

Subsampling is a Ubiquitous Challenge



Disease Propagation

"I don't know what these dots are ...
but ya mind if I connect 'em?"



Protein Networks

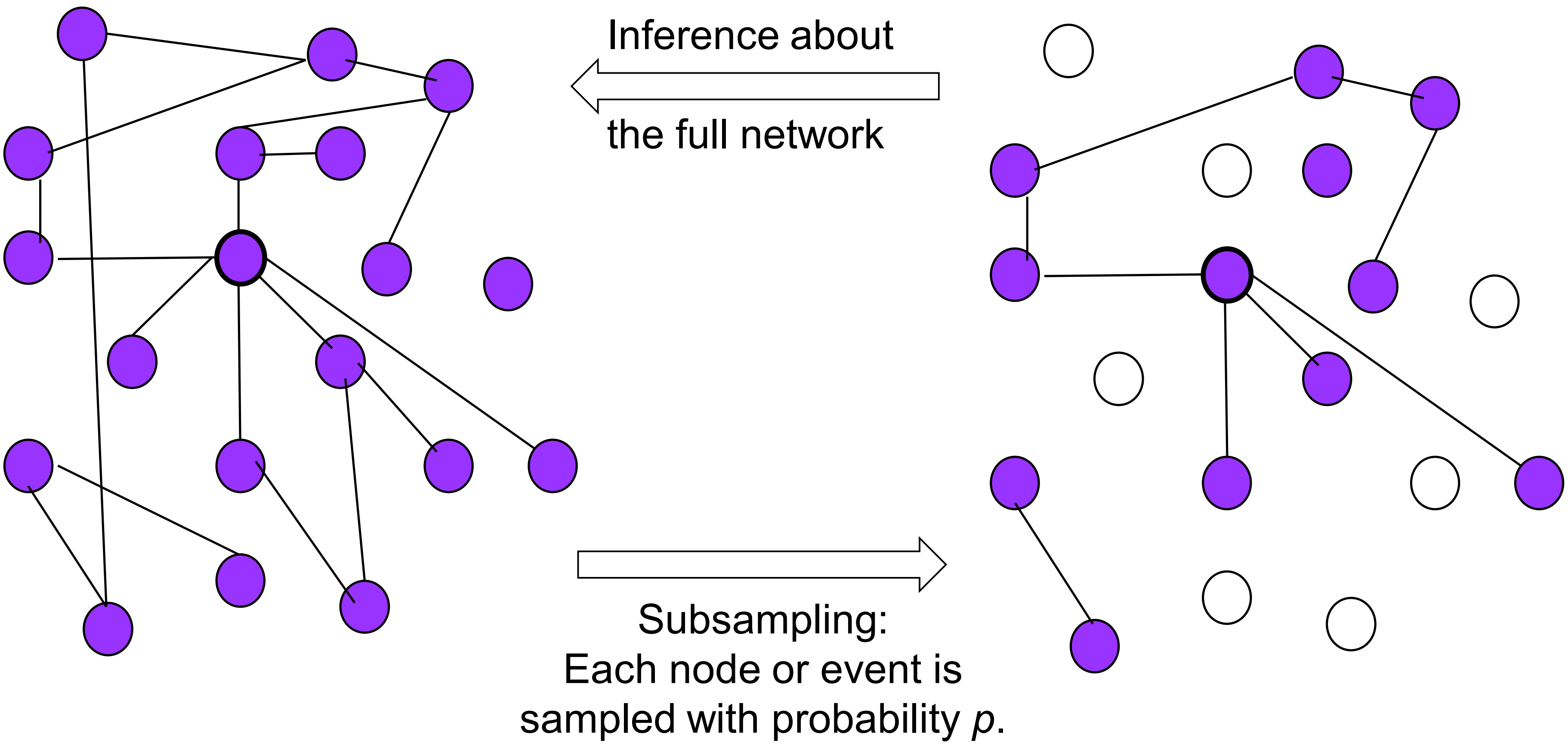
[Rajagopala et al., 2014]

Social or Ecological Systems

[Grandjean, 2014]

Subsampling Scaling Theory

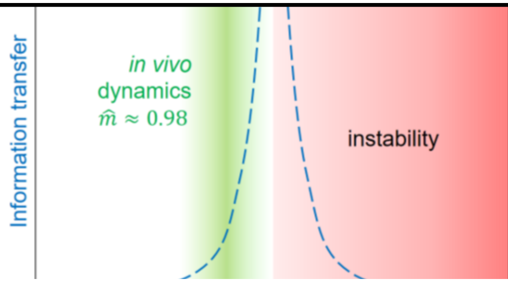
Levina & Priesemann, Nature Communications, 2017



→ Subsampling scaling theory
for graph degree distributions,
clustering, or avalanche size distributions

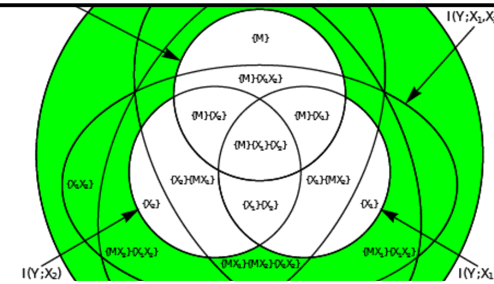
Physics of Neural Systems

Spreading Dynamics and Phase Transitions



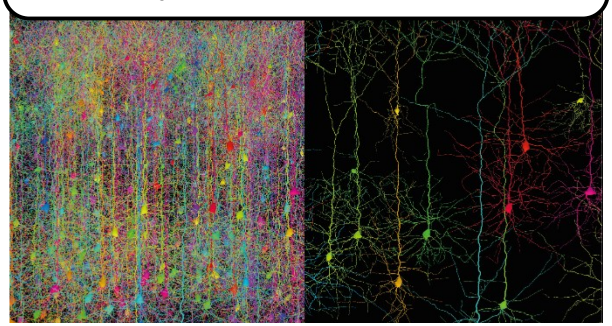
VP et al., Plos Comp Biol., 2013
Wilting & VP, Cerebr. Ctx, 2019
Wilting & VP, Curr Op Neurosci, 2019
Neto, Spitzner & VP, arxiv; Spitzner et al., arxiv

Information Theory to Quantify & Design Computation



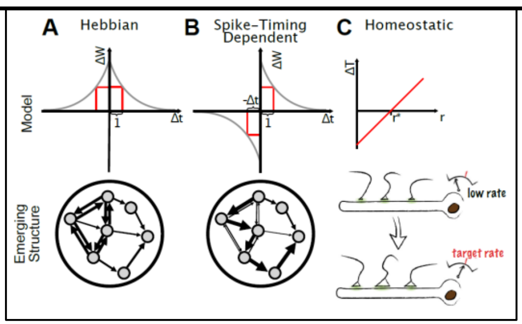
Wibral, Lizier & VP, Matter to Life, 2017
Wollstadt et al., Plos CB, 2017
Wibral et al., Entropy, 2017
Rudelt, … VP, biorxiv, 2020

Subsampling Theory



VP et al., 2009, 2013, 2014
Levina & VP, Nat. Commun., 2017
Wilting & VP, Nat. Commun., 2018
Zierenberg et al., PRE & PRR, 2020

Local Learning Rules to Optimize Computation



Zierenberg, … VP, Phys Rev X, 2018
del Papa, VP & Triesch, 2017, 2019
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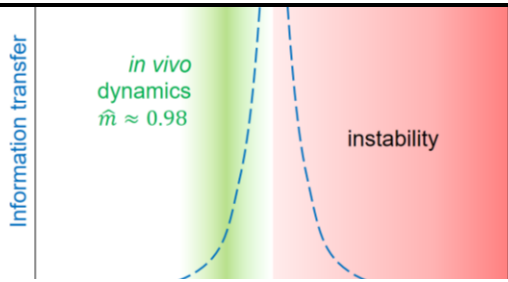

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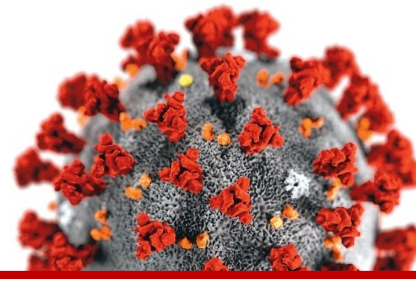
Wilting & VP, Curr Op Neurosci, 20
Neto, Spitzner & VP, arxiv; Spitzner et al., arxiv



COVID-19
Dehning, … VP, Science, 2020
Linden, … VP, Dtsch Arztebl Int, 2020
Bauer, … VP, Plos Comp Biol, 2021
Contreras … VP, Nat Commun, 2021
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VP et al., The Lancet, 2021a,b,c

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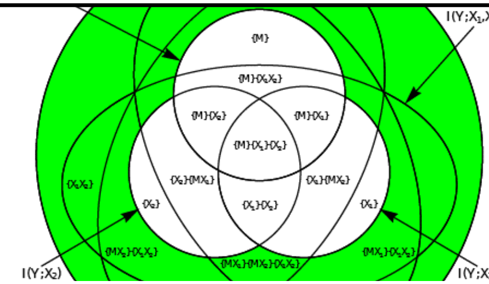

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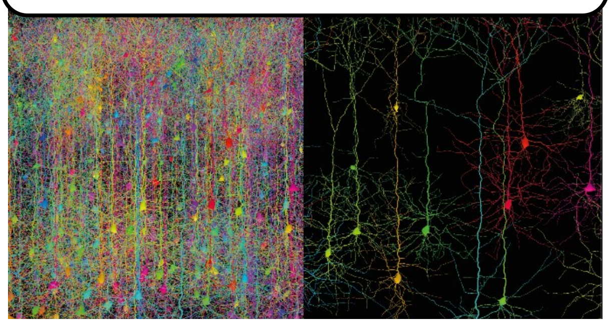

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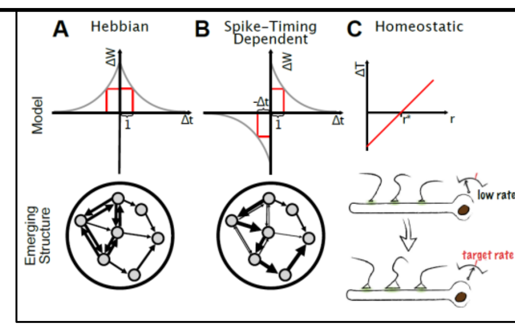

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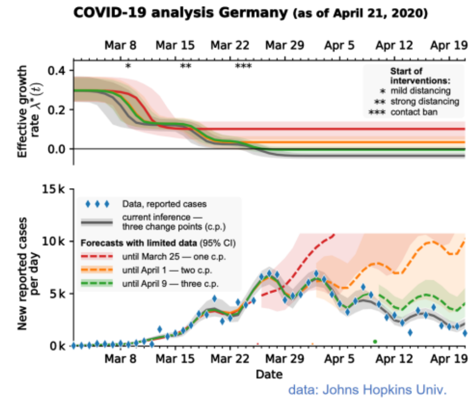
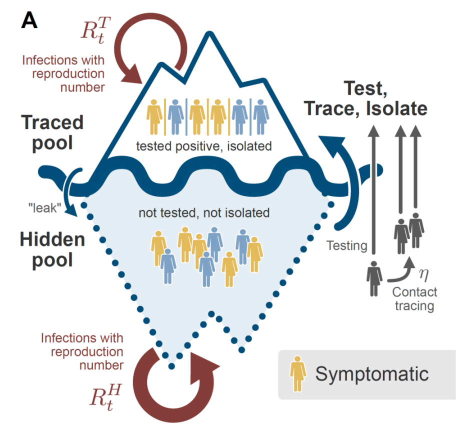
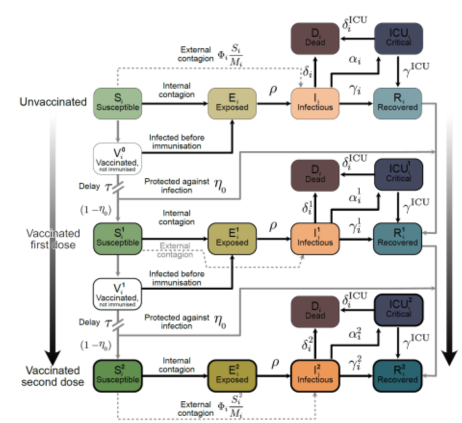
- **Quantifying the Effectiveness of COVID-19 Interventions using Bayesian Inference**
  (Dehning et int. VP, Science 2020)



- **Mitigating the Spread of COVID-19 via Test-Trace-Isolate (TTI)**
  (Contreras et int VP, Nat Commun 2021)
  (Contreras et int VP, Science Adv., 2021)



- **The Progress of Vaccination Determines the Pace to Lift Restrictions**
  (Bauer, et int VP, Plos Comp Biol., 2021)



- **Estimation of the Underreporting**
  (Linden et int VP, Dt. Arztebl Int, 2020)

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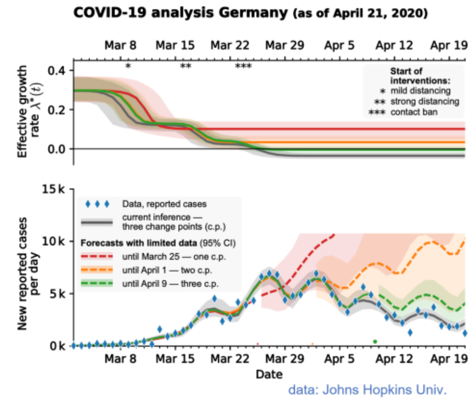
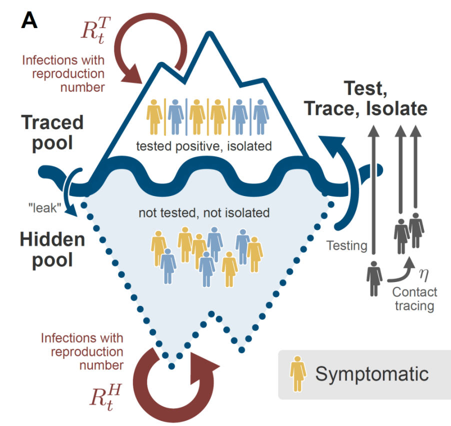
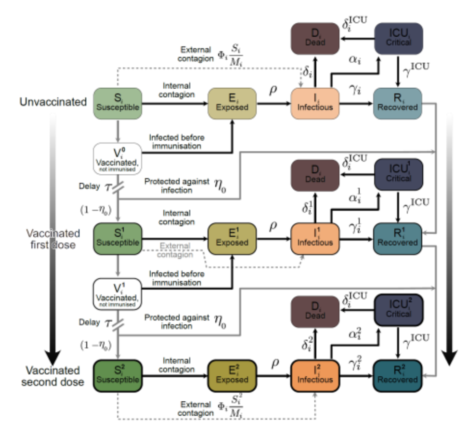
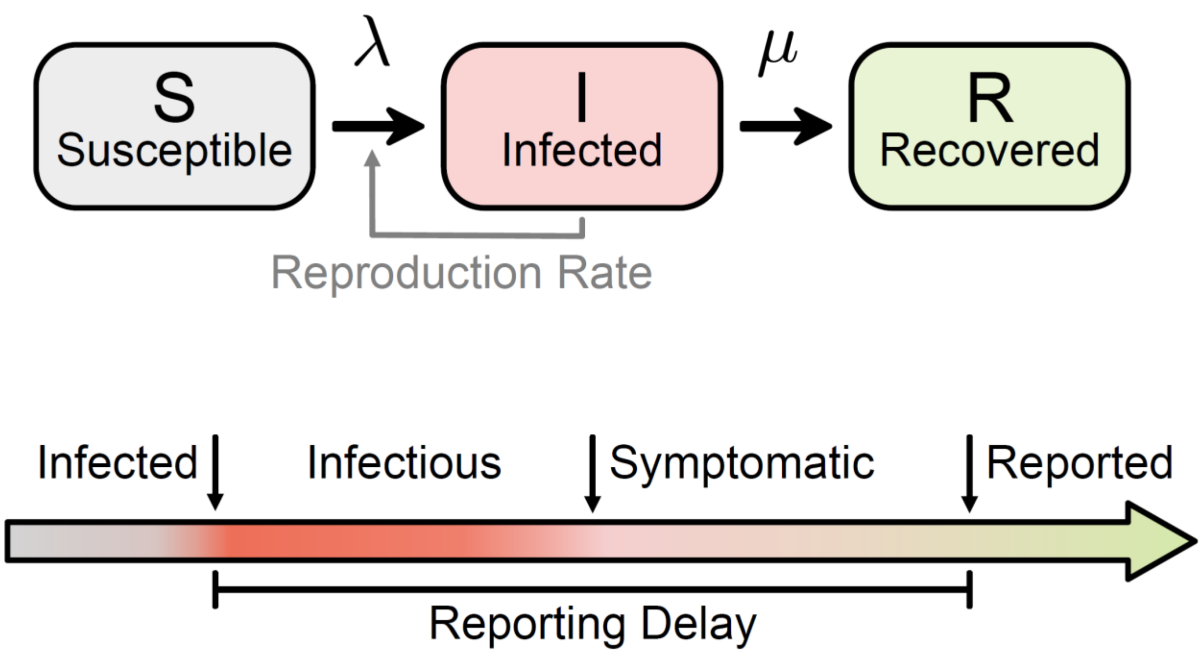






SIR: Susceptible-Infected-Recovered

SIR Model



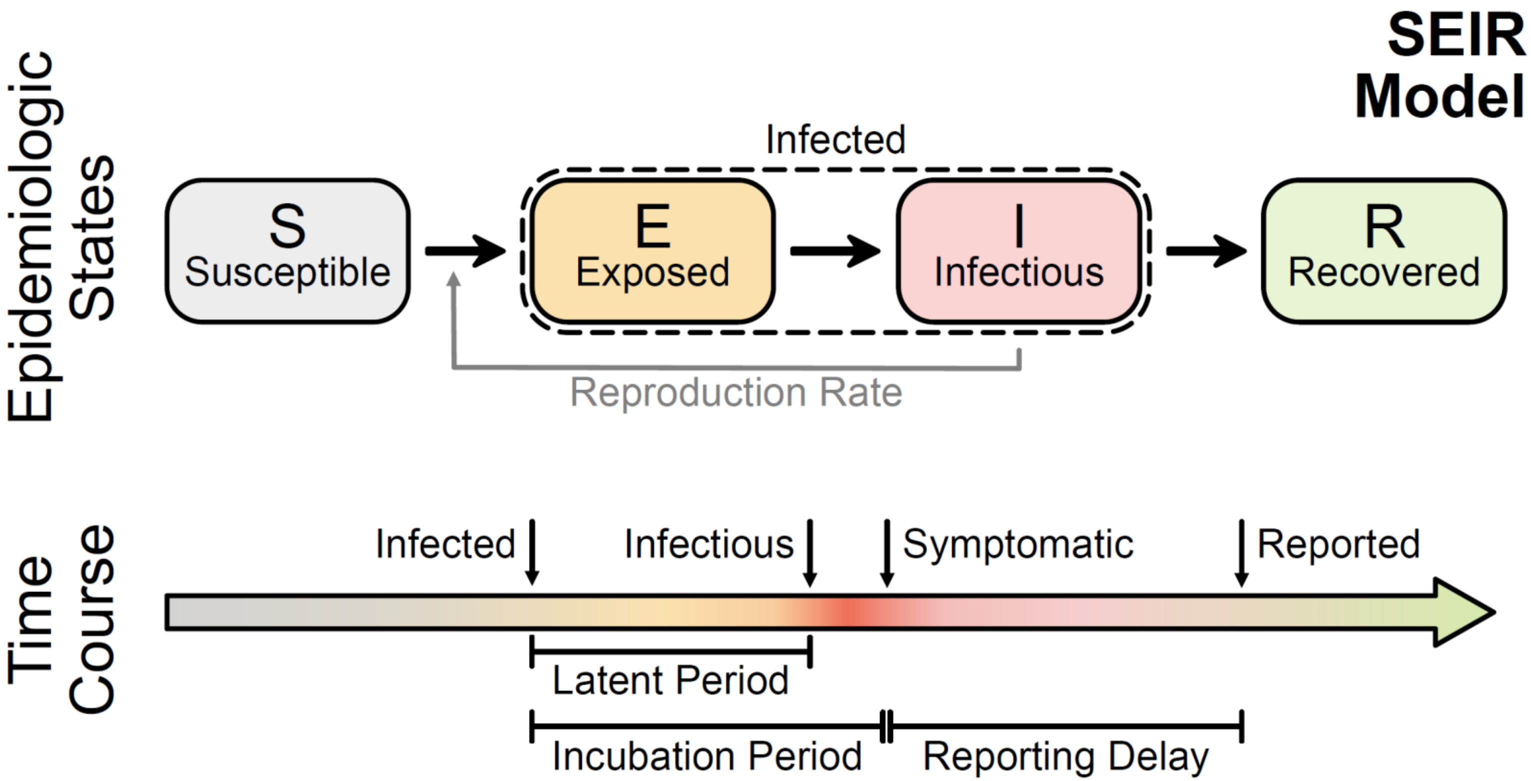
$$\frac{dS}{dt} = -\lambda \frac{SI}{N}$$

$$\frac{dI}{dt} = \lambda \frac{SI}{N} - \mu I$$

$$\frac{dR}{dt} = \mu I$$

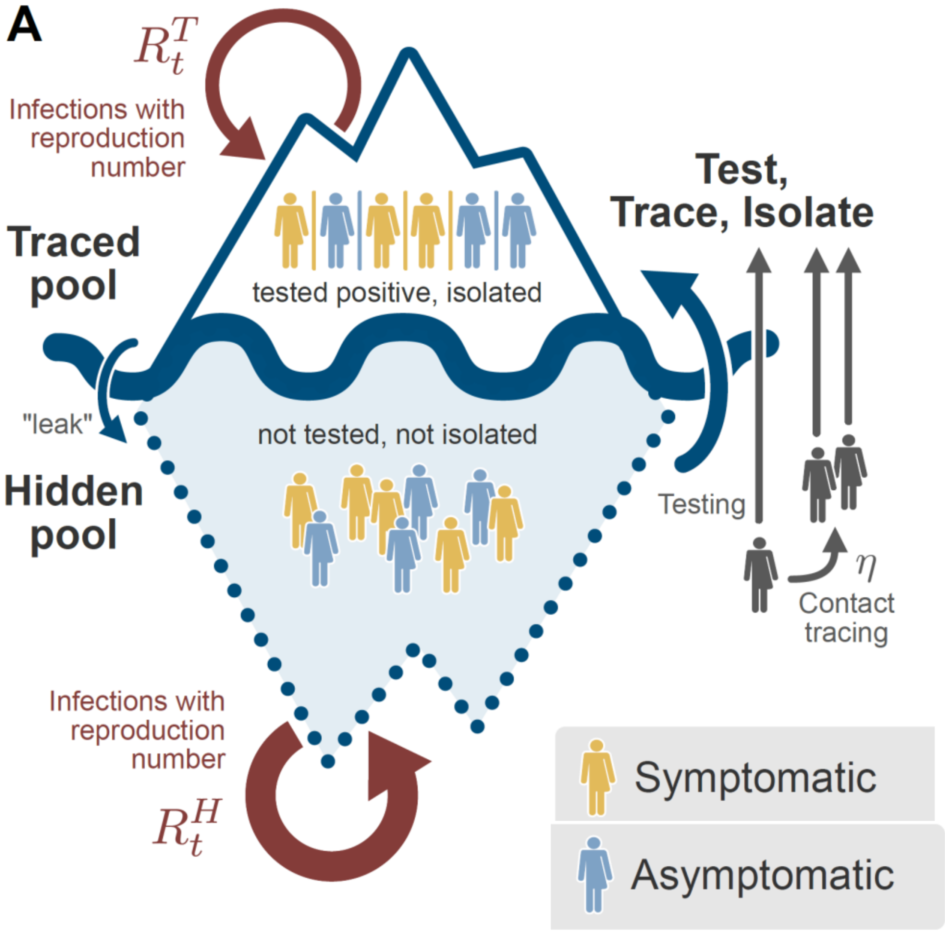
[Dehning et int., Priesemann, arxiv /medRxiv / Science, 2020]

SEIR: Susceptible-Exposed-Infected-Recovered



[Dehning et int., Priesemann, arxiv / medRxiv / Science, 2020]

Test-Trace-and-Isolate (TTI) contributes to containment



Test-Trace-Isolate (TTI) is not perfect:

- Pre- und asymptomatic infection are hard to detect
- Contacts are missed (1/3)
- Quarantine is not perfect
- People who do not get tested (20%)
- Introduction of new infectious from abroad
- Limited capacities of health offices for testing and tracing

[Contreras et int., Priesemann, Nature Communications, 2021]

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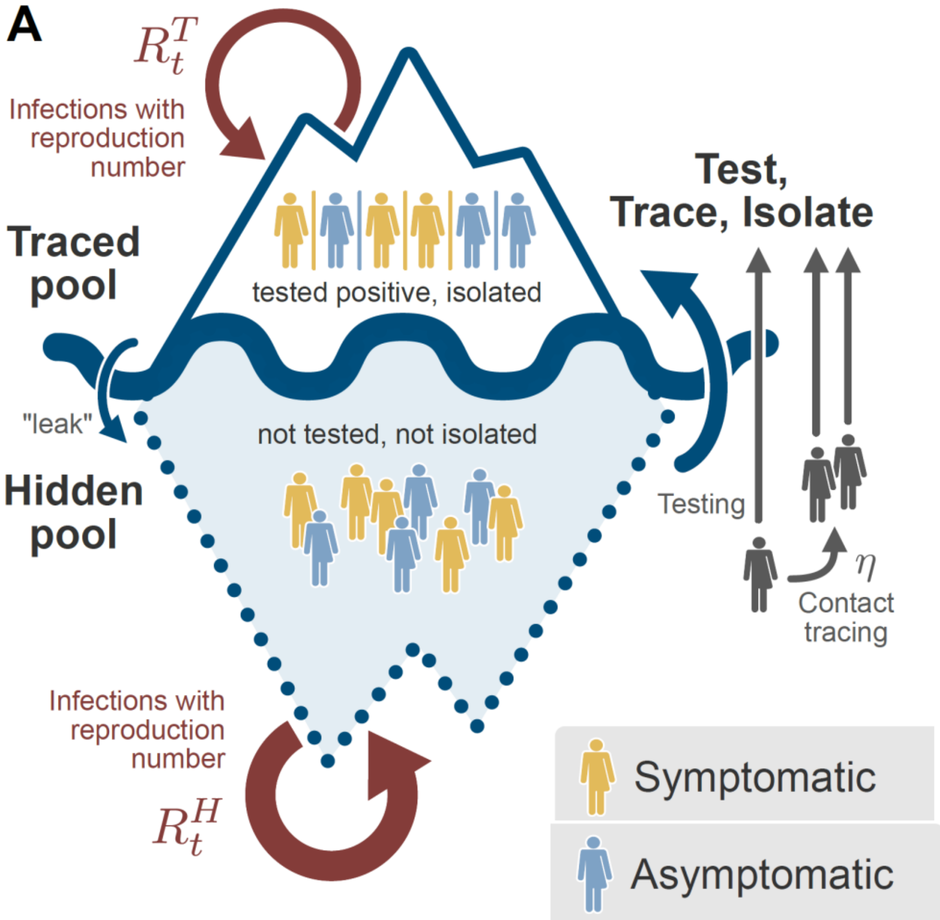
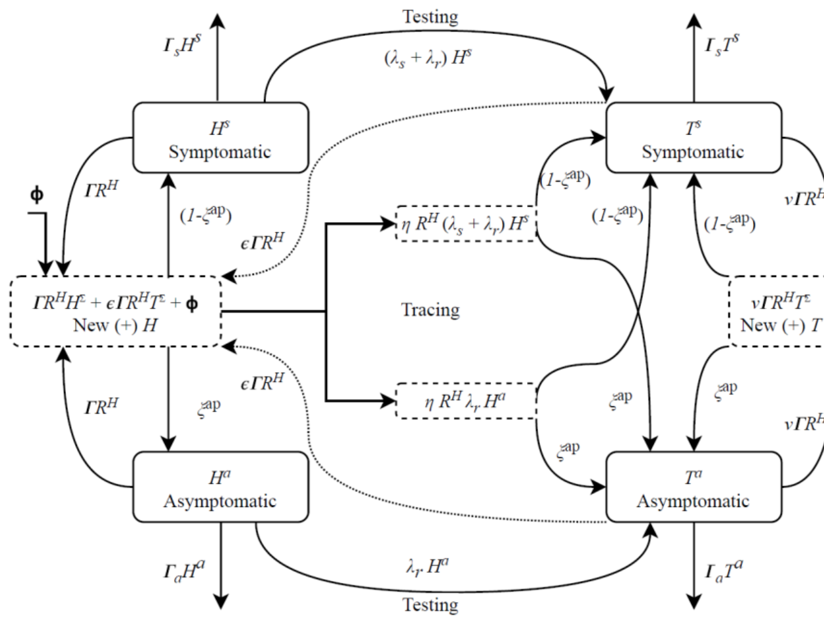
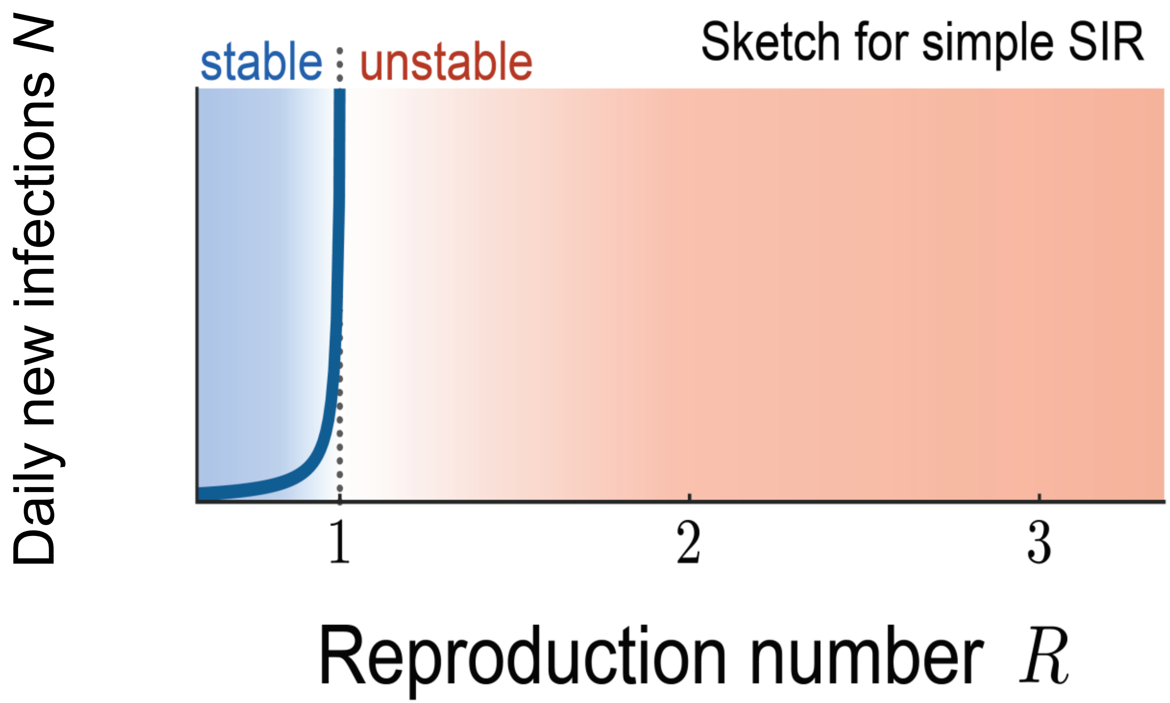


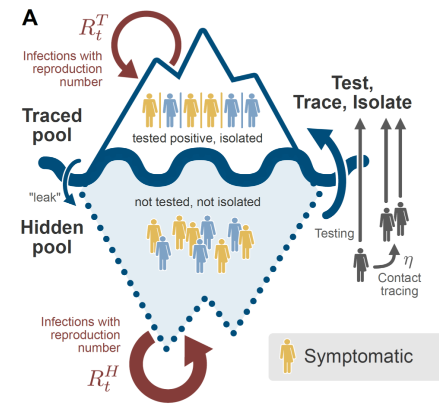


[Contreras et int., Priesemann, Nature Communications, 2021]

The reproduction number *R* and the external influx of new cases Φ determine the level of new infections *N*

$$N \approx \frac{\Phi}{R_c - R} = \frac{\Phi}{1 - R}\,, \qquad \text{for } R < 1$$



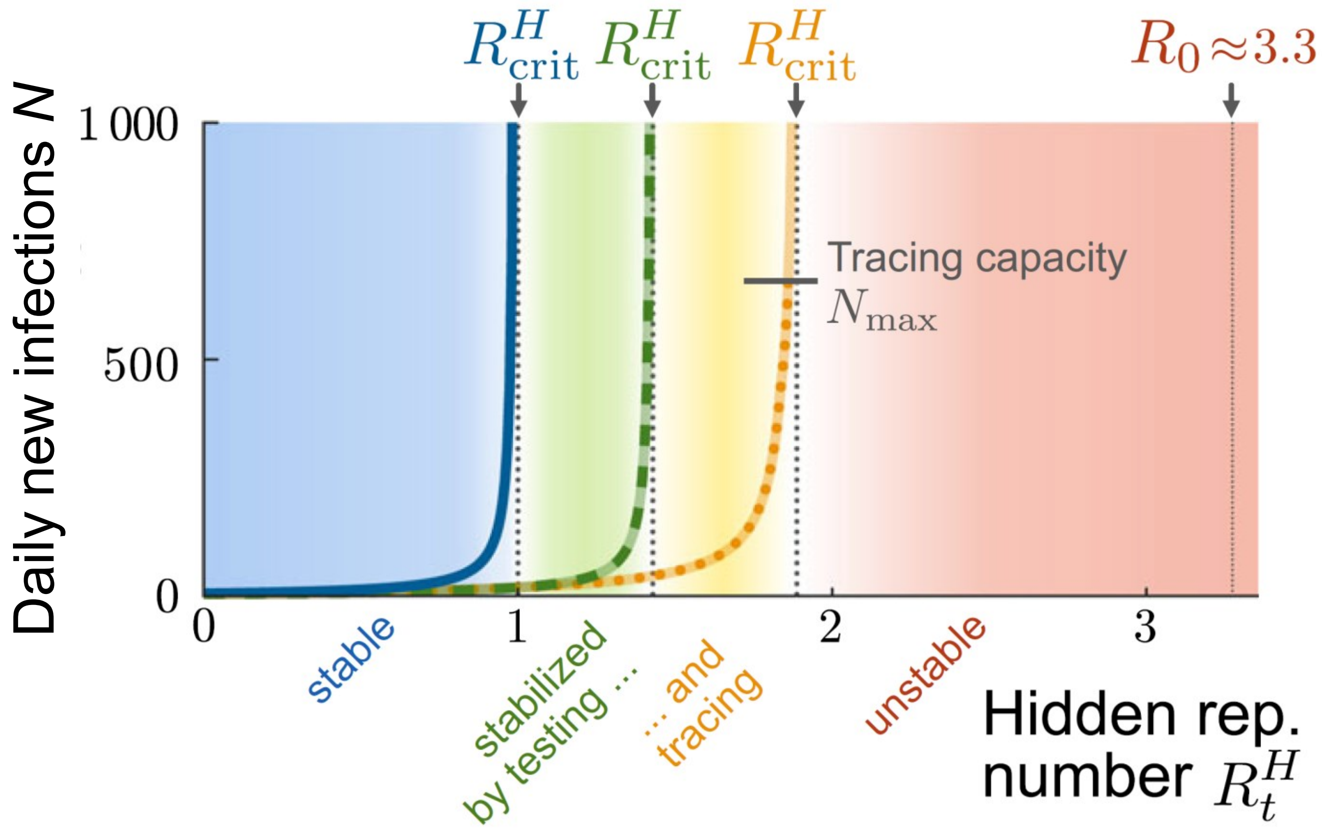


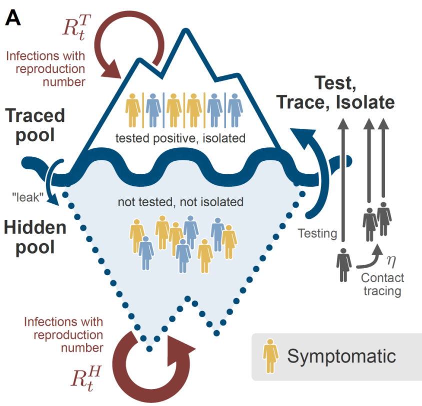
[Contreras et int., Priesemann, Nature Communications, 2021]

Test-Trace-Isolate (TTI)

pushes the transition to instability R_c to higher contact rates

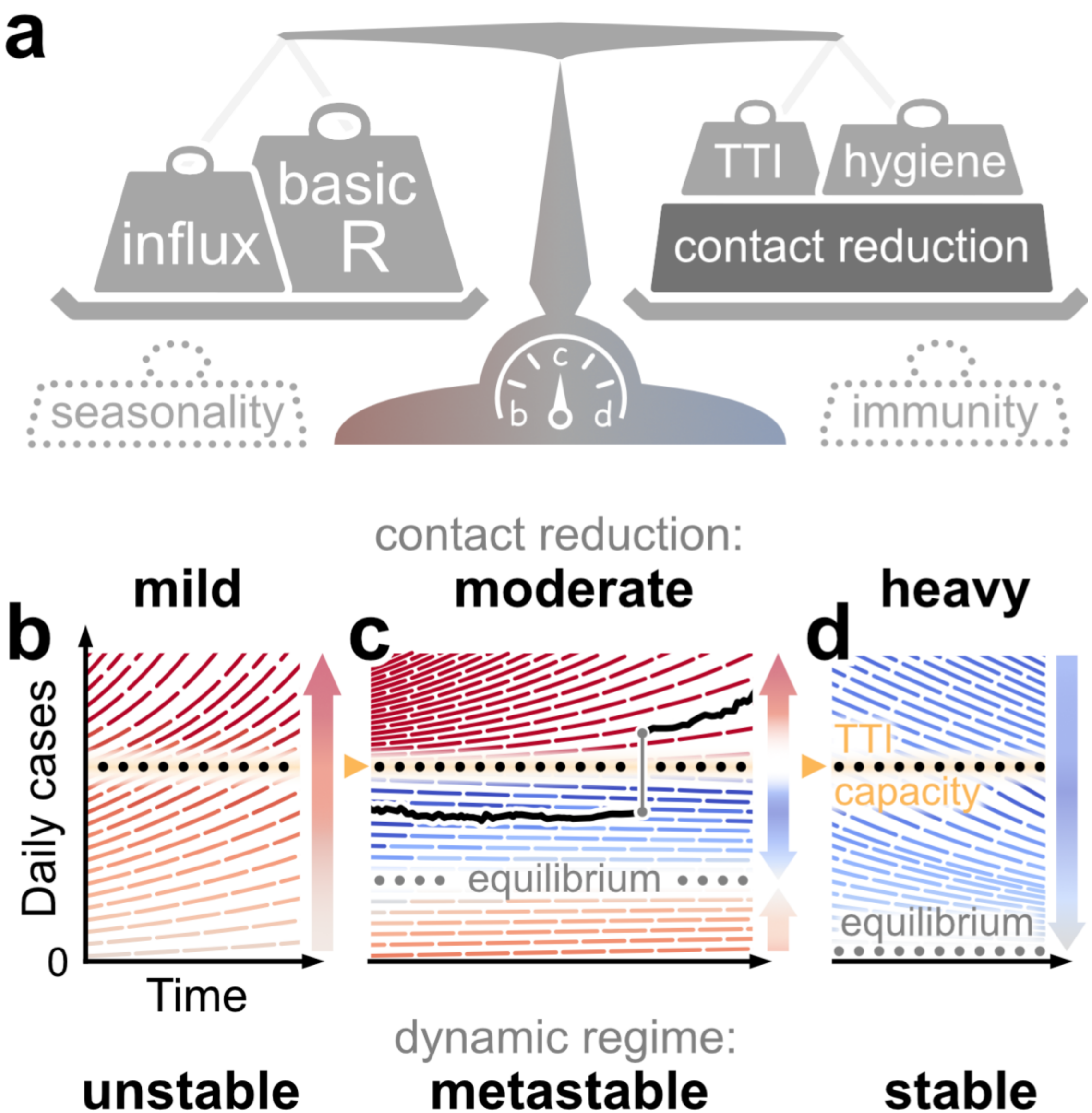
$$N \approx \frac{\Phi}{R_c - R} = \frac{\Phi}{1 - R}, \qquad \text{for } R < 1$$





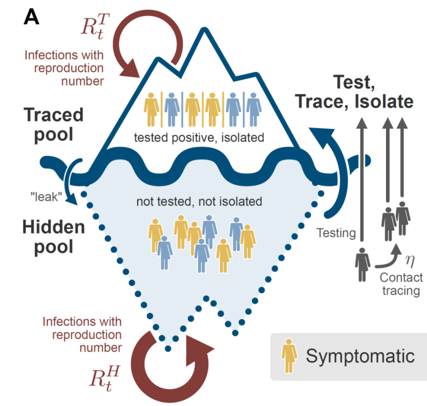
[Contreras et int., Priesemann, Nature Communications, 2021]

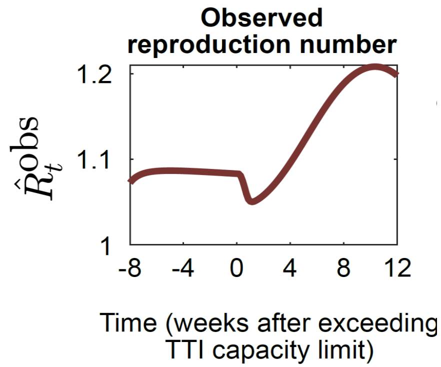
Combined measures to contain COVID-19

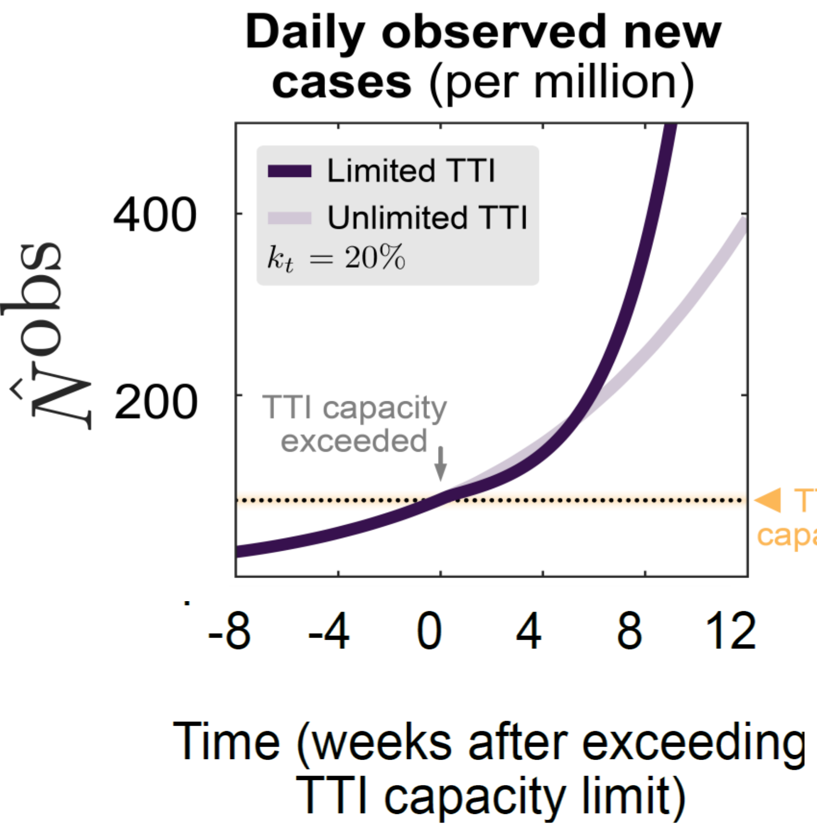


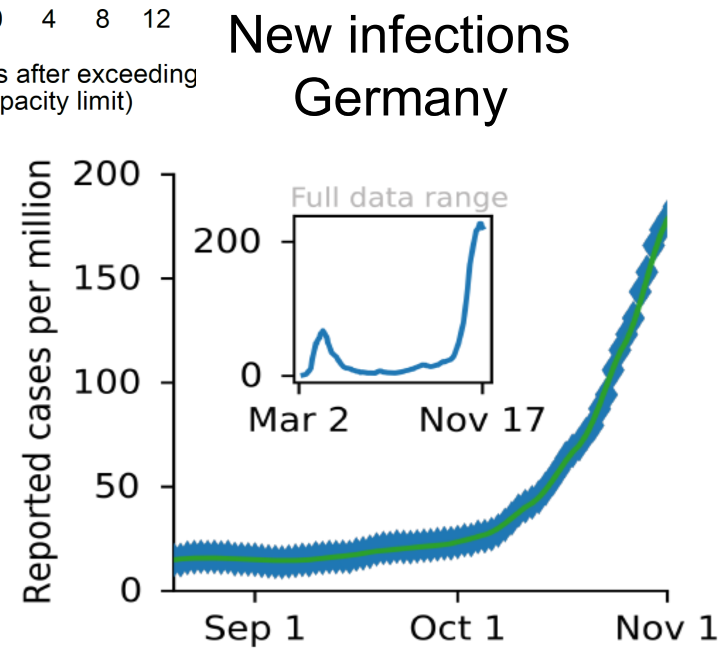
[Contreras et int., Priesemann, Science Advances, 2021]

Crossing the TTI Limit: Case numbers grow faster than exponential



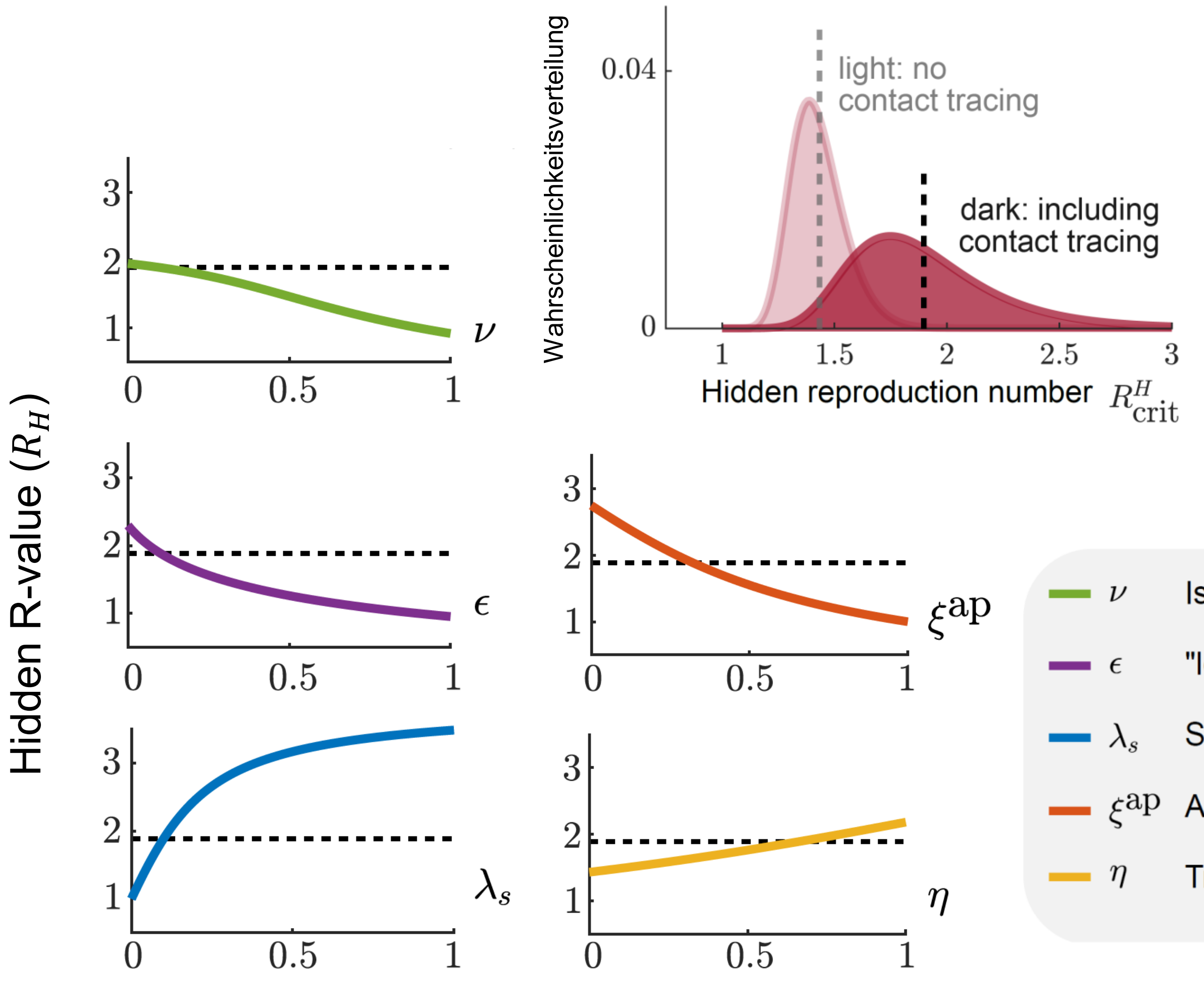


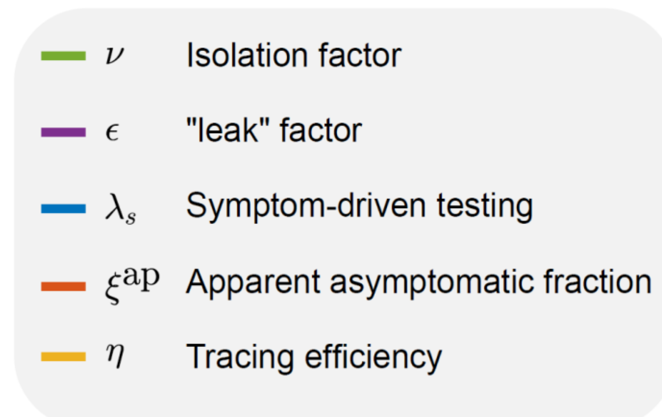


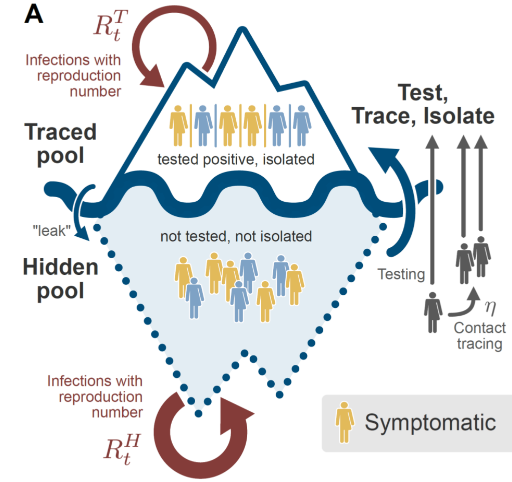


[Contreras et int., Priesemann, Nature Communications, 2021, and arxiv]

Sensitivity Analysis



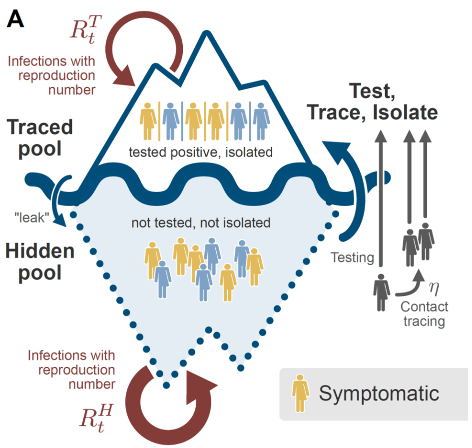


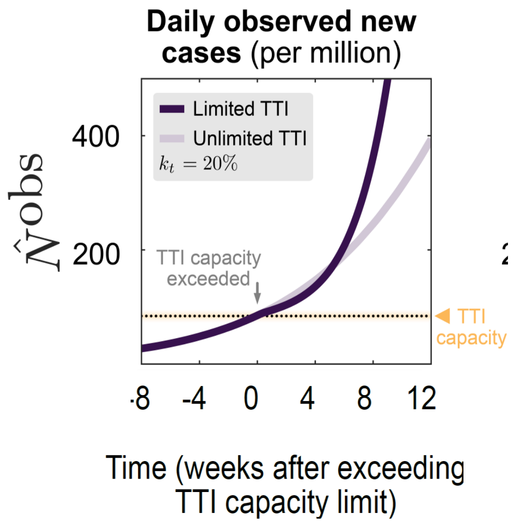


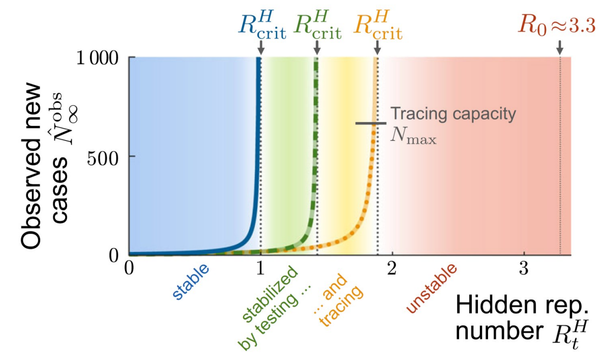
[Contreras et int., Priesemann, Nature Communications, 2021]

Summary of the TTI strategy

Test-Trace-Isolate (TTI) contributes to containing COVID-19:







The undetected cases contribute most strongly to the spread

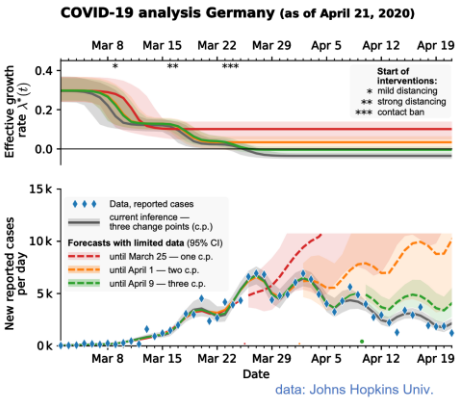
If the TTI capacity is surpassed, a tipping point is crossed, and growth self-accelerates.

TTI enables every single person to have more contacts: Instead of one, about two persons can be infected → Compensaiton by TTI.

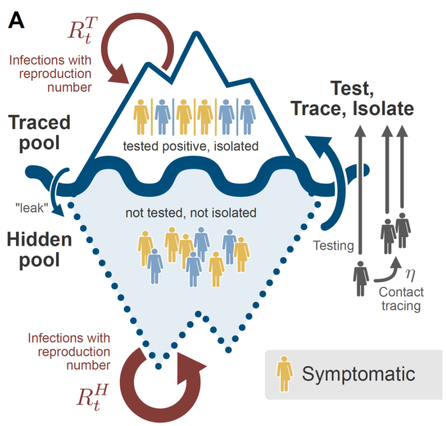
https://arxiv.org/pdf/2011.11413 [Contreras et int., Priesemann, Science Advances, 2021]
https://arxiv.org/pdf/2009.05732 [Contreras et int., Priesemann, Nature Communications, 2021]

Overview

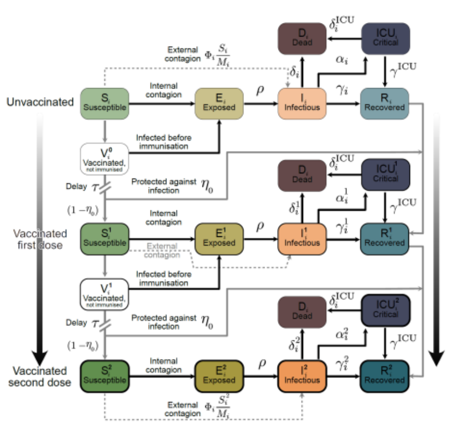
- **Quantifying the Effectiveness of COVID-19 Interventions using Bayesian Inference**
  (Dehning et int. VP, Science 2020)



- **Mitigating the Spread of COVID-19 via Test-Trace-Isolate (TTI)**
  (Contreras et int VP, Nat Commun 2021)
  (Contreras et int VP, Science Adv., 2021)



- **The Progress of Vaccination Determines the Pace to Lift Restrictions**
  (Bauer, et int VP, Plos Comp Biol., 2021)



- **Estimation of the Dark Figure**
  (Linden et int VP, Dt. Arztebl Int, 2020)

Transdisciplinary Position Papers

- → **Initiating discourse and coordinating consensus among dozens of scientists across disciplines**
  (Virology, Sociology, Epidemiology, Economy, Public Health…)
- → **Timely handling of urgent policy questions**
- → **Clear communication** of current state of knowledge *and* of uncertainty
- → Public outreach (print, radio, TV, social media)
- → Political advising
- → Expert papers: The Leopoldina, The Lancet, Zeit, SZ, FAZ, Politico […]

Published Online
December 18, 2020
https://doi.org/10.1016/
S0140-6736(20)32625-8

Calling for pan-European commitment for rapid and sustained reduction in SARS-CoV-2 infections

Across Europe, the COVID-19 pandemic is causing excess deaths, placing a burden on societies and health systems and harming the economy. European governments have yet to develop a common vision to guide the management of the pandemic. Overwhelming evidence shows that not only public health, but also society and the economy benefit greatly from reducing cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Vaccines will help control the virus, but not until late 2021.

If European governments do not act now, further waves of infection are to be expected, with consequential damage to health, society, jobs, and businesses. With open borders across Europe, a single country alone cannot keep the number of COVID-19 cases low; joint action and common goals among countries are therefore essential. We therefore call for a strong, coordinated European response and clearly defined goals for the medium and long term. Achieving and maintaining low case numbers should be the common, pan-European goal for the following reasons.

First, low case numbers save lives, and fewer people will die or suffer from long-term effects of COVID-19. In addition, medical resources will not be diverted from other patients in need.

Second, low case numbers save jobs and businesses. The economic impact of COVID-19 is driven by viral

Panel: **A joint European strategy for the COVID-19 pandemic**

1 Achieve low case numbers

(i) Aim for a target of no more than ten new COVID-19 cases per million people per day. This target has been reached in many countries, and can be reached again throughout Europe by spring, 2021, at the latest.

(ii) Take firm action to reduce case numbers quickly. Strong interventions have proven efficient and balance the rapid achievement of low case numbers against the strain on mental health and the economy.

(iii) To avoid a ping-pong effect of importing and reimporting severe acute respiratory syndrome coronavirus 2 infections, the reduction should be synchronised across all European countries and start as soon as possible. This synchronisation will allow European borders to stay open.

2 Keep case numbers low

(i) When case numbers are low, easing of restrictions is possible but should be carefully monitored. Continue and improve targeted mitigation measures, such as mask wearing, hygiene, moderate contact reduction, testing, and contact tracing.

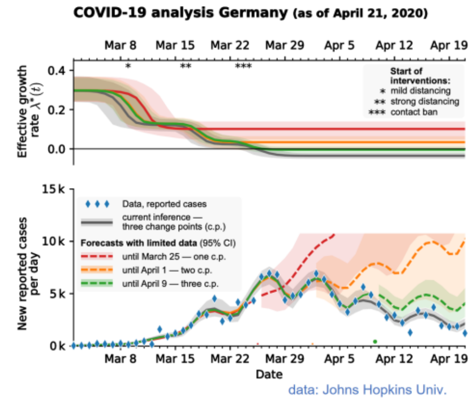
Expert Paper signed by more than 1000 European scientists.

C. Altmann, K. Becker, M. Brinkmann, S. Ciesek, C. Drosten, C. Fuest, G. Haug, M. Kleiner, H. Kroemer, R. Neugebauer, B. Prainsack, M. Stratmann, H. Streeck, L. Wieler, O. Wiestler […]

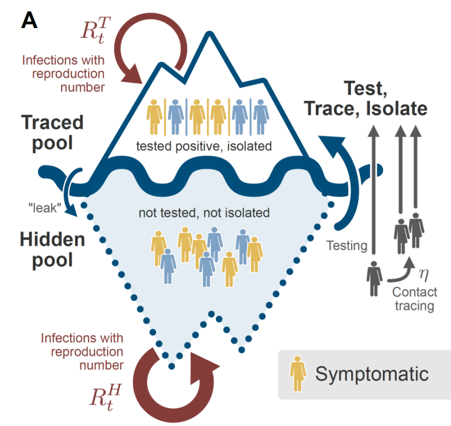
[Priesemann et al., The Lancet, 2021a,b,c] Text and Supporters https://www.containcovid-pan.eu

Overview

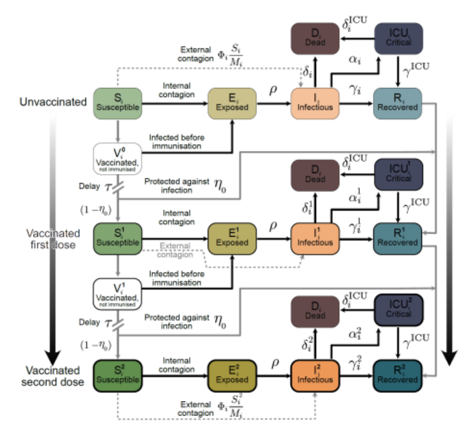
- **Inferring the Magnitude of Change Points and Interventions for the Spread of COVID-19**
  (Dehning et int. VP, Science 2020)



- **Mitigating the Spread of COVID-19 via test-trace-isolate (TTI)**
  (Contreras et int VP, Nat Commun 2021)
  (Contreras et int VP, Science Adv., 2021)



- **The progress of vaccination determines the pace to lift restrictions**
  (Bauer, et int VP, Plos Comp Biol., 2021)



- **Estimation of the Underreporting**
  (Linden et int VP, Dt. Arztebl Int, 2020)

Overview

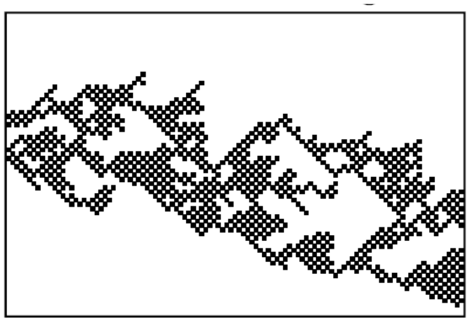
Overview

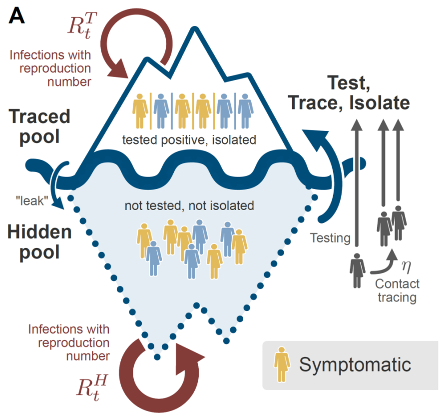
- **Subsampling Theory:** Inferring collective properties even under sparse spatial sampling
  Levina & VP, Nat Commun, 2017
  Wilting & VP, Nat Commun, 2018

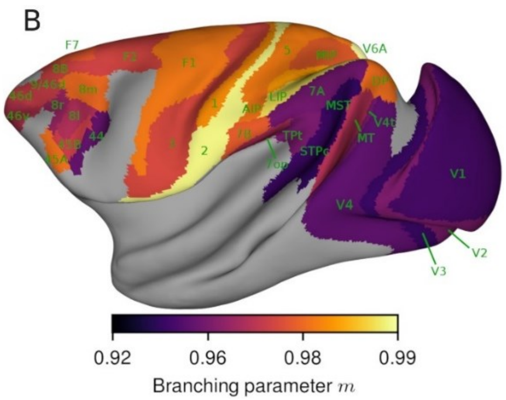
- **COVID-19 Pandemic:** Predicting future scenarios & developing mitigation strategies
  Bauer et int., Priesemann, Plos Comp Biol, 2021
  Contreras et int., VP, Nat Commun, 2021
  Contreras et int., VP, Science Adv, 2021
  Dehning et int., VP, Science, 2020
  VP et al., The Lancet, 2021a,b,c

- **Collective Computation in Living Neural Networks:** Critical phenomena, fine-tuning of computation, and clinical implications
  Cramer et int., VP. Nat Commun, 2020
  Hagemann et int., VP, Plos Comp Biol., 2021
  Zierenberg, Wilting & Priesemann, PRX, 2018

- **Research Perspective**



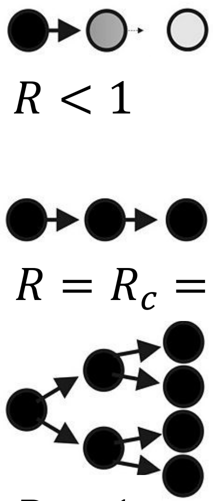




Why are we interested in branching processes?

Inferring Spreading Dynamics

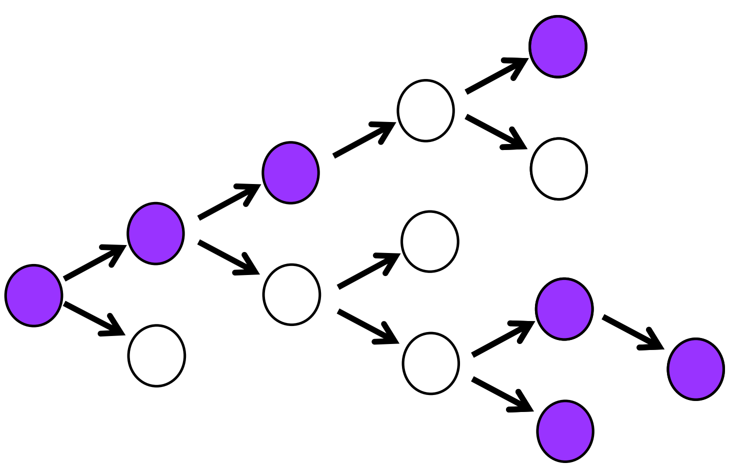
control parameter *R*
expected number of "children"



$R < 1$ subcritical

$R = R_c = 1$ critical

$R > 1$ supercritical



- ➢ returns the control parameter R, instead of a binary test for or against criticality

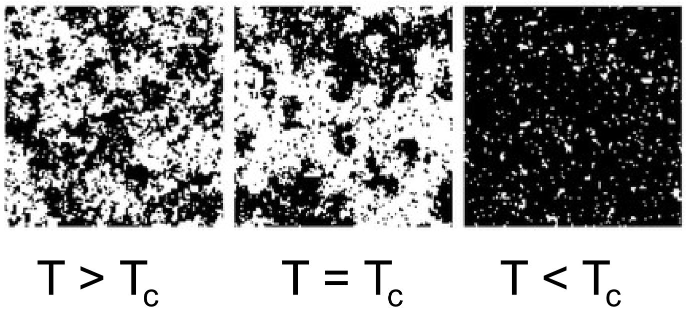
Efficient, precise, easily applicable:

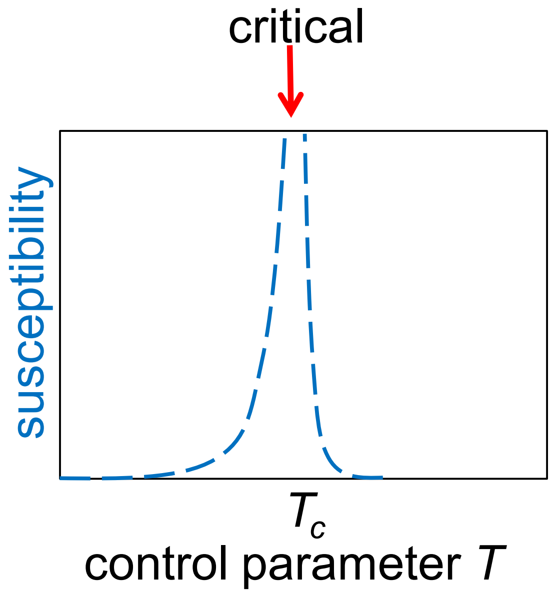
- ➢ It only requires knowing a(t), i.e. the *sampled* activity at each time step
- ➢ It does not require knowing the system size N, the number of sampled units n, or any of the moments of the process.
- ➢ Ideal conditions: Estimation of control parameter from a single unit!

Adopted by: J.Beggs, K.Hengen, C.Butfering; e.g. Ma et al., Neuron, 2019

[Dehning et int. VP, Science, 2020]
[Wilting & VP, Nature Communications, 2018]
[Levina & VP, Nature Communications, 2017]

Critical Phenomena





Ising Model

Divergence at $T = T_c$:

- Susceptibility
- Specific heat
- Correlation length

Neural Network

Control parameter: Effective coupling strength

- Sensitivity to input
- Coding space
- Long-range communication (space)
  Active memory (time)

→ Criticality can maximize information processing properties

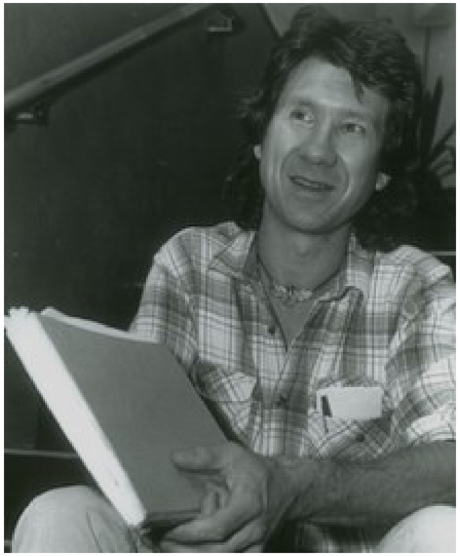
[Ising, 1924; Onsager, 1944]

Quantifying Information Processing

Chris Langton / Alain Turing

Information processing can be decomposed into:

- Transfer
- Storage
- Modification



Chris Langton

information transfer:

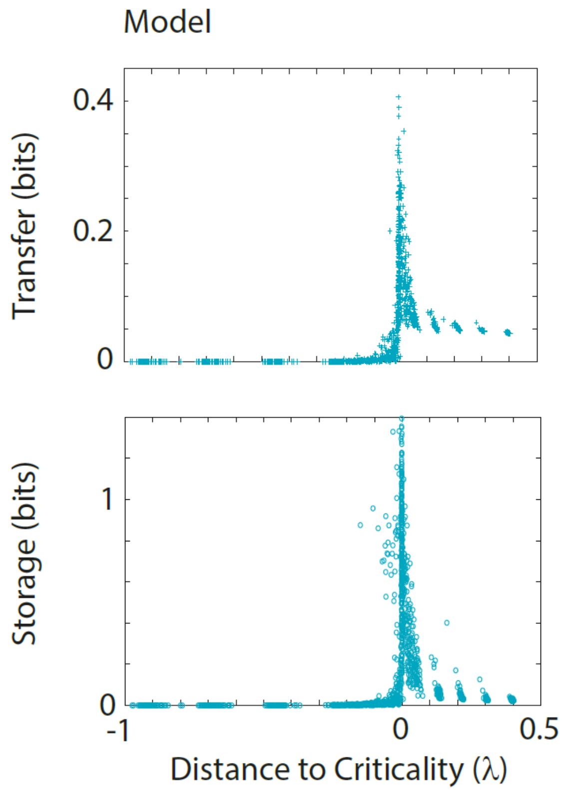
$$TE(\mathbf{X}^- \rightarrow Y^t) = I(Y^t; \mathbf{X}^- | \mathbf{Y}^-)$$

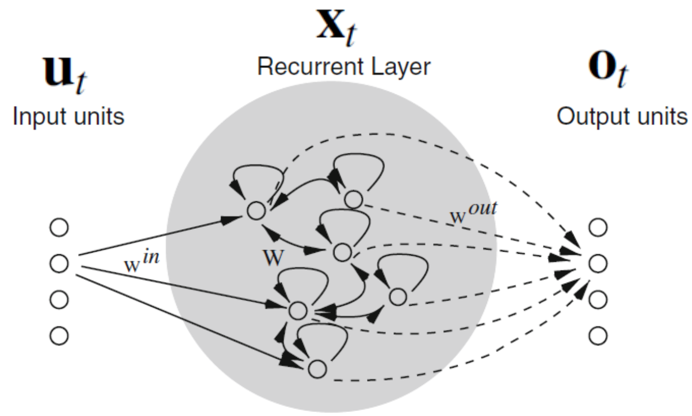
active information storage:

$$AIS(\mathbf{X}^- \rightarrow X^t) = I(X^t; \mathbf{X}^-)$$

[Langton, 1990; Lindner et al., 2011; Lizier et al., 2014; **Wibral, Lizier & VP, 2015**]

Computational Properties at Criticality





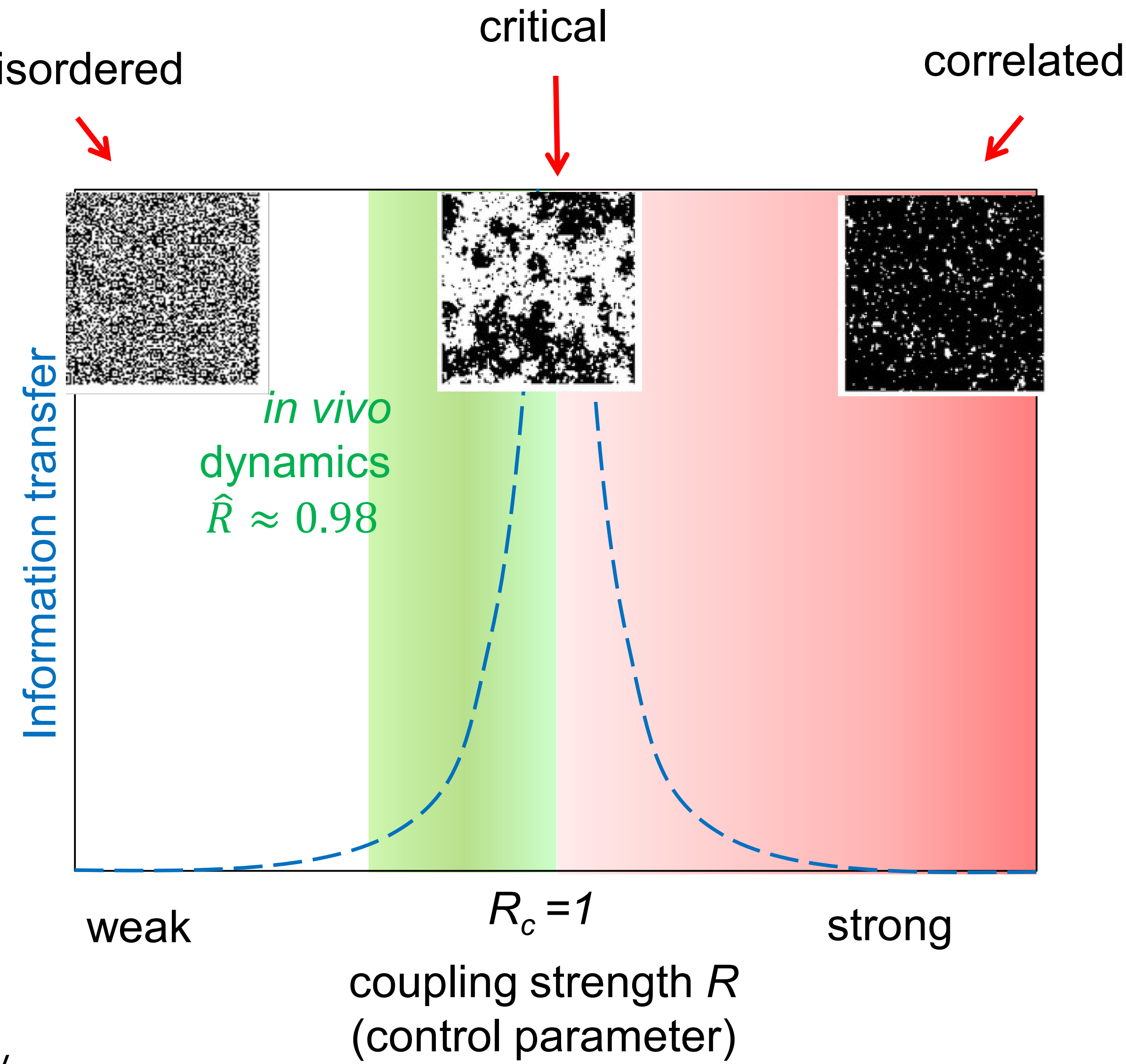
Task performance
that requires information storage
is optimal if the reservoir network
is close to a **critical state**

Crutchfield & Young, 1989, 1990
Hubermann, 1990
Langton, 1990
Li et al., 1990
Kauffmann, 1990
Arnold, 1996
Kentridge, 1997
Greenfield & Lecar, 2001
Bertschinger & Natschlaeger, 2004
Haldemann & Beggs, 2005
Kinouchi & Kopelli, 2006
Legenstein & Maass, 2007
Larremore et al., 2011a,b
Lizier et al., 2011
Shew et al., 2011
Boedecker et al., 2012
Barnett et al., 2013
Beggs & Timme, 2013
Shew & Plenz, 2013
Tomen et al., 2014
[…]

maximal entropy
minimal redundancy

strong amplification
long reverberations

instability
epilepsy



Reverberating regime in rat, cat, monkey & human:

VP et al., 2014
Wilting & VP, 2018
Wilting et al., 2018
Wilting & VP, 2019
Neto, Spitzner & VP, arxiv
Hagemann et al., 2021

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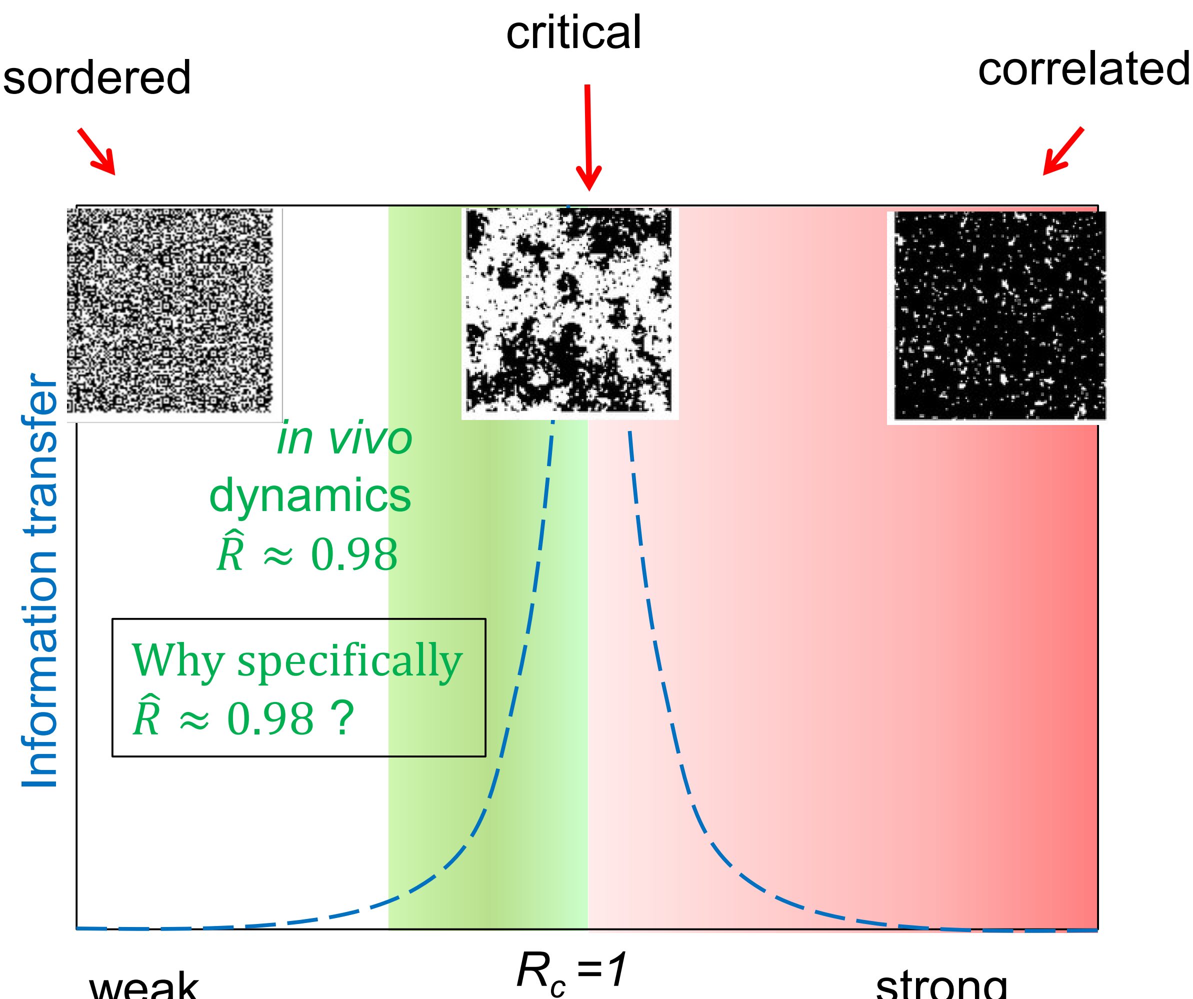

coupling strength R
(control parameter)

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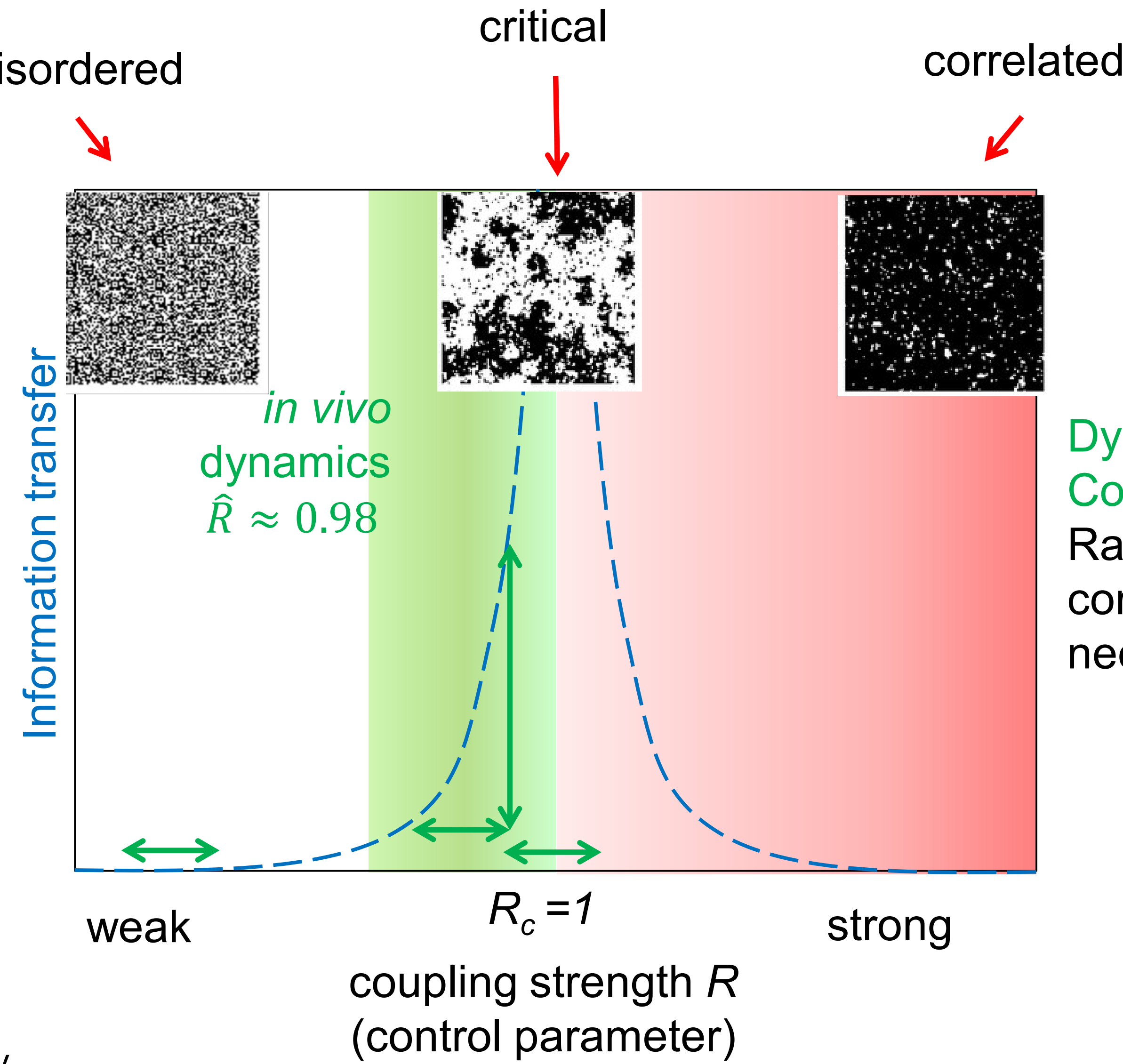

Reverberating regime in rat, cat, monkey & human:

Dynamic Computation: Rapid tuning to computational needs

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Wilting & VP, 2018
Wilting et al., 2018
Wilting & VP, 2019
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Hagemann et al., in prep

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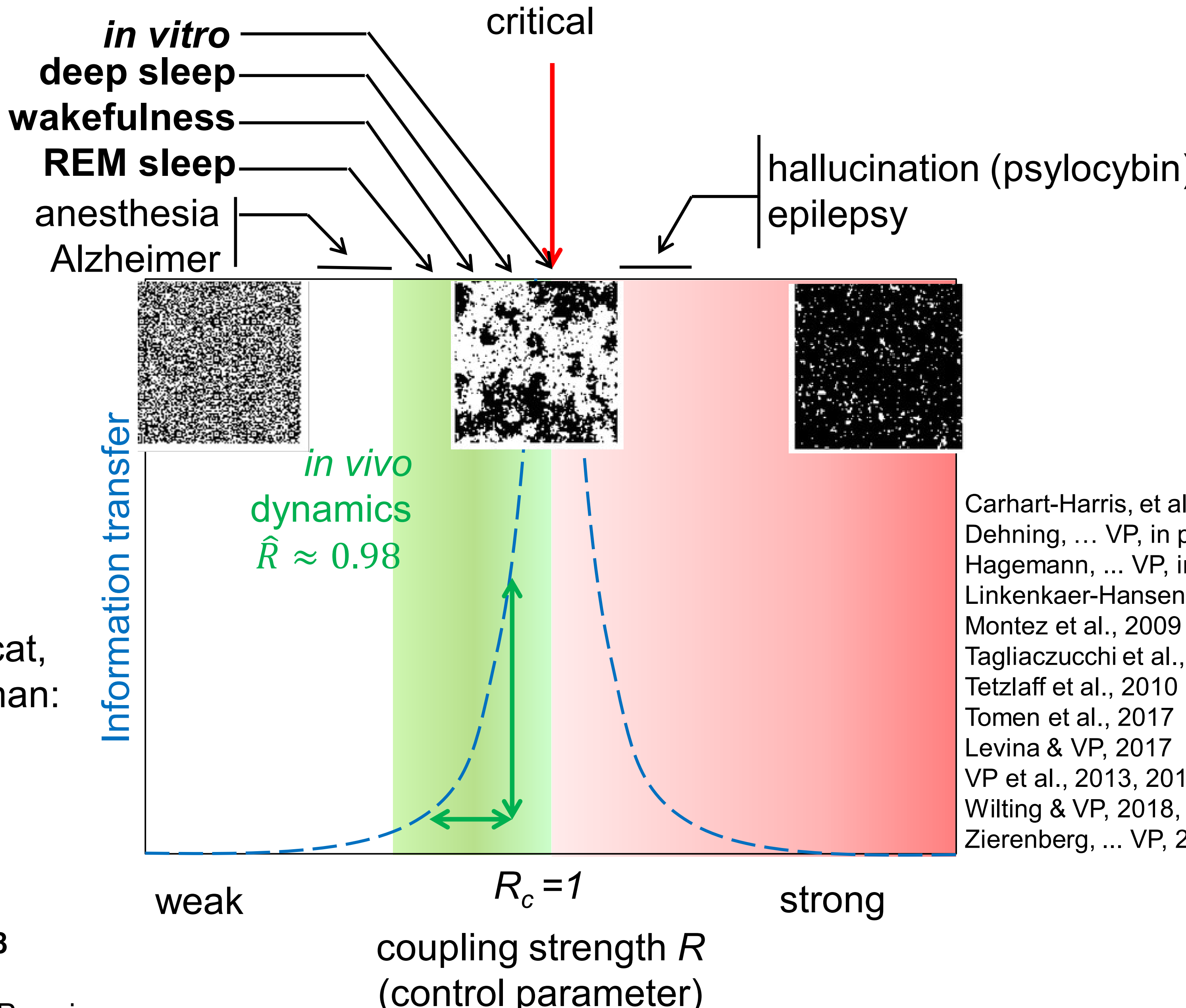

Carhart-Harris, et al., 2013
Dehning, … VP, in prep
Hagemann, ... VP, in prep
Linkenkaer-Hansen, 2001
Montez et al., 2009
Tagliaczucchi et al., 2014ff
Tetzlaff et al., 2010
Tomen et al., 2017
Levina & VP, 2017
VP et al., 2013, 2014
Wilting & VP, 2018, 2019
Zierenberg, ... VP, 2018

VP et al., 2014
Wilting & VP, 2018
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Hagemann et al., in prep

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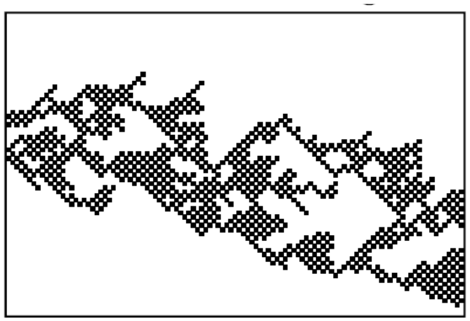

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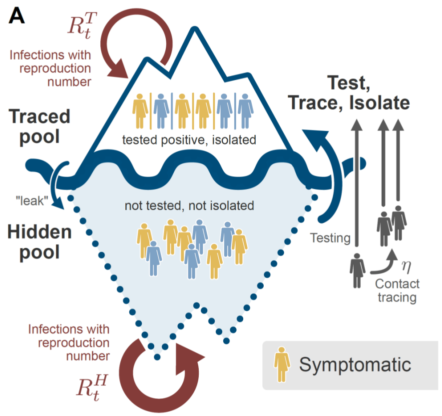

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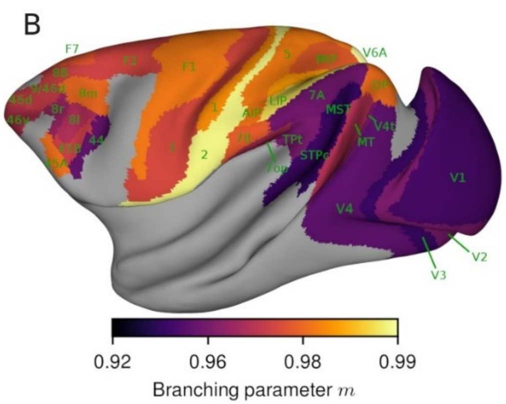
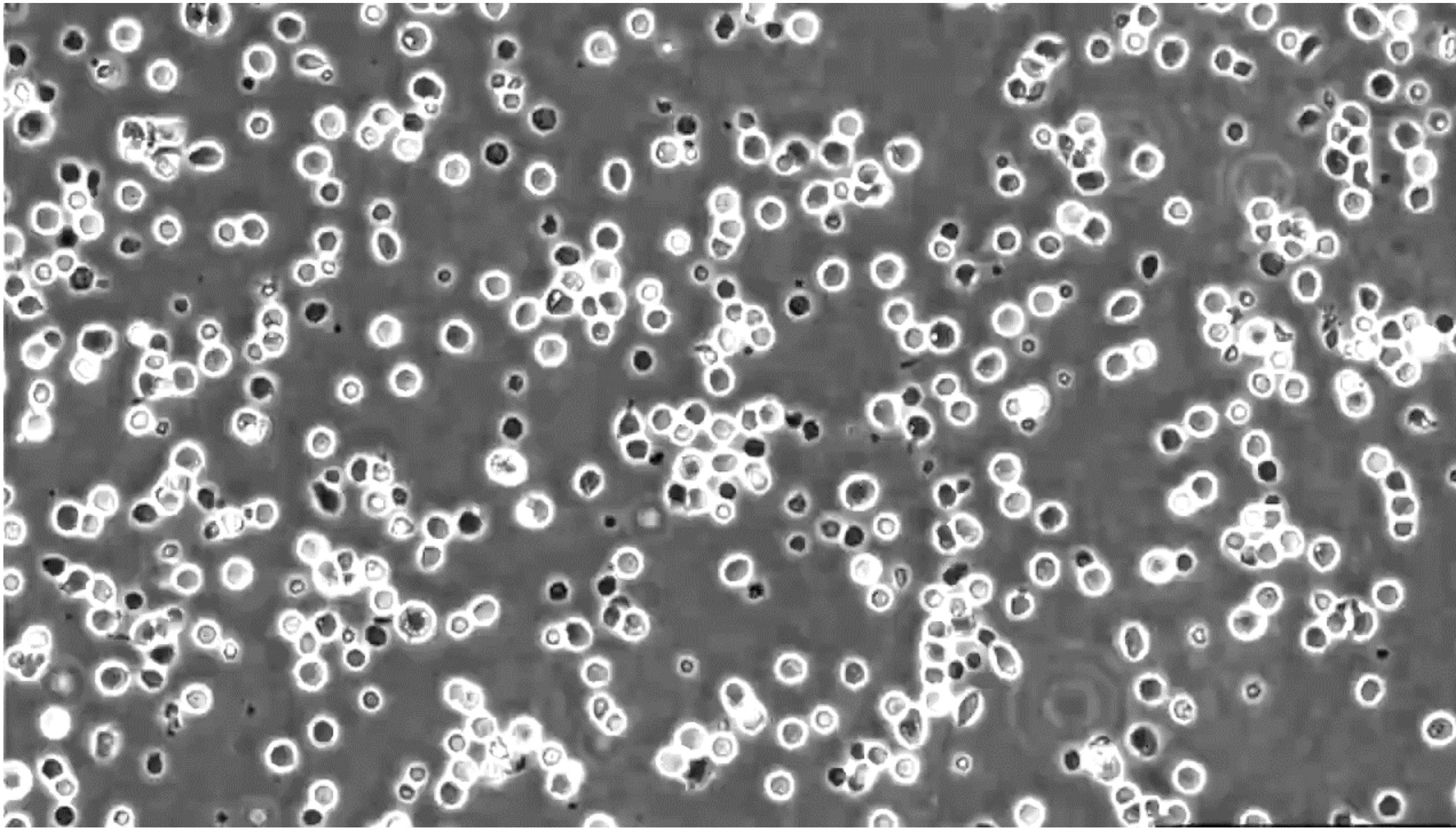


- **Self-Organization towards Criticality – or Subcriticality**
  Zierenberg, Wilting & Priesemann, PRX, 2018

Neurons forming a network *in vitro*

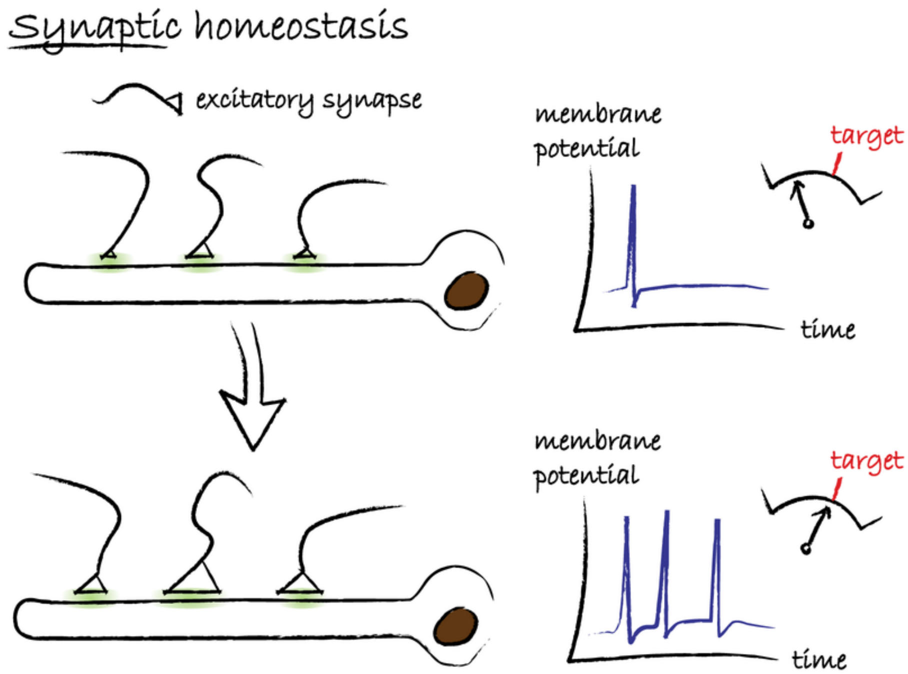


[Cellular Dynamics International]

see e.g. [Levina & VP, Nature Communications, 2017]

Homeostatic Plasticity

Homeostatic plasticity maintains a *target activity rate* $\boldsymbol{r}^*$ for each neuron by regulating the synaptic strength (or excitability) – i.e. the “coupling” $\boldsymbol{\alpha}$ between neurons.



Turrigiano & Nelson, Nat Rev Neurosci., 2004
Williams, O’Leary & Marder, Scholarpedia, 2013
Zierenberg, Wilting, VP, Phys Rev X, 2018

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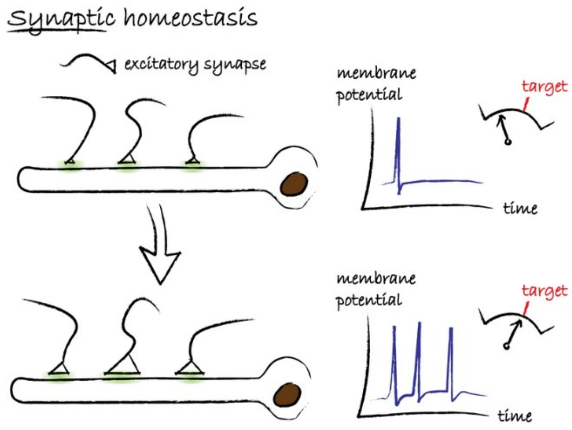


Small increase if not spiking

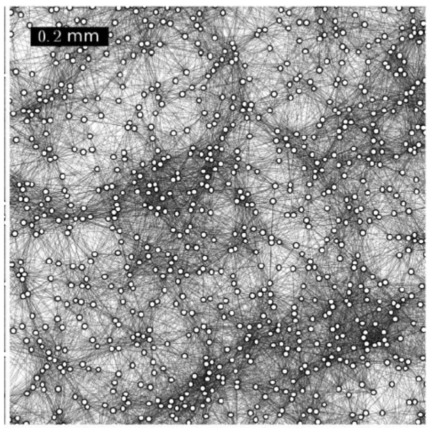
Decrease upon a spike

$$\Delta\alpha_{j,t} = (\Delta t\, r_j^* - s_{j,t})\left(\frac{\Delta t}{\tau_{\mathrm{hp}}}\right)$$

Change in incoming exc. synaptic strength

Very slow timescale

Topology

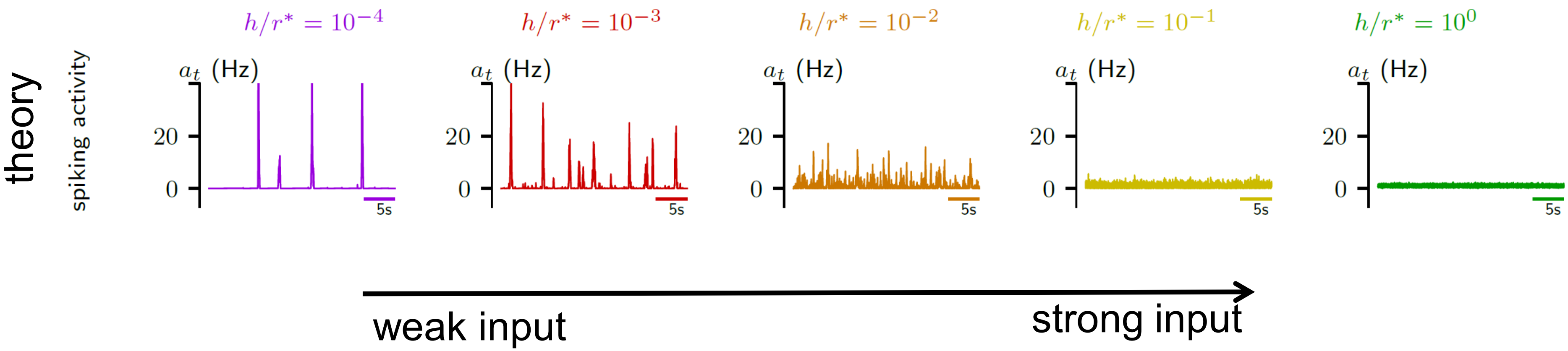


Advantages:

- Only *local information* required
- No "*memorization*" of past spiking required
- Different target rates *r** for each neuron j can be implemented

Turrigiano & Nelson, Nat Rev Neurosci., 2004
Williams, O'Leary & Marder, Scholarpedia, 2013
Zierenberg, Wilting, VP, Phys Rev X, 2018

From Collective Dynamics to Computation



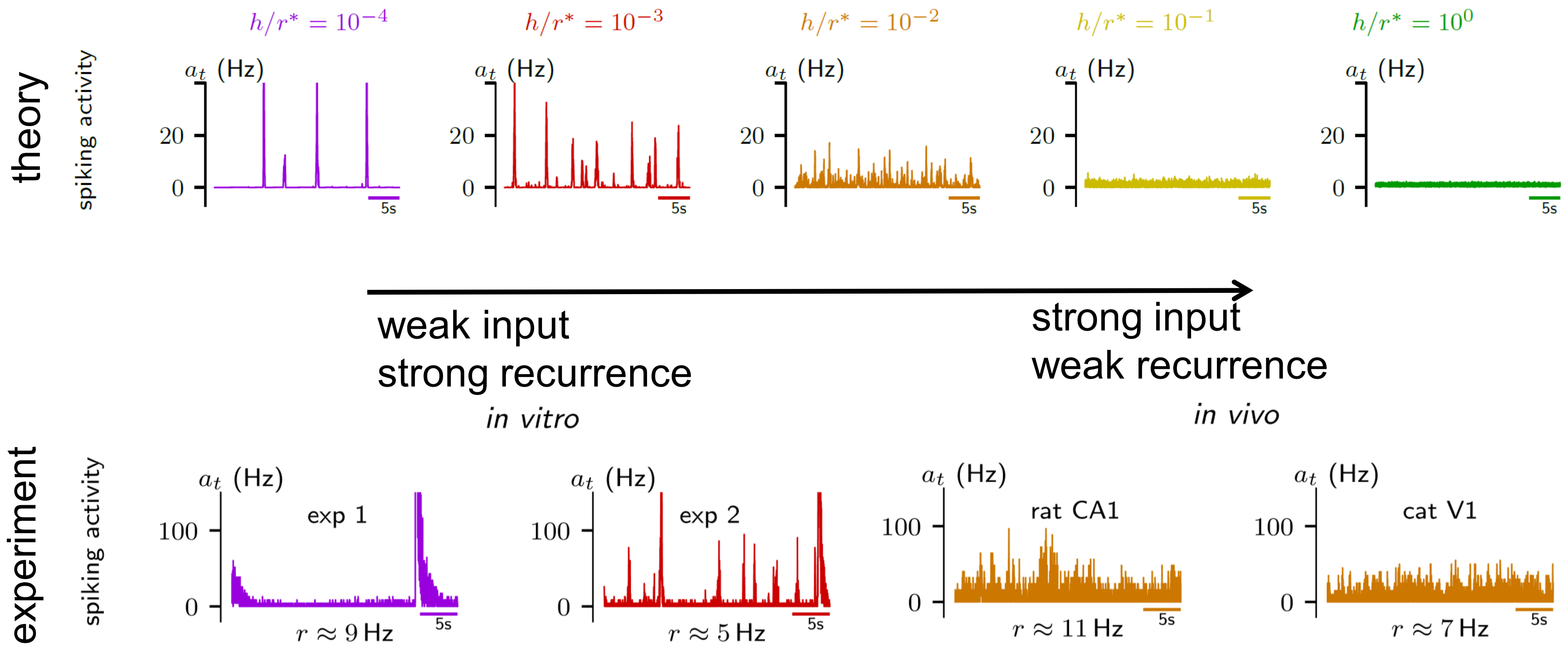
Long intrinsic timescales
Long “active memory”
High variability
Stronger “recurrence”

Short intrinsic timescales
Fast “forgetting”
Less variability
Closely mirroring input

Under homeostatic plasticity, **the input strength** changes collective dynamics, functional recurrence *R* and hence abstract computational properties.
→ Making use of this in generic tasks!

[Zierenberg, Wilting & Priesemann, Phys Rev X, 2018]
[Cramer et int., Priesemann, Nature Communications, 2020]

Increasing input strength abolishes bursts under homeostatic plasticity



Under homeostatic plasticity, **the input strength** becomes the **control parameter.**
Differences of input strength can explain the emergence of bursts *in vitro.*

[Zierenberg, Wilting & Priesemann, Phys Rev X, 2018]
[Cramer et int., Priesemann, Nature Communications, 2020]

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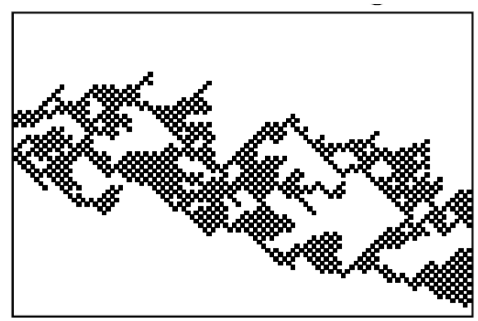
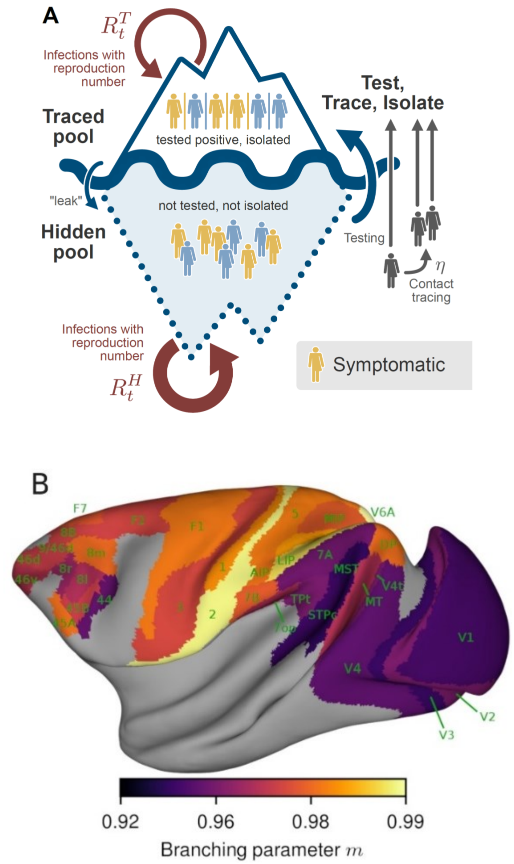
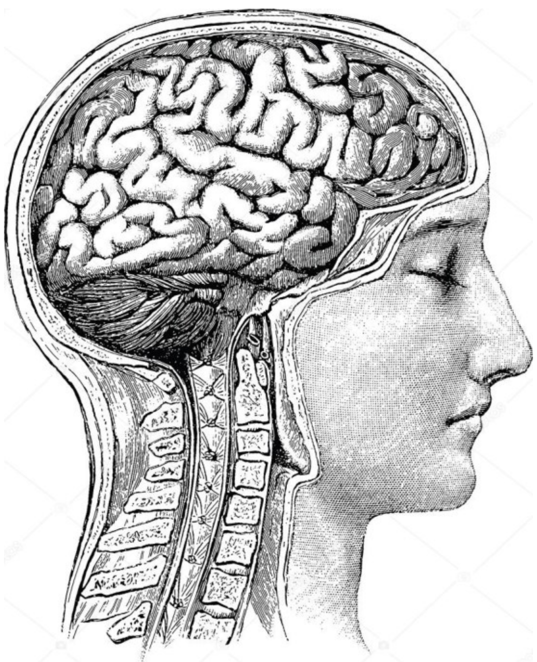
  Zierenberg, Wilting & Priesemann, PRX, 2018





Research Perspective



Self-Organization of Living Neural Networks

- "Infogenesis"
- Learning
- Information Flow
- Spreading Dynamics

Pandemic – Infodemic

- Entangled Spread of Information and Disease
- Self-Regulation and Self-Stabilization

Goals

- Energy-efficient, living future AI
- Self-regulation of neural networks and its pathology
- Pandemic and crisis preparedness

→ PostDoc Position

Levina & Priesemann, Nature Communications, 2017
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Contreras et int., Priesemann, Nature Communications, 2021
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Image: unorobus.gmail.com, ID:106167644

Thank you!

Priesemann Group
Simon Bauer
Sebastian Contreras
Jonas Dehning
David Ehrlich
Daniel Gonzalez Marx
Kira Herff
Emil Iftekhar
Matthias Linden
Matthias Loidolt
Fabian Mikulasch
Sebastian Mohr
Joao Neto
Valentin Neuhaus
Lucas Rudelt
Alexander Schmidt
Andreas Schneider
Julian Schulz
Paul Spitzner
Patrick Vogt
Johannes Zierenberg

MAX-PLANCK-GESELLSCHAFT

COVID-19 Expert Consortium
of the Göttingen Campus and beyond:
Heike Bickeböller, Philip Bittihn, Eberhard Bodenschatz, Wolfgang Brück, Alexander Ecker, Andreas Leha, Theo Geisel, Ramin Golestanian, Helmut Grubmüller, Stephan Herminghaus, Gerald Haug, Reinhard Jahn, Jürgen Jost, Norbert Lossau, Vladimir Zykov, Michael Meyer-Hermann, Iris Pigeot, Simone Scheithauer, Anita Schöbel, Fredi Schüth,
Michael Wibral & Michael Wilczek

bccn göttingen

GIF
German-Israeli Foundation for Scientific Research and Development

External PhD students (co-supervised)
Benjamin Cramer (U Heidelberg)
Madhura Ketkar (ENI Göttingen)
Corentin Nelias (MPI-DS)

egePan Unimed

SPP 2205
Evolutionary optimization of neuronal processing

Alumni
Bruno del Papa (MERK)
Jan Geisler (Max Planck School)
Bettina Royen (Max Planck School)
Jorge de Heuvel (U Mainz)
Annika Hagemann (Bosch)
Helge Heuer (U Göttingen)
Leonhard Leppin (MPI Garching)
Jens Wilting (Bosch)
Matthias Loidolt (Oxford)
Henrik von der Emde (Cambridge)
Mathias Sogorski (PSI, Berlin)
Moritz Layer (Cambridge)
Victor Brasch (EPFL)

MBExC Multiscale Bioimaging

P2M Physics-to-Medicine

SFB 1286
Quantitative Synaptology

Bundesministerium für Bildung und Forschung