HETEROGENEITY AND STOCHASTICITY OF DISEASE SPREAD

Antoine Allard

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The COVID-19 pandemic brought to the public eye the role mathematical models play in infectious disease epidemiology :

- generate forecast;
- estimate the effectiveness of non-pharmaceutical interventions (NPIs);
- understand the underlying factors influencing the spread of the virus.



Lockdown professor steps down after breaking rules to meet married lover



ledevoir.com

Voir par-delà le sommet de la courbe

Alexis Riopel

theguardian.com

Coronavirus exposes the problems and pitfalls of modelling

lan Sample



Julien Arino, Marc Brisson, Caroline Colijn et Mathieu Maheu-Giroux

Les travaux de dizaines de modélisateurs ont permis aux autorités de mesurer l'effet potentiel des diverses mesures sanitaires mises en place pour contrer la COVID-19. À titre de représentants de leur spécialité, quatre d'entre eux se partagent le prix du Scientifique de l'année 2020 de Radio-Canada : Julien Arino, de l'Université du Manitoba; Marc Brisson, de l'Université Laval; Caroline Colijn, de l'Université Simon Fraser, en Colombie-Britannique; et Mathieu Maheu-Giroux, de l'Université McGill.

Lire l'article détaillé





Background in mathematical modeling in epidemiology...



BC Centre for Disease Control

J. Math. Biol. (2014) 69:1627–1660 DOI 10.1007/s00285-013-0744-9

Mathematical Biology

Spreading dynamics on complex networks: a general stochastic approach

Pierre-André Noël · Antoine Allard Laurent Hébert-Dufresne · Vincent Marceau · Louis J. Dubé

Asymmetric percolation drives a double transition in sexual contact networks

ntoine Allard^a, Benjamin M. Althouse^{b,c,d}, Samuel V. Scarpino^{e,f}, and Laurent Hébert-Dufresne^{b,g,h,1} e de Recerca Matemàtica, E-08193 Bellaterra (Barcelona). Spain; ^bInstitute for Disease Modeling, Bellevue, WA 98005; ^cInformation School, University ihington, Seattle, WA 98105; "Department of Biology, New Mexico State University, Las Cruces, NM 88003; "Department of Mathematics and cs, University of Vermont, Burlington, VT 05405; ^cComplex Systems Center, University of Vermont, Burlington, VT 05405; ^oSanta Fe Institute, Santa I 87501; and ^hDepartment of Computer Science, University of Vermont, Burlington, VT 05405 ntre de Recerca Ma

nature

physics

SANG Edited by Burton H. Singer, University of Florida, Gainesville, FL, and approved July 10, 2017 (received for review February 22, 2017)



SCIENTIFIC

LETTERS

disease transmission

PUBLISHED ONLINE: 1 AUGUST 2016 | DOI: 10.1038/NPHYS3832

The effect of a prudent adaptive behaviour on

Samuel V. Scarpino^{1,2*}. Antoine Allard³ and Laurent Hébert-Dufresne¹

Propagation dynamics on networks featuring complex topologies

Laurent Hébert-Dufresne, Pierre-André Noël, Vincent Marceau, Antoine Allard, and Louis J. Dubé

PHYSICAL REVIEW E 84, 026105 (2011)

Modeling the dynamical interaction between epidemics on overlay networks

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OPEN Global efficiency of local immunization

Adaptive networks: Coevolution of disease and topology

Vincent Marceau, Pierre-André Noël, Laurent Hébert-Dufresne, Antoine Allard, and Louis J. Dubé

RESEARCH ARTICLE The risk of sustained sexual transmission of Zika is underestimated

Antoine Allard¹, Benjamin M. Althouse^{2,3,4}, Laurent Hébert-Dufresne^{2,5,6}, Samuel V. Scarpino⁷



Robert Smith? University of Ottawa Pres

PHYSICAL REVIEW E 79, 036113 (2009)

Heterogeneous bond percolation on multitype networks with an application to epidemic dynamics

Antoine Allard, Pierre-André Noël, and Louis J. Dubé Département de physique, de génie physique et d'optique, Université Laval, Québec, Québec, Canada GIV 0A6

Babak Pourbohloul University of British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada V5Z 4R4 and, School of Population & Public Health, University of British Columbia, Vancouver, British Columbia, Canada V6T 1Z3





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SANC

The effect of a prudent adaptive behaviour on disease transmission

Samuel V. Scarpino^{1,2*}. Antoine Allard³ and Laurent Hébert-Dufresne¹

... and then January 2020 came along.

statnews.com

Cause of Wuhan's mysterious pneumonia cases still unknown, Chinese officials say

By Helen Branswell Jan. 5. 2020

Notes from the Field

A Novel Coronavirus Genome Identified in a Cluster of Pneumonia Cases — Wuhan, China 2019–2020

Wenjie Tan^{1,2,#}; Xiang Zhao¹; Xuejun Ma¹; Wenling Wang¹; Peihua Niu¹; Wenbo Xu¹; George F. Gao¹; Guizhen Wu^{1,2,}

WHO Statement regarding cluster of pneumonia cases in Wuhan, China

9 January 2020 | Statement | China

SCIENCEINSIDER

Novel human virus? Pneumonia cases linked to seafood market in China stir concern

The health department of Wuhan initially reported 27 cases, but the tally stands at 59 as of 6 January

3 JAN 2020 · BY DENNIS NORMILE



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The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

A Novel Coronavirus from Patients with Pneumonia in China, 2019

Na Zhu, Ph.D., Dingyu Zhang, M.D., Wenling Wang, Ph.D., Xingwang Li, M.D., Bo Yang, M.S., Jingdong Song, Ph.D., Xiang Zhao, Ph.D., Baoying Huang, Ph.D., Weifeng Shi, Ph.D., Roujian Lu, M.D., Peihua Niu, Ph.D., Faxian Zhan, Ph.D., Xuejun Ma, Ph.D., Dayan Wang, Ph.D., Wenbo Xu, M.D., Guizhen Wu, M.D., George F. Gao, D.Phil., and Wenjie Tan, M.D., Ph.D., for the China Novel Coronavirus Investigating and Research Team

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Babak Pourbohloul University of British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada V5Z 4R4 and, School of Population & Public Health, University of British Columbia, Vancouver, British Columbia, Canada V6T 123

cbc.ca

Previously unknown virus may be causing pneumonia outbreak in China, WHO says | CBC News

Thomson Reuters · Posted: Jan 09, 2020 11:27 AM ET I Last Updated: January 9. 2020

China CDC Weekly



COMMENTARY

MEDICAL VIROLOGY WILEY

Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle

Hongzhou Lu¹ | Charles W. Stratton² | Yi-Wei Tang³









Outline :

- 1. Basic epidemiological models.
- 2. How COVID-19 challenges some assumptions made by "traditional" models.
- 3. Contact network epidemiology (CNE).
- 4. How COVID-19 allows CNE to shine, and what can we learn from it.









Main epidemiological assumptions

- the disease results either in complete immunity or death (SIR)
- the disease is not fatal and conveys no immunity (SIS)
- all individuals are equally susceptible

Main *structural* assumptions

- the disease is transmitted in a closed population
- contacts occur according to the law of mass-action
- the population is large enough to justify a deterministic analysis







Susceptible-Infected-Susceptible (SIS) dynamics

- the disease is not fatal and conveys no immunity
- -S: fraction of the pop. susceptible to the disease
- I : fraction of the pop. infected by the disease
- susceptible and infected individuals come into contact at a rate $\propto SI$ (mass-action assumption)

$$\frac{dS}{dt} = -\beta SI + \alpha I \qquad \qquad \frac{dI}{dt} = \beta SI - \alpha I$$

a trajectory

$$I(t) = \frac{I^*}{1 - (1 - I^*/I(0))e^{(1 - R_0)\alpha t}}$$

settles to

$$I^* = \begin{cases} 0 & \text{if } R_0 < 1\\ 1 - \frac{1}{R_0} & \text{if } R_0 > 1 \end{cases}$$

with $R_0 = \beta/\alpha$ being the basic reproduction number (expected number of secondary cases directly caused by one case in an otherwise fully susceptible population)







Susceptible-Infected-Recovered (SIR) dynamics

- the disease results either in complete immunity or death
- -S: fraction of the pop. susceptible to the disease
- I: fraction of the pop. infected by the disease
- -R: fraction of the pop. having recovered from the disease
- susceptible and infected individuals come into contact at a rate $\propto SI$ (mass-action assumption)

$$\frac{dS}{dt} = -\beta SI \qquad \qquad \frac{dI}{dt} = \beta SI - \alpha I \qquad \qquad \frac{dI}{dt} = \alpha I$$

- the fraction of the population who will be infected by the disease eventually is a solution of

$$R(\infty) = 1 - S(0)e^{-R_0(R(\infty) - R(0))} \simeq 1 - e^{-R_0R(\infty)}$$

with $R_0 = \beta/\alpha$ being the basic reproduction number

- there will be an epidemic wave if $R_0 > 1$, otherwise the outbreak will die out
- there is herd immunity if a fraction $1 1/R_0$ of the population is already immune









Models used in more realistic settings are more complex, but the basic ingredients remain largely the same.

COVID-19 Scenario Projections: The Emergence of Omicron in the US – January 2022





Potential for large outbreaks of Ebola virus disease

A. Camacho^{a,*,1}, A.J. Kucharski^{a,**,1}, S. Funk^a, J. Breman^b, P. Piot^c, W.J. Edmunds^a



Data-driven model for the assessment of Mycobacterium tuberculosis transmission in evolving demographic structures

Sergio Arregui^{a,b,1}, María José Iglesias^{c,d}, Sofía Samper^{d,e}, Dessislava Marinova^{c,d}, Carlos Martin^{c,d,f}, Joaquín Sanz^{g,h,2}, and Yamir Moreno^{a,b,i,1,2}

^aInstitute for Biocomputation and Physics of Complex Systems, University of Zaragoza, 50018 Zaragoza, Spain; ^bDepartment of Theoretical Physics, University of Zaragoza, 50009 Zaragoza, Spain; ^cDepartment of Microbiology, Faculty of Medicine, University of Zaragoza, 50009 Zaragoza, Spain; ^dCentro de Investigación Biomédica en red Enfermedades Respiratorias (CIBER), Carlos III Health Institute, 28029 Madrid, Spain; ^eInstituto Aragonés de Ciencias de la Salud, Instituto de Investigación Sanitaria (IIS) Aragon, 50009 Zaragoza, Spain; [†]Service of Microbiology, Miguel Servet Hospital, Instituto de la Salud, Instituto de Investigación Sanitaria (IIS) Aragon, 50009 Zaragoza, Spain; [†]Service of Microbiology, Miguel Servet Hospital, Instituto de restigación Sanitaria (IIS) Áragon, 50009 Zaragoza, Spain; 9 Department of Genetics, Sainte-Justine Hospital Research Centre, Montreal, QC H3T1C5, Canada; hDepartment of Biochemistry, Faculty of Medicine, University of Montreal, Montreal, QC H3T1J4, Canada; and Institute for Scientific Interchance Foundation, 10126 Turin, Italy







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Challenged assumption #1 : contacts occur according to the law of mass-action

* many outbreaks are not shaped by the "average" individuals but rather by a minority of superspreading events



Superspreading and the effect of individual variation on disease emergence

J. O. Lloyd-Smith^{1,2}, S. J. Schreiber³, P. E. Kopp⁴ & W. M. Getz¹

Spatial and temporal dynamics of superspreading events in the 2014–2015 West Africa Ebola epidemic

Max S. Y. Lau^{a,1}, Benjamin Douglas Dalziel^{b,c}, Sebastian Funk^d, Amanda McClelland^e, Amanda Tiffany^f, Steven Riley^g, C. Jessica E. Metcalf^a, and Bryan T. Grenfell^{a,h}

^aDepartment of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544; ^bDepartment of Integrative Biology, Oregon State University, Corvallis, OR 97331; ^cDepartment of Mathematics, Oregon State University, Corvallis, OR 97331; ^dCentre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine, London WC1E 7HT, United Kingdom; eInternational Federation of Red Cross and Red Crescent Societies, CH-1211 Geneva 19, Switzerland; ^fEpicentre, CH-1211 Geneva 6, Switzerland; ⁹Medical Research Council Centre for Outbreak Analysis and Modelling, Department Infectious Disease Epidemiology, Imperial College London, London SW7 2AZ, United Kingdom; and ^hFogarty International Center, National Institutes of Health, Bethesda, MD 20892

THE LANCET

CORRESPONDENCE | VOLUME 395, ISSUE 10227, E47, MARCH 14, 2020

Secondary attack rate and superspreading events for SARS-CoV-2

Yang Liu • Rosalind M Eggo • Adam J Kucharski

THE LANCET Infectious Diseases

COMMENT | VOLUME 21, ISSUE 9, P1203-1204, SEPTEMBER 01, 2021

Understanding why superspreading drives the COVID-19 pandemic but not the H1N1 pandemic

Paul Z Chen Marion Koopmans David N Fisman Frank X Gu

SCIENTIFIC AMERICAN.

How 'Superspreading' Events Drive Most COVID-19 Spread

As few as 10 percent of infected people may drive a whopping 80 percent of cases in specific types of situations

By Christie As



Available online at www.sciencedirect.com science



Journal of Theoretical Biology 232 (2005) 71-81

Network theory and SARS: predicting outbreak diversity

Lauren Ancel Meyers^{a,b,*,1}, Babak Pourbohloul^{c,1,2}, M.E.J. Newman^{b,d} Danuta M. Skowronski^{c,2}. Robert C. Brunham^{c,2}





Challenged assumption #2 : the population is large enough to justify a deterministic analysis

 \star at the early stage, the outcome of an outbreak depends on stochastic events





Available online at www.sciencedirect.com SCIENCE Journal of Theoretical Biology 232 (2005) 71-81



www.elsevier.com/locate/yjtbi

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PLOS BIOLOGY

ESSAY

Superspreading events in the transmission dynamics of SARS-CoV-2: Opportunities for interventions and control

Benjamin M. Althouse^{1,2,3©}*, Edward A. Wenger^{1©}, Joel C. Miller®⁴, Samuel V. Scarpino®^{5,6,7,8,9,10}, Antoine Allard®^{11,12}, Laurent Hébert-Dufresne^{11,13,14}, Hao Hu^{15©}

Main ideas :

- takes into account the contact network between individuals.
- infectious disease transmitted from an infected individual to their susceptible neighbors in the contact network.
- the structure of this contact network shapes the spreading dynamics.

Mathematical abstraction :

- nodes (vertices) : individuals
- links (edges) : (potential) disease-causing contacts between two individuals
- network (graph) : contact network of a population



Modelling disease outbreaks in realistic urban social networks

Stephen Eubank 🖾, Hasan Guclu, V. S. Anil Kumar, Madhav V. Marathe, Aravind Srinivasan, Zoltár Toroczkai & Nan Wang

Nature 429, 180-184 (2004)

BULLETIN (New Series) OF THE AMERICAN MATHEMATICAL SOCIETY Volume 44, Number 1, January 2007, Pages 63–86 S 0273-0979(06)01148-7 Article electronically published on October 17, 200

CONTACT NETWORK EPIDEMIOLOGY: BOND PERCOLATION APPLIED TO INFECTIOUS DISEASE PREDICTION AND CONTROL

LAUREN ANCEL MEYERS

lisciplinary Perspectives on Infectious Disease Volume 2011, Article ID 284909, 28 pages doi:10.1155/2011/284909

Review Article Networks and the Epidemiology of Infectious Disease

> Leon Danon,¹ Ashley P. Ford,² Thomas House,³ Chris P. Jewell,² Matt J. Keeling,¹, Gareth O. Roberts.² Joshua V. Ross.⁴ and Matthew C. Vernon







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Epidemic percolation networks (EPNs) :

- previous slide : stochastic process is taking place on the contact network to produce an outcome
- EPNs : consider an ensemble of random networks encoding all possible outcomes
 - \rightarrow links indicate contacts that will transmit the disease
- \Rightarrow studying the EPNs random network ensemble becomes equivalent to studying the spreading dynamics



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Probability generating functions (PGFs)

- a PGF is a formal power series whose coefficients are a probability mass function $\{a_n\}_{n\geq 0}$

$$A(x) = \sum_{n \ge 0}^{\infty} a_n x^n = a_0 + a_1 x + a_2 x^2 + a_3 x^3 + \dots$$

computing the moments

$$A(1) = \sum_{n \ge 0}^{\infty} a_n = 1; \qquad \langle n \rangle = \sum_{n \ge 0}^{\infty} n \, a_n = \left. \frac{dA(x)}{dx} \right|_{x=1} = A'(1); \qquad \langle n^p \rangle = \sum_{n \ge 0}^{\infty} n^p \, a_n = \left(x \frac{d}{dx} \right)^p A(x) \right|_{x=1}$$

extracting the coefficients

$$a_n = \frac{1}{n!} \left. \frac{d^n A(x)}{dx^n} \right|_{x=0} = \frac{1}{2\pi} \int_0^{2\pi} A(e^{i\theta}) e^{-in\theta} d\theta$$

sum of a fix/random number of variables drawn independently

$$B_2^{\text{fix}}(x) = \sum_{l \ge 0} b_l x^l = \sum_{l \ge 0} \sum_{n=0}^l a_n a_{l-n} x^l = \sum_{n \ge 0}^\infty a_n x^n \sum_{m \ge 0}^\infty a_m x^m = [A(x)]^2; \qquad B_p^{\text{fix}}(x) = [A(x)]^p; \qquad C^{\text{rand}}(x) = \sum_{n \ge 0}^\infty a_n [A(x)]^2; \qquad B_p^{\text{fix}}(x) = [A(x)]^p; \qquad C^{\text{rand}}(x) = \sum_{n \ge 0}^\infty a_n [A(x)]^2; \qquad B_p^{\text{fix}}(x) = [A(x)]^p; \qquad C^{\text{rand}}(x) = \sum_{n \ge 0}^\infty a_n [A(x)]^2; \qquad B_p^{\text{fix}}(x) = [A(x)]^p; \qquad C^{\text{rand}}(x) = \sum_{n \ge 0}^\infty a_n [A(x)]$$



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$\left[A(x)\right]^n = A(A(x))$



Probability generating functions (PGFs) formalism

- assuming a very, very large population (i.e. neglecting finite-size effects)
- patient zero causes k secondary infections with probability p_k (degree distribution of the EPN)

$$G_0(x) = \bullet + \bullet x + \forall x^2 + \forall x^3 + \ldots = \sum_{k \ge 0}^{\infty} p_k x^k ; \qquad \langle k \rangle = \sum_{k \ge 0}^{\infty} k \, p_k = G'_0(1) ; \qquad \langle k^2 \rangle = \sum_{k \ge 0}^{\infty} k^2 \, p_k$$

—

$$G_1(x) = \mathbf{\Phi} + \mathbf{\Phi} x + \mathbf{\Psi} x^2 + \mathbf{\Psi} x^3 + \ldots = \sum_{k \ge 0}^{\infty} \frac{(k+1)p_{k+1}}{\langle k \rangle} x^k = \frac{G'_0(x)}{G'_0(1)}$$

average number of secondary infections a newly infected individual causes ____

 $G'_1(1)$

- all outbreaks will eventually die out when $R_0 < 1$
- some outbreaks will eventually die out when $R_0 > 1$



PHYSICAL REVIEW E 66, 016128 (2002)

Spread of epidemic disease on networks

M. E. J. Newman

a newly infected individual causes k new infections with probability $(k+1)p_{k+1}/\langle k \rangle$ (excess degree distribution of the EPN)

$$= \frac{\langle k^2 \rangle - \langle k \rangle}{\langle k \rangle} \equiv R_0$$



Probability generating functions (PGFs) formalism

- probability u that an outbreak eventually dies out



- the fraction of the population infected in an epidemic wave (and the probability of such wave) is

$$R(\infty) = \sum_{k\geq 0}^{\infty} p_k (1 - u^k) = 1 - G_0(u)$$

 $-H_0(x)$: PGF of the distribution of the size of outbreaks that will eventually die out

$$H_1(x) = \mathbf{Q} = \mathbf{P} + \mathbf{P} + \mathbf{P} + \mathbf{P} + \mathbf{P} + \dots = x \sum_{k \ge 0}^{\infty} \frac{(k+1)p_{k+1}}{\langle k \rangle} [H_1(x)]^k = x G_1(H_1(x))$$

- the distribution of the size of outbreaks that will eventually die out can be extracted from



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$$+ \underbrace{\bigotimes}_{k \ge 0}^{\infty} + \ldots = \sum_{k \ge 0}^{\infty} \frac{(k+1)p_{k+1}}{\langle k \rangle} u^k = G_1(u)$$

 $H_0(x) = xG_0(H_1(x))$



Lesson #1 : the friendship paradox

- on average, your friends have more friends than you do
 - \rightarrow a random individual has k friends with probability p_k
 - \rightarrow however, their friends have k friends with probability $\propto kp_k$
- by spreading on a contact network, the disease naturally oversamples individuals more likely to cause a larger number of secondary infections
- ignoring this effect leads back to the mass-action assumption

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Lesson #2 : the effect of superspreading events

 the PGF formalism falls back to the outcome of the SIR dynamics when p_k is a Poisson distribution

$$G_0(x) = G_1(x) = e^{R_0(x-1)};$$
 $R(\infty) = 1 - e^{-R_0R(\infty)}$

- the mass-action assumption is not appropriate for diseases whose propagation is driven by superspreading events



Lesson #3 : we need to look beyond R_0 for overdispersed infectious diseases like COVID-19

negative binomial distribution for secondary cases

$$G_1(x) = \left[1 + \frac{R_0(x-1)}{\gamma}\right]^{-\gamma}$$

shows the great impact overdispersion (small γ) has on the spreading dynamics

- in other words, if $R_0 > 1$, our attention should not be focused on whether R_0 equals 2.5 or 3.5, but rather be focused on figuring out how much heterogeneity there is behind it (what is γ ?)



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Lesson #4 : COVID-19 is particularly overdispersed

- plans prepared with pandemic Influenza in mind might fall short to contain the spread of COVID-19





Lesson #5 : distinction between "risk" and "spread"

- mass-action assumes the risk for individuals to become infected is uniformly distributed (i.e. in-degree in the EPN distributed according to a Poisson)
- following links in the EPN in their opposite direction oversamples individuals that will cause a larger number of secondary cases
 - \rightarrow backward contact tracing
 - \rightarrow "cluster busting"



The effectiveness of backward contact tracing in networks

Sadamori Kojaku 1, Laurent Hébert-Dufresne 2.3, Enys Mones4, Sune Lehmann Yong-Yeol Ahn [16,7]



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Lesson #6 : assessing the pandemic potential of an emerging disease

- parameters of the EPN can be inferred from early incidence data
- doing so provides an assessment on the risk of a pandemic
- validation using data from the 2014-2016 Ebola Virus Disease (EVD) epidemic in Sierra Leone indicates that the PGF formalism provides realistic forecasts











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Fonds de recherche Nature et technologies Québec 🏼 🔹



Samuel V. Scarpino (Pandemic Prevention Institute, The Rockefeller Foundation)



Benjamin M. Althouse (Truveta)

...and many other collaborators

Slides available at antoineallard.info





