Webinar: Modeling for a Globally Connected World - What Models are Good for and How they Work

Presented by:

Professor Louis Gross

National Institute for Mathematical and Biological Synthesis, University of Tennessee, Knoxville

With support from the National Science Foundation (DBI-1300426)

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MEET YOUR MODERATOR

Suzanne Lenhart, PhD

Chancellor's Professor of *Mathematics, University of Tennessee*

Associate Director for Education and Outreach, *National Institute for Mathematical and Biological Synthesis (NIMBioS)*

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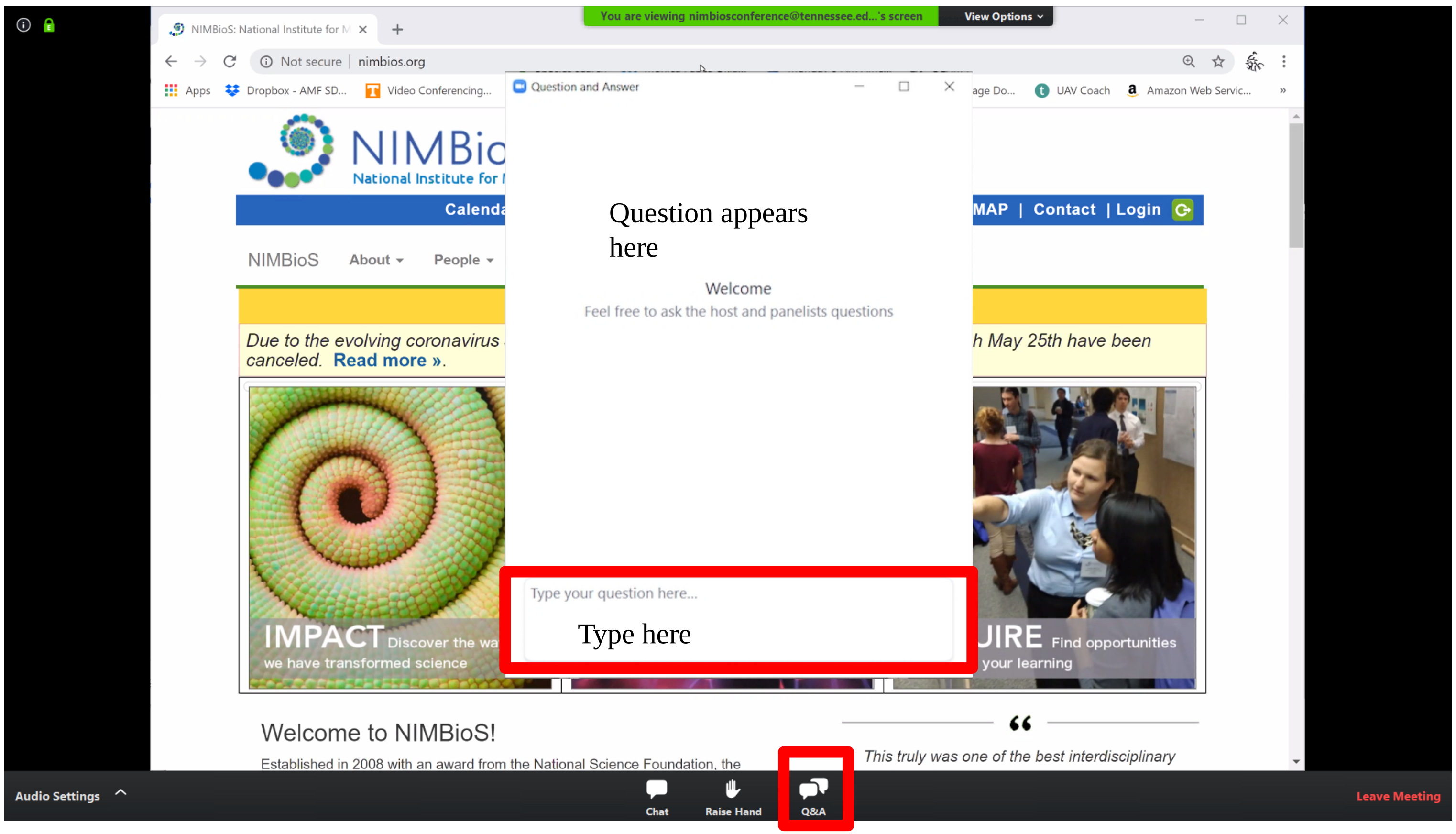

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NIMBioS Webinar Series

NIMBioS is hosting a series of webinars focusing on topics at the interface of mathematics and biology. Unable to attend the live presentation? That's ok! Register to attend, and you will receive a link to the webinar recording.

Upcoming Webinars

Mathematical modeling of malaria transmission by mosquitoes

Date: 3:30 EDT Tuesday, April 21, 2020

Speaker: Dr. Vitaly Ganusov, Assoc. Professor, Microbiology, University of Tennessee, Knoxville

Moderator: Dr. Louis Gross, NIMBioS Director and Chancellor's Professor of Ecology and Evolutionary Biology and Mathematics at the University of Tennessee

Abstract: Malaria is a disease caused by parasites from the genus *Plasmodium*. Every year, 200 million individuals experience malaria, and approximately 500,000 of these individuals die. It is well established that malaria is transmitted from person to person by mosquitoes. Yet, quantitative details of how likely a bite by an infected mosquito results in infection remains poorly understood. In my talk I will analyze experimental data in which mosquitoes, carrying *Plasmodium yoelii* sporozoites, bite individual mice, and mathematically model the likelihood of infection as a function of several parameters (number of sporozoites per mosquito, feeding time, blood take probability) that were recorded in the data. Our results suggest that infection probability depends strongly on the number of sporozoites mosquitoes carry, and less on the probing time, and is independent of whether a mosquito takes the blood meal or not. I will also discuss implications of these results for modeling epidemiological dynamics of malaria and for clinical trials of malaria vaccines.

NIMBioS.org   A recording of this webinar will be posted within two days

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MEET YOUR PRESENTER

Louis J. Gross, PhD

Chancellor's Professor *of Ecology and Evolutionary Biology and Mathematics, University of Tennessee*

Director, *The National Institute for Mathematical and Biological Synthesis, (NIMBioS), University of Tennessee*

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Webinar Objectives

- Provide an overview of modeling objectives and the process of developing a model
- Describe different types of models and their applications
- Discuss the limitations of models and how they are evaluated

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Fear, Access, and the Real-Time Estimation of Etiological Parameters for Outbreaks of Novel Pathogens

Authors: Nina H. Fefferman[*1,2], Eric T. Lofgren[3], Nianpeng Li[4], Pieter Blue[5], David J. Weber[6] and Abdul-Aziz Yakubu[4].

[*] Corresponding Author: N.H. Fefferman, 447 Hesler Biology Building, Department of Ecology and Evolutionary Biology, University of Tennessee, Knoxville, TN, 37996, email: nfefferm@utk.edu

An SIR-type model of an epidemic that accounts for the "observed" data from testing and the "real" spread, accounting for sensitivity of surveillance to clinical testing errors.

Nina Fefferman, Univ. of Tennessee

JAMA Insights

ONLINE FIRST FREE

March 26, 2020

Turbulent Gas Clouds and Respiratory Pathogen Emissions

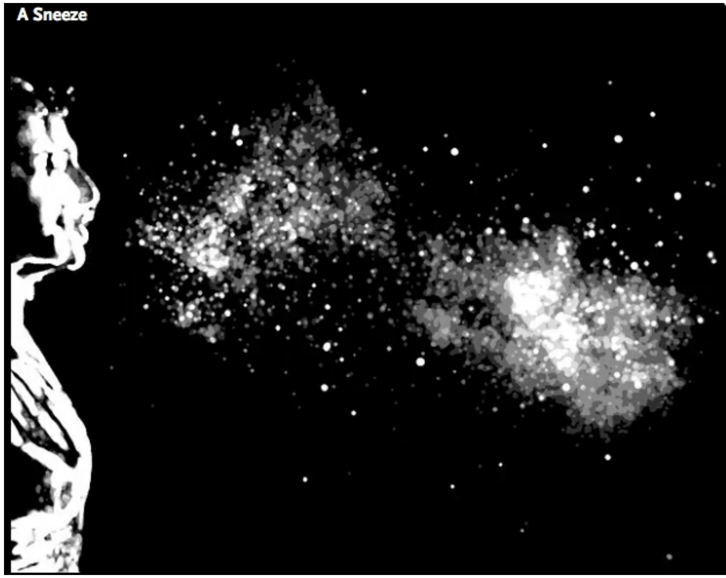
Potential Implications for Reducing Transmission of COVID-19

Lydia Bourouiba, PhD[1]

Author Affiliations | Article Information

JAMA. Published online March 26, 2020. doi:10.1001/jama.2020.4756

A model that uses experimental data on sneezes linked to mathematical analysis of turbulent fluid dynamics

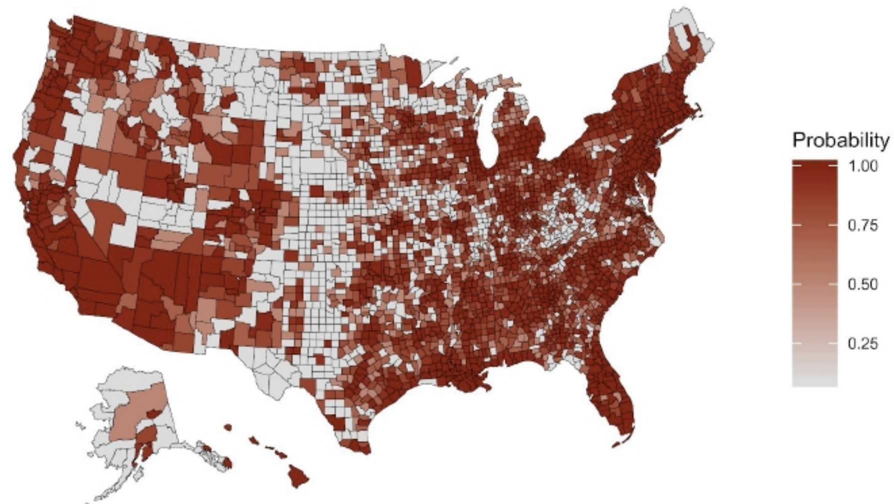


Lydia Bourouiba, MIT

Probability of current COVID-19 outbreaks in all US counties

Emily Javan, Dr. Spencer J. Fox, Dr. Lauren Ancel Meyers

Corresponding author:
Lauren Ancel Meyers
The University of Texas at Austin
laurenmeyers@austin.utexas.edu

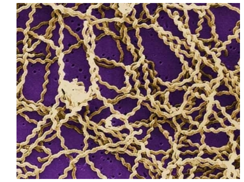


A model that uses a branching process to project the spread of COVID-19 in different US counties.

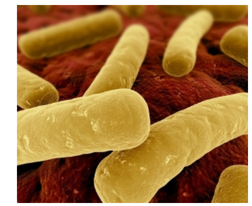
Lauren Ancel Meyers, Univ. of Texas

Infectious Disease Modeling at NIMBioS

Mathematical modeling of *Leptospira* transmission and intervention strategies



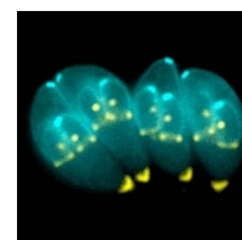
Evaluating the shifts in antimicrobial use practices and resistance resulting from risk mitigation strategy



Climate change and vector-borne diseases

Synthesizing and predicting infectious disease while accounting for endogenous risk

Integrated modeling and analysis of within-host infection and between-host transmission for *Toxoplasma gondii*



Optimal control of neglected tropical diseases

Order of topics

- Science and models
- Methods of investigation and theory
- Constraints on models
- Evaluating models
- Some lessons

What is science?

Science is thought to be a process of pure

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n on measuring things and counting them up.
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Lewis Thomas - Sierra Club Bulletin, March/April 1982, P. 52

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What is science?

Science is thought to be a process of pure reductionism, taking the meaning out of mystery, explaining everything away, concentrating all our attention on measuring things and counting them up. It is not like this at all. The scientific method is guesswork, the making up of stories. The difference between this and other imaginative works of the human mind is that science is then obliged to find out whether the guesses are correct, the stories true. Curiosity drives the enterprise, and the open acknowledgement of ignorance.

Lewis Thomas - Sierra Club Bulletin, March/April 1982, P. 52

Models

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What is science?

Science is thought to be a process of pure reductionism, taking the meaning out of mystery, explaining everything away, concentrating all our attention on measuring things and counting them up. It is not like this at all. The scientific method is guesswork, the making up of stories. The difference between this and other imaginative works of the human mind is that science is then obliged to find out whether the guesses are correct, the stories tr

Data

Curiosity drives the enterprise, and the open acknowledgement of ignorance.

Lewis Thomas - Sierra Club Bulletin, March/April 1982, P. 52

Expressing Theory

Verbally

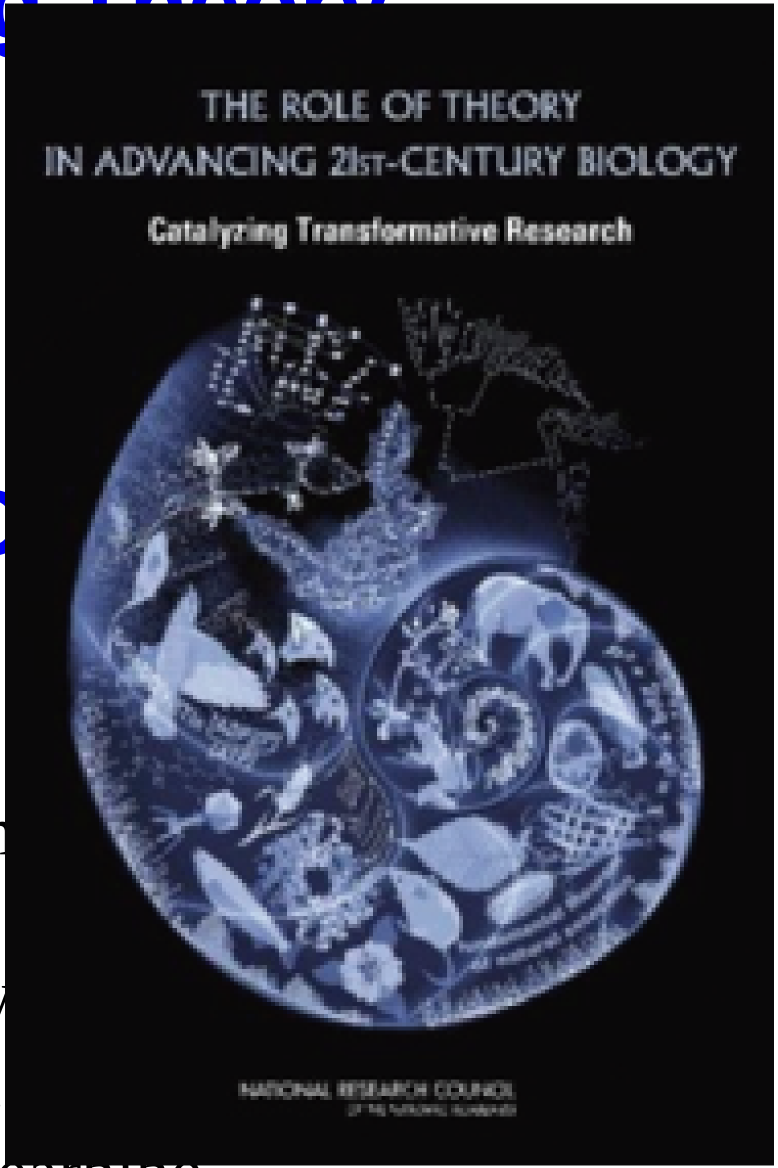
Graphically

Mathematically

Through Simulation

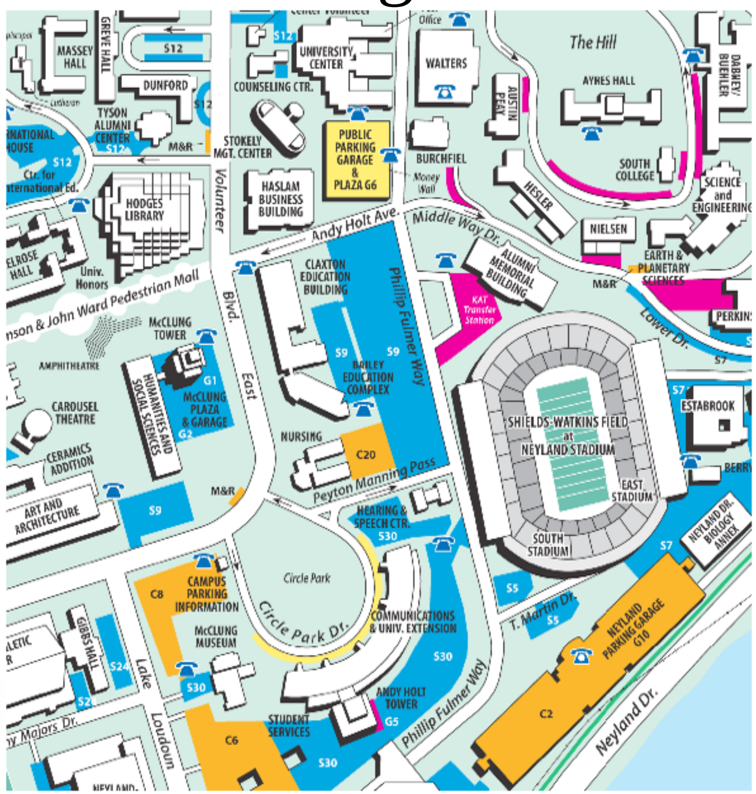
Approaches to D

1. Descriptive: (a) Empirical
   Comparative
2. Mechanistic (a) Compartm
   adaptationist
3. Systems - hierarchy theory
4. Individual- or agent-based
5. Expert systems, machine learning



The “stories” in science are models

A model is a simplification of reality. Think of it as a map - it includes some features that represent what we observe but not others. Modeling is the process of *selective ignorance* - we select what to include and what to ignore.



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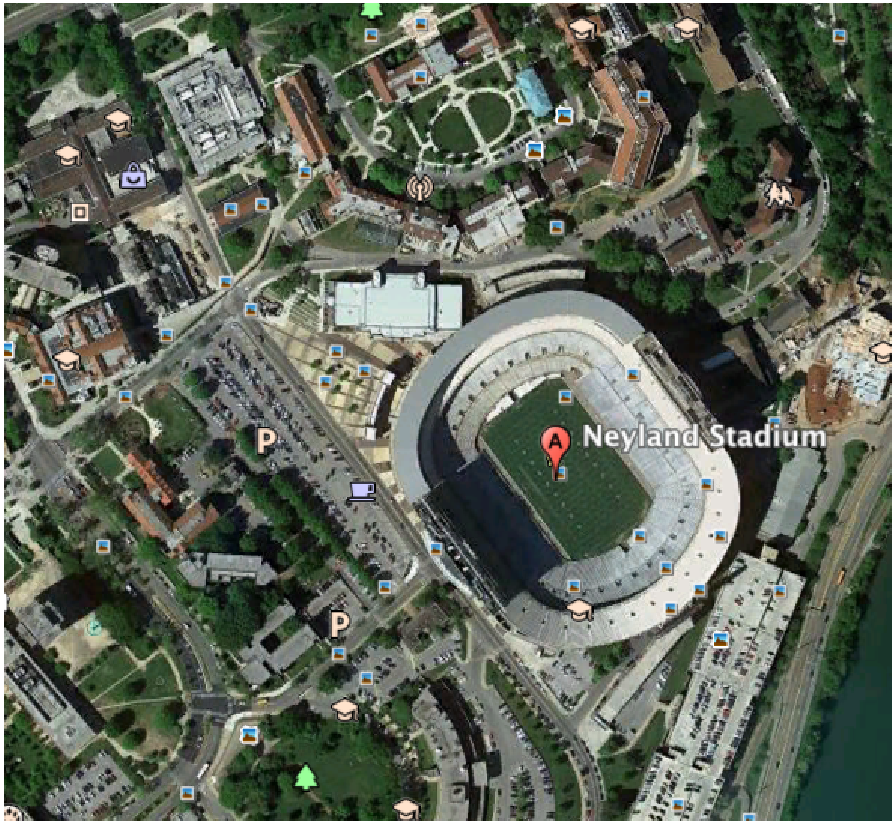
The "stories" in science are models

Is this less of a simplification? Is it closer to "reality"?



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You make models all the time:

In the current pandemic, you are taking account of many factors, data from sources you trust, and your personal values/beliefs to decide who to interact with, whether to leave your home, and how often to do so. You may not be making a "formal" calculation of your personal risk of harm, but an underlying "model" is involved.

So you are deciding what is "best" for you

You make models all the time:

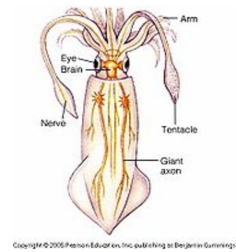
What decision do you make in more “normal” times when faced with:

So you are deciding what is “best” for you quite regularly

Models in Biology

Physiology

Disease



Neurobiology

Microbiology

Development

Genetics

Model Systems

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Taxonomy of Models

This could be based on the model objectives, on the general approaches used, or on the methodology. One possibility is:

conceptual

verbal

quantitative

physical (e.g. real, such as a physical model for an animal to evaluate heat-loading)

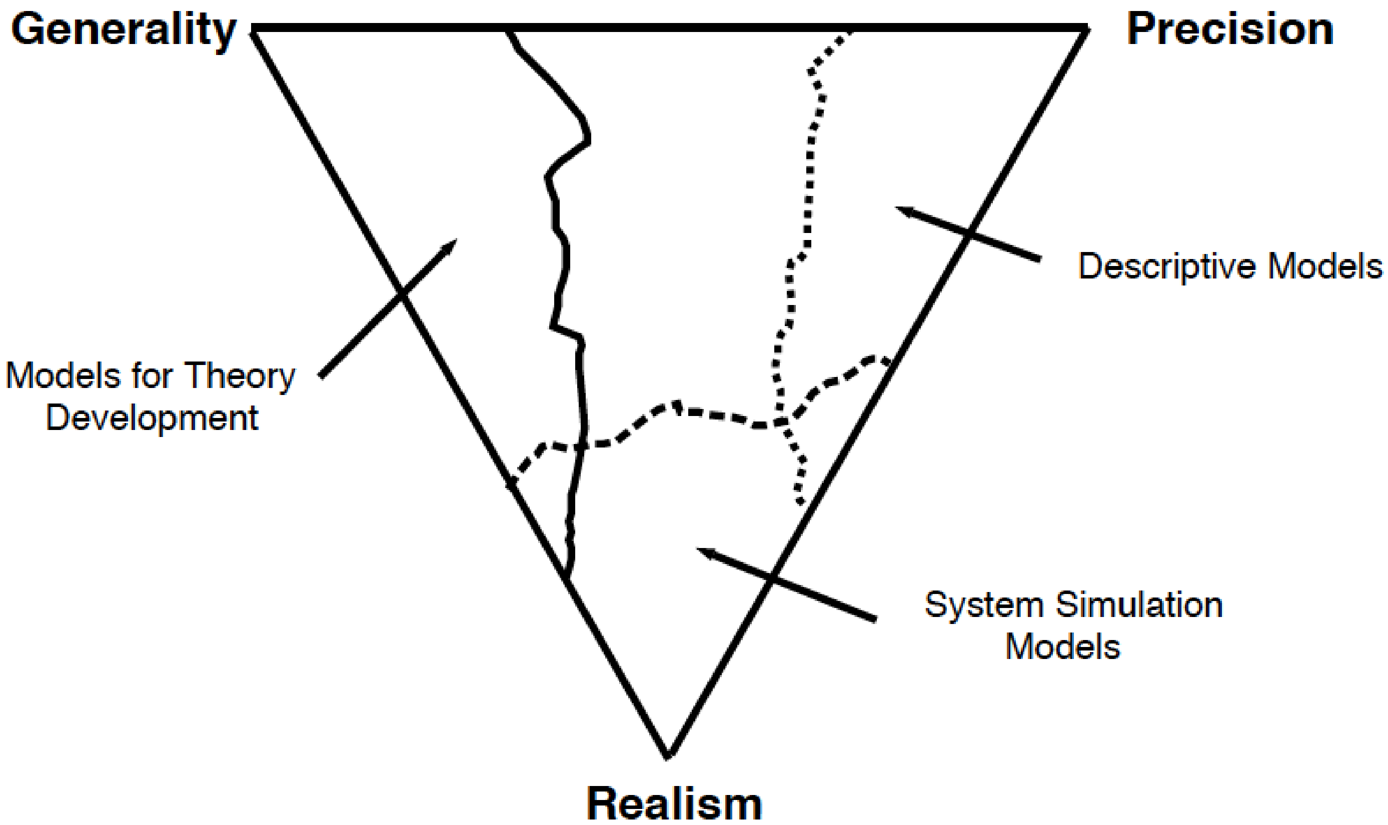
biological (including animal models used for experiments, cell lines, and tissue cultures)

Note that modeling text books typically classify models based on mathematical approach.

Possible Model Objectives

1. Suggest observations and experiments
2. Provide a framework to assemble bodies of facts - provide a means to standardize data collection
3. "Allows us to imagine and explore a wider range of worlds than ours, giving new perceptions and questions about how our world came to be as it is" F. Jacob - The Possible and the Actual, 1982
4. Clarifies hypotheses and chains of argument
5. Identifies key components in systems
6. Allows simultaneous consideration of spatial and temporal change
7. Extrapolate to broad spatial or long temporal scales for which data can not easily be obtained
8. Prompts tentative and testable hypotheses
9. Serves as a crude guide to decision making in circumstances where action cannot wait for detailed studies
10. Provides an antidote to the helpless feeling that the world is too complex to understand in any generality - provides a means to get at general patterns and trends
11. To predict how a system will behave under different management, and control the system to meet some objective

Models and tradeoffs



No one model can do everything

Environmental Modeling

Species densities

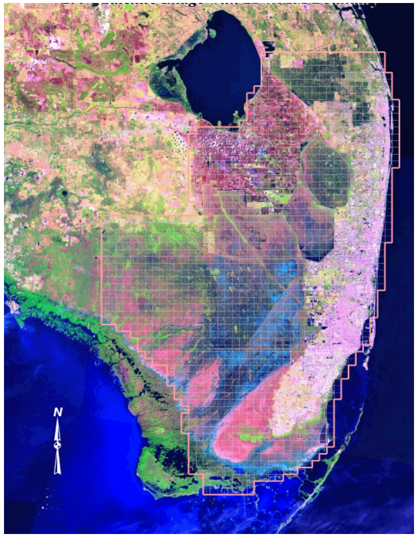
Animal telemetry

Physical conditions

Data sources

GIS map layers (Vegetation, hydrology, elevation),Weather, Roads, Species densities

Monitoring



Models

Statistical

Differential equations

Matrix

Agent-based

Management input

Harvest regulation

Water control

Reserve design

Evaluation/Analysis

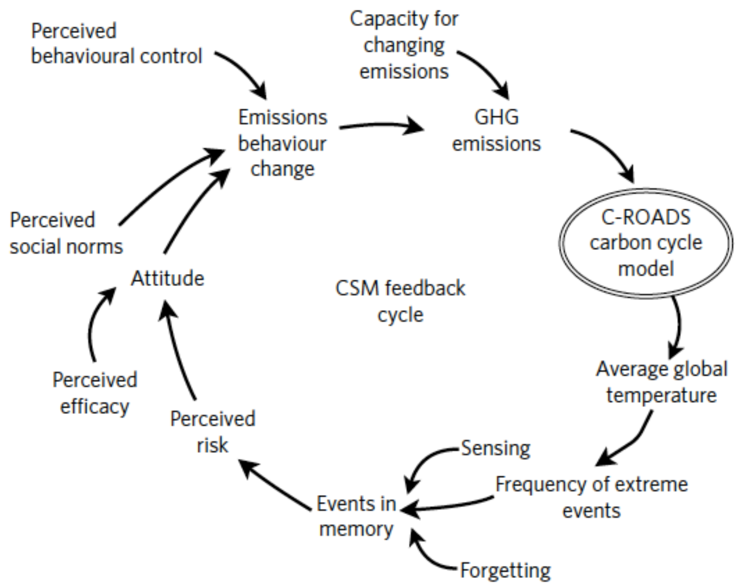
Simulation

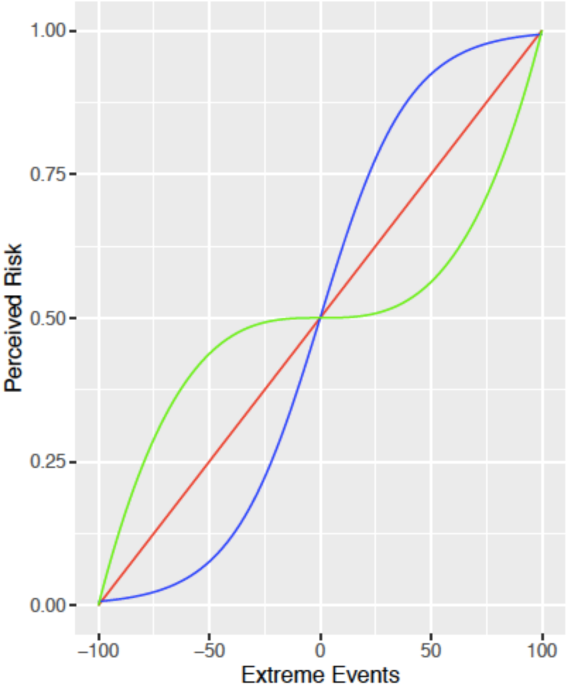
Visualization, corroboration, sensitivity, uncertainty

Matlab, C++, Distributed, Parallel

Describing Models

There is no single protocol to describe models. Some are described graphically





Beckage, B., L. J. Gross, K. Lacasse, E. Carr, S. S. Metcalf, J. M. Winter, P. D. Howe, N. Fefferman, T. Franck, A. Zia, A. Kinzig and F. M. Hoffman. 2018. Linking models of human behavior and climate alters projected climate change. *Nature Climate Change* **8**, 79–85

Describing Models

Some are described mathematically with definition of the variables and parameters

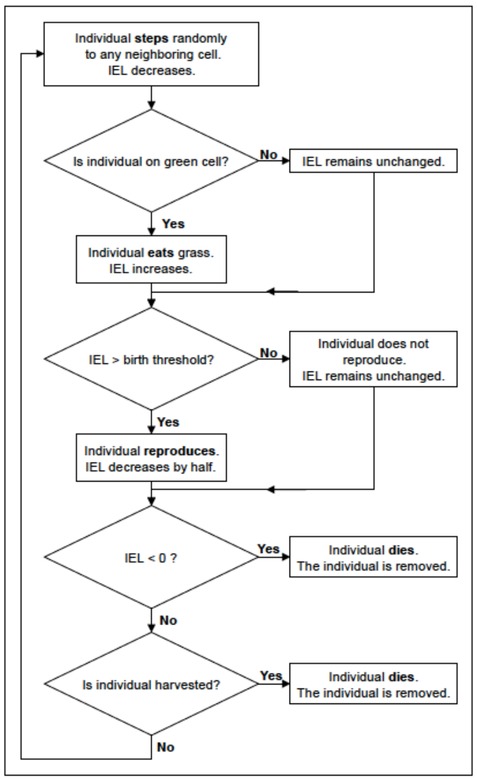
$$\frac{dN_1(t)}{dt} = a_1(a_2 - N_1) - f(N_1)N_2,$$
$$\frac{dN_2(t)}{dt} = b_1 f(N_1)N_2 - b_2N_2 - u(t)N_2, \tag{1}$$

$$f(N_1) = \frac{a_1 a_3 N_1}{1 + a_3 a_4 N_1}, \tag{2}$$

Federico, P., L. J. Gross, S. Lenhart, and D. Ryan. 2013. Optimal control in individual-based models: implications from aggregated methods. *American Naturalist* **181**: 64-77

Describing Models

Described through the code that simulates the system and associated documentation and metadata



Federico, P., L. J. Gross, S. Lenhart, and D. Ryan. 2013. Optimal control in individual-based models: implications from aggregated methods. *American Naturalist* **181**: 64-77

```
# Filename: EcoSuccessionPlot.R
# R script to
# - Print out a table showing landscape structure over time

# A function to perform matrix exponentiation
"%^%"<-function(A,n){
  if(n==1) A else {B<-A; for(i in (2:n)){A<-A%*%B}}; A
  }

# Enter the transfer matrix
T = matrix(c( 0.94, 0.05, 0.01,
              0.02, 0.86, 0.12,
              0.01, 0.06, 0.93 ), ncol = 3)

# Enter the initial state
x0 = matrix(c( 1, 0, 0 ), ncol = 1)

# We will create a matrix x that has three columns.
# Each column will contain time series data for one class.
# Each row will correspond to a time step.
x = matrix(rep(0, 201*3), ncol = 3)

x[1, ] = x0     # Data for time step t = 0

# Use for loop to generate times series data
for (t in 1:200){
   x[t+1, ] = T%^%t %*% x0 # Data for time step t
   }

# Time series information for proportion underwater is
# in the first column
u = x[ ,1]

# Time series information for proportion saturated but
# not underwater is in the second column
s = x[ ,2]

# Time series information for proportion dry is in the
# thid column
d = x[ , 3]
```

F Bodine, E., S. Lenhart and L. J. Gross. ***Mathematics for the Life Sciences.*** Princeton University Press (2014).

Describing Models

Some are described by the statistical methodology used, data and metadata

Event Number	Event	Rate	Change(s) to state variable(s) (ΔX)
1	Infection of uninfected host by pathogen 1	$F_1 J_\varnothing \Delta t + o(\Delta t)$	$J_\varnothing \to J_\varnothing - 1$ $J_1 \to J_1 + 1$
2	Infection of uninfected host by pathogen 2	$F_2 J_\varnothing \Delta t + o(\Delta t)$	$J_\varnothing \to J_\varnothing - 1$ $J_2 \to J_2 + 1$
3	Infection by pathogen 1 of host singly infected by pathogen 2	$F_1 J_2 \Delta t + o(\Delta t)$	$J_2 \to J_2 - 1$ $J_{1,2} \to J_{1,2} + 1$
4	Infection by pathogen 2 of host singly infected by pathogen 1	$F_2 J_1 \Delta t + o(\Delta t)$	$J_1 \to J_1 - 1$ $J_{1,2} \to J_{1,2} + 1$
5	Death of host singly infected by pathogen 1 and replacement with an uninfected host	$\mu J_1 \Delta t + o(\Delta t)$	$J_1 \to J_1 - 1$ $J_\varnothing \to J_\varnothing + 1$
6	Death of host singly infected by pathogen 2 and replacement with an uninfected host	$\mu J_2 \Delta t + o(\Delta t)$	$J_2 \to J_2 - 1$ $J_\varnothing \to J_\varnothing + 1$
7	Death of coinfected host and replacement with an uninfected host	$\mu J_{1,2} \Delta t + o(\Delta t)$	$J_{1,2} \to J_{1,2} - 1$ $J_\varnothing \to J_\varnothing + 1$

https://doi.org/10.1371/journal.pbio.3000551.t001

		Observed counts, O_k										Total
Pathogens with *n* distinct types, strains, or clones	***n***	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	***N***
Human papillomavirus	25	2,933	140	64	26	102	39	12	2	2	-	5,412
Anther smut (*M. violaceum*)	102	285	74	60	32	14	3	3	2	1	1	475
B. afzelii on bank voles	7	807	33	26	13	10	11	6	-	-	-	906
Malaria (*P. vivax*)	57	1,023	404	291	208	118	50	16	5	1	1	2,117

Abbreviation: NiSP, Noninteracting Similar Pathogens

https://doi.org/10.1371/journal.pbio.3000551.t002

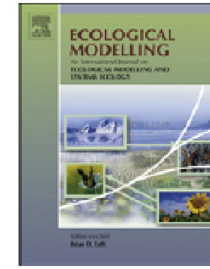
Hamelin, F. M., L. J.S. Allen, V. A. Bokil, L. J. Gross, F. M. Hilker, M. J. Jeger, C. A. Manore, A. G. Power, M. A. Rúa, N. J. Cunniffe. 2019. Co-infections by non-interacting pathogens are not independent and require new tests of interaction. https://doi.org/10.1371/journal.pbio.3000551

Ecological Modelling 221 (2010) 2760–2768

Contents lists available at ScienceDirect

Ecological Modelling

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



The ODD protocol: A review and first update

Volker Grimm[a,*], Uta Berger[b], Donald L. DeAngelis[c], J. Gary Polhill[d], Jarl Giske[e], Steven F. Railsback[f,g]

[a] Helmholtz Centre for Environmental Research-UFZ, Department of Ecological Modelling, Permoserstr. 15, 04318 Leipzig, Germany
[b] Institute of Forest Growth and Computer Science, Dresden University of Technology, P.O. 1117, 01735 Tharandt, Germany
[c] USGS/Biological Resources Division and Dept. of Biology, University of Miami, PO Box 249118, Coral Gables, FL 33124, USA
[d] Macaulay Land Use Research Institute, Craigiebuckler, Aberdeen, AB15 8QH, United Kingdom
[e] University of Bergen, Department of Biology, P.O. Box 7803, N-5020 Bergen, Norway
[f] Department of Mathematics, Humboldt State University, Arcata, CA 95521, USA
[g] Lang, Railsback & Associates, 250 California Avenue, Arcata, CA 95521, USA

An example of a general protocol developed specifically for agent-based models but useful across other model types is the **ODD Protocol.** This is an update of a protocol first published in 2006 for "Overview, Design Concepts and Details"

Elements of the updated ODD protocol
1. Purpose 2. Entities, state variables, and scales 3. Process overview and scheduling
4. Design concepts • Basic principles • Emergence • Adaptation • Objectives • Learning • Prediction • Sensing • Interaction • Stochasticity • Collectives • Observation
5. Initialization 6. Input data 7. Submodels

Grimm et al. (2010) Ecological Modelling 221: 2760-2768

Constraints on models

Data constraints: Available data may not be sufficient to specify appropriate functional forms, interrelationships, or parameters. May force aggregation of components. May not be sufficient to elaborate criteria for evaluation of model performance.

Effort constraints: Resource constraints may limit the amount of detail it is feasible to include. Limits on time modelers and collaborators may invest as well as pressure to produce results.

Computational constraints: Despite great enhancements in computational resources, there are many problems still not feasible to carry out computationally.

Other constraints: ethical or other societal considerations.

Constructing models

Given the above, the entire modeling process involves evaluation of alternative approaches to assess the most appropriate procedures for the questions of concern. This is part of the process of ***selective ignorance*** *involved in constructing models.*

Just as public policy decisions involve a balancing act between various alternatives which satisfy to varying degrees the desires of different stakeholders, realism in modeling involves balancing different approaches to meet a goal.

Realistic modeling is the science of the actual rather than the science of the ideal.

Model evaluation – some terminology

Verification - model behaves as intended, i.e. equations correctly represent assumptions; equations are self-consistent and dimensionally correct. Analysis is correct. Coding is correct - there are no bugs.

Calibration - use of data to determine parameters so the model "agrees" with data. This is specific to a given criteria for accuracy. Some call this Tuning or Curve-fitting.

Corroboration - model is in agreement with a set of data independent from that used to construct and calibrate it.

Validation - model is in agreement with real system it represents with respect to the specific purposes for which it was constructed. Thus there is an implied notion of accuracy and domain of applicability.

Evaluation (testing) - appropriateness to objectives; utility; plausibility; elegance; simplicity; flexibility.

Evaluation and model objectives

Given the many objectives for models, we should expect there to be multiple criteria for evaluating whether a model is useful.

Before developing a model in any detail, criteria should be established for evaluating its use

Evaluation procedures should account for constraints of Data, Effort and Resources, Computation

Evaluation criteria should be taken into consideration in assessing methods, level of detail, scale, and what to ignore in deciding on a model.

Evaluating different types of models

Models for theory development –

General, some realism, little precision.

Make qualitative comparisons to patterns, not quantitative ones, over some parameter space. No calibration or corroboration performed, except theoretical corroboration (meaning that model agrees with the general body of theory in the field).

Evaluating different types of models

Descriptive models-

Precise, little realism, not general

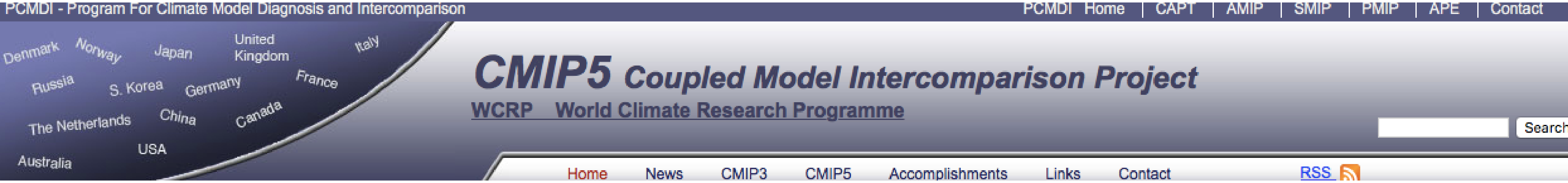
Statistical hypothesis testing; time series analysis methods applied.

Models for specific systems -

Realism, some precision, not general

Quantitative comparisons, constrained by available data. Compare component-by-component if data are available.

Example of complex model evaluation – Global Climate Models



CMIP5 promotes a standard set of model simulations from 20 different GCMs in order to:

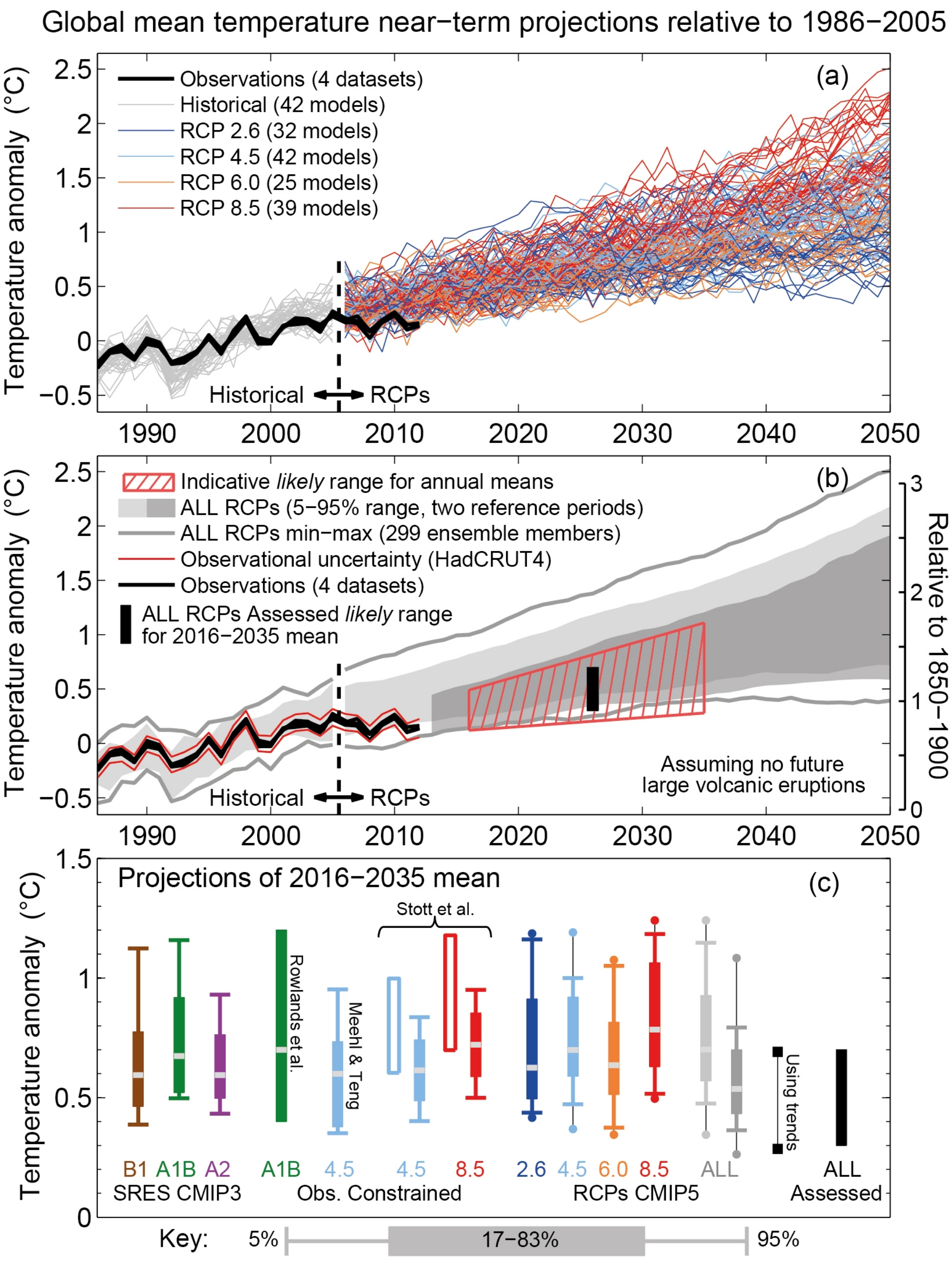
- evaluate how realistic the models are in simulating the recent past,
- provide projections of future climate change on near term (out to about 2035) and long term (out to 2100 and beyond), and
- understand factors responsible for differences in model projections, including quantifying some key feedbacks such as those involving clouds and the carbon cycle

https://pcmdi.llnl.gov/mips/cmip5

Global Mean Surface Temperature to 2050

Climate models assume **<u>static representative concentration pathways (RCPs)</u>** for anthropogenic GHG emissions.

Kirtman et al. 2013: Near-term Climate Change: Projections and Predictability. In: Climate Change 2013: Fifth Assessment Report of the Intergovernmental Panel on Climate Change.



Despite the importance of evaluation, many published models lack explicit criteria or consideration of this. Why?

1. It's difficult and requires potentially different skill sets from those constructing and using models.
2. Science is very much a human enterprise and it is natural that once one has devoted considerable effort to developing a particular model, it is difficult to critique yourself.
3. Modern settings with a great amount of team effort to develop models or experimental protocols can constrain individuals who do not wish to be an outcast in a lab.

Criteria I use in Reviewing Modeling Papers

1. Are the models appropriate to the biological questions being addressed?
2. Are the underlying biological questions of potential interest to a significant fraction of the journal's audience?
3. Does the mathematics/model teach us anything new that is biologically significant?
4. Is the mathematics/modeling correct?
5. If the paper is strictly theoretical, does it point out broadly useful new insights?
6. Are the model parameters and variables estimable from observations?
7. Is there some effort devoted to model evaluation?

Take home lessons

- Model evaluation for all types of biological models is relatively rare.
- Set criteria for model evaluation prior to expending a lot of effort on a model.
- Tie evaluation criteria to model objectives.
- Encourage consideration of evaluation in all your educational initiatives.
- Multiple models are good – encourage this.
- Consider whether an evaluation has been done or discussed whenever you review a paper.

Thank you for your participation

Questions/comments? Please use the Questions Button on Zoom to post these.

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