Models and Meta-Models for Public Health Decision Making

Vaccine Decision-making as an Exemplar

Don Burke
Dean, Graduate School of Public Health
University of Pittsburgh
19 Jan 2012
What Is Public Health?
( Don Burke’s 10 Second Elevator Speech )

• Public health is prevention of disease in populations
• Examples include
  – Vaccines
  – Sanitation
  – Diet
  – Healthy behaviors
• Inherently interdisciplinary
Public Health Dynamics: Building on three Pittsburgh legacies

Jonas Salk
Herb Simon
Fred Rogers
Some former residents of my Squirrel Hill neighborhood

Jonas Salk
Fred Rogers
Herb Simon
LECTURE OUTLINE

1. ABOUT PUBLIC HEALTH AND PUBLIC HEALTH DYNAMICS
2. BASICS OF EPIDEMIC MODELING
3. MODELING FOR DECISION-MAKING: VACCINES
   DATA
   PATTERN DETECTION
   EQUATION BASED MODELS
   AGENT AND NETWORK MODELS
   MODELING OF INTERVENTIONS
   MODELING OF PRAGMATICS
   COST-BENEFIT MODELING
   DECISIONS
4. CONCLUSIONS
5. AREAS FOR COLLABORATION
Modeling Steps

- Equation Based Models
- Agent & Network Models
- Modeling of Interventions
The Vaccine Meta-Model

Data
Patterns & Parameters
Equation Based Models
Agent & Network Models
Modeling of Interventions
Modeling of Pragmatics
Cost Benefit Analyses
Decision
Modeling Steps

Support / Clients

Software
Academic Disciplines

Systems Thinking
Data mining
Time series decomposition
Social networks
GIS
Game theory
Remote sensing
Machine learning & A.I.
High-performance computing

Info Sci
Epid
Biostat
Math
Comp Sci
Indust Engin
Enviro Engin
Behavior
Law
Econ
Policy
Philos

Benter Foundation

CDC
Bill & Melinda Gates Foundation

The Vaccine Meta-Model
Aerodynamics, the study of gases in motion

Fluid dynamics, the study of fluid flow

Molecular dynamics, the study of motion on the molecular level

Thermodynamics, the study of the relationships between heat and mechanical energy
Some Academic Units Focusing on Disease Dynamics
The Vaccine Meta-Model

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Data mining
Time series decomposition
Social networks
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Game theory
Remote sensing
Machine learning & A.I.
High-performance computing

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Policy
Philos

Bcenter Foundation

NATIONAL INSTITUTES
OF HEALTH

CDC

Bill & Melinda Gates Foundation

PITT

Clara

Tycho

FRED

Francis

LEO

HERMES

GAIA

The Vaccine Meta-Model
Decision making: Computer simulation models can compensate for weaknesses in mental models.

Prior knowledge

Expert opinion

Modeling & Simulation

Data
Infectious Disease Dynamics:
The Standard Simple “S-I-R” conceptual model
The **Kermack-McKendrick** epidemic model / simplest version

- closed fixed size population (i.e., no births, deaths)
- incubation period of the infectious agent is instantaneous
- duration of infectivity is same as length of the disease
- completely homogeneous population
- no age, spatial, or social structure.

The model consists of a system of three coupled nonlinear ordinary differential equations,

\[
\begin{align*}
\frac{dS}{dt} &= -\beta SI \\
\frac{dI}{dt} &= \beta SI - \gamma I \\
\frac{dR}{dt} &= \gamma I
\end{align*}
\]

where \( t \) is time, \( S(t) \) is the number of susceptible people, \( I(t) \) is the number of people infected, \( R(t) \) is the number of people who have recovered and developed immunity to the infection, \( \beta \) is the infection rate, and \( \gamma \) is the recovery rate.

Revived by Anderson and May (1979)
Demographics (e.g., age)

Weather & Environment

Human Behavior

Interactions with other contagions

Mosquito Dynamics

Microbial Evolution

S → I → R
“Individual-Based” or “Agent-Based” Models

Some toy (simple) models of system dynamics in public health
Growing Artificial Societies
Joshua M. Epstein
Robert Axtell
Brookings Institution 1996

Generative Social Science
Joshua M. Epstein
Princeton Univ Press 2007

“If you can’t grow it, you don’t understand it.”

Josh
H1N1 pandemic decision support using large scale agent based simulations
Model of a USA pandemic

Ferguson NM, Cummings DA, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza epidemic
Nature July 27, 2006; 442: 448-52
Typical MIDAS - ASPR /BARDA decision support team meeting at Pitt

• Don Burke, PI
• Ron Vorhees, Allegheny County Epidemiologist
• Rick Zimmerman, Community Health Physician
• John Grefenstette, Computer Scientist
• Cho-Cho Lin, Economist
• Sandra Quinn, Behavioral Scientist
• Jim Stark, Epidemiology Graduate student
• Shanta Zimmer, Infectious Disease Physician
• Shawn Brown, Computational Scientist
• Roni Rosenfeld, Computer Scientist
• Maggie Potter, Lawyer & Public Health Practice
• Bruce Lee, Internal Med Physician & Operations Research

Bruce or Shawn on phone in DC
Washington DC Metro Visualization
Data Access
A project to digitize and render computable all the data in the US weekly National Notifiable Disease Surveillance System, since the beginning of disease reporting, and provide open access to these data

- 1888 to present (more than 120 years)
- 50 states and 1500 cities and towns
- 55 reportable infectious diseases
- 6,300 weekly reports
- 100 million cases and 4 million deaths
Danish nobleman who made accurate and comprehensive observations of the positions of the stars and planets. After his death, Tycho’s assistant Johannes Kepler used these data to derive the laws of planetary motion.
Endangered public health data: USA and world-wide

- USA
- Laos
- India
- Nigeria
## City Morbidity Reports: 1906-1953

### Pneumonia (All Forms)

City Reports for Week Ended June 5, 1920

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<thead>
<tr>
<th>Place</th>
<th>Cases</th>
<th>Deaths</th>
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<td>Attleboro, Mass.</td>
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<tr>
<td>Aurora, Ill.</td>
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<td>Billings, Mont.</td>
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Jamestown, N. Y.   | 1
Jersey City, N. J. | 1
Kalamazoo, Mich.  | 1
Kansas City, Kans. | 1
Kansas City, Mo.  | 6
Kearny, N. J.      | 2
Lackawanna, N. Y.  | 5
La Salle, Ill.     | 1
Lawrence, Mass.    | 2
Lexington, Ky.     | 1
Lima, Ohio.        | 2
Lincoln, Nebr.     | 1
Logansport, Ind.   | 2
Long Beach, Calif. | 1
Lorain, Ohio.      | 1
Los Angeles, Calif.| 24
Louisville, Ky.    | 4
Lynn, Mass.        | 6
Manchester, N. H.  | 2
Mankato, Minn.     | 1
Marion, Ind.       | 1
Marquette, Mich.   | 1
Melrose, Mass.     | 1
Memphis, Tenn.     | 5
Methuen, Mass.     | 1
Milwaukee, Wis.    | 2
Minneapolis, Minn. | 2
Mishawaka, Ind.    | 2
Montgomery, Ala.   | 1
Morristown, N. J.  | 1
Mount Vernon, N. Y.| 3
Nashua, N. H.     | 1
Nashville, Tenn.   | 3
New Britain, Conn. | 1
New Haven, Conn.   | 7
New London, Conn.  | 2
STATE MORBIDITY REPORTS: 1928-CURRENT

TABLE II. Cases of selected notifiable diseases, United States, weeks ending January 7, 1995, and January 8, 1994 (1st Week)

<table>
<thead>
<tr>
<th>Reporting Area</th>
<th>AIDS*</th>
<th>Gonorrhea</th>
<th>Hepatitis (Viral), by type</th>
<th>Legionellosis</th>
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<td>2</td>
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<td>64</td>
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<td>250</td>
<td>637</td>
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<td>Upstate N.Y.</td>
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<td>N.J.</td>
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<td>E.N. CENTRAL</td>
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<td>Ohio</td>
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<td>N. Dak.</td>
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<td>S. Dak.</td>
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<td>Nebr.</td>
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<td>Kans.</td>
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<td>S. ATLANTIC</td>
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<td>-</td>
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<td>S.C.</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>Ga.</td>
<td>-</td>
<td>313</td>
<td>192</td>
<td>-</td>
</tr>
</tbody>
</table>

MMWR: 1995 January

"Count"
Data entry by “Digital Divide Data” in Phnom Penh

- 6,300 weekly reports
- 35,000 worksheets
- 200 million keystrokes
History of disease reporting in the US
The history of measles control in the US

Weekly incidence rates (per 100,000) for US states: 1928-1980
The history of polio eradication in the US

Weekly incidence rates (/100,000) in US states: 1928-1964
- First mass vaccination campaign in 1955-56 (red line)
Welcome

Project Tycho was started in 2009 at the University of Pittsburgh Graduate School of Public Health to address the lack of access to detailed public health data for analysis and policy making. This project was funded by the Bill & Melinda Gates Foundation as part of the Vaccine Modeling Initiative. The goal of project Tycho is to provide a central global public health data access point. Historical as well as current public health data are of great value if accessible for research and analysis. Open access will enable the use of analytical capacity from around the globe for new discoveries of disease patterns and control policies.

The Tycho database currently contains the digital version of the entire US weekly nationally notifiable disease surveillance system. This system was initiated in 1888 and data continues today. All weekly reports between 1888 and 2009 (6300 reports) have been entered from PDF files or hard copies using double data entry (200 million keystrokes). Currently, the Tycho database contains 10 million records that each represent a weekly report from a location for a specific disease. All 50 states, 9 overseas territories and over 4,000 cities have been included. The records include a total of 90 million reported cases and 4 million reported deaths due to notifiable diseases in the United States for the last 122 years.

Currently, the Tycho database is being tested. Invited users have been provided with access to all features of the website and database. A general open access release is planned for later in 2011.

Features accessible after login
Example: Patterns of measles in three cities over four years: Why?

Opportunities:

• Detect historical spatial-temporal patterns

• Use time series decomposition techniques borrowed from the physical sciences (e.g., electrical engineering, oceanography)

• Build up body of "epidemic case law"
Pattern Detection
USA STATE “GEO-SPACE” MAP
NINE CENSUS DIVISIONS SHOWN AS DIFFERENT COLORS
USA STATE “INFLUENZA SPACE” MAP
SIMILARITY OF INFLUENZA TIME SERIES = CONTIGUITY IN “INFLUENZA SPACE”
USA STATE “INFLUENZA-SPACE” MAP
MOST POPULOUS STATES SHIFTED TO CENTER OF THE MAP
Pattern Detection
Decomposition of Thailand Dengue Time Series Using the Empiric Mode Decomposition
Country-level DHF epidemic wave structure in Thailand
Traveling waves in the occurrence of dengue hemorrhagic fever in Thailand
DEREK A.T. CUMMINGS, RAFAEL A. IRIZARRY, NORDEN E. HUANG, TIMOTHY P. ENDY,
ANANDA NISALAK, KUMNUAN UNGCHUSAK & DONALD S. BURKE
Spatial distribution of Basic Reproductive Number, $R_0$
Agent-based simulations
• Individuals commute to schools/workplaces with realistic distances based on travel data.
• Disease transmission probabilities depend on where transmission occurs, and who infects whom.
Agent-Based Models for Infectious Disease

Small-pox (Epstein et al 2002) 5000 agents

H5N1 Thailand (Ferguson et al 2005) 85M agents

Influenza Pandemic US (Ferguson et al, 2006) 273M agents

MIDAS H1N1pdm Model (Cooley, Brown et al 2009) Pandemic Planning

FRED: (Pitt, 2011) Dynamic Demographics, Health Behavior Models
FRED: Framework for Reconstruction of Epidemic Dynamics

- FRED Core
- Synthetic Population
- Pathogen Parameters
- Intervention Policies
- Behavior Change Model
- Analysis and Visualization Tools
- Request Queue
- FRED Simulation Engine
- Request DB
- Results DB
- FRED Web Service
- FRED Web Page
- FRED Client
- Simulation Information Management System (FRED SIMS)

Natural History, Viral Evolution
Vaccination
Antivirals
School Closure
Preventive Behaviors
Health Belief Model
Social Network Influences
FRANCIS
GAIA
Modeling mosquito transmission of disease

For Dengue (Aedes)

For Malaria (Anopheles)

“Computational ARthropod Agents”
Ratchaburi Thailand, site of the dengue vaccine efficacy trial
Pragmatics
Individual Health Behaviors in an Epidemic Model

Integrating FRANCIS

into FRED:
Individual Behaviors and Epidemic Dynamics

Cases → Decision to take action → Vaccination → Cases

Cases → Case
FRED: Framework for Reconstruction of Epidemic Dynamics

- Synthetic Population
- Simulation Engine
- Pathogen Parameters
- Analysis and Visualization

Behavior Change Model (Francis)

School → Household → Workplace → Hospital → Community

GAIA

- Sample Scenario
- Number of Infections/day
- Percent
- Days infectious

MIDAS
Models of Infectious Disease Agent Study
Integrating FRANCIS in FRED

• Agents in FRED may decide to adopt various *health behaviors*
  ▪ accept a vaccine, wear facemasks, etc

• Each behavior is controlled by a *cognitive model*, which may include:
  ▪ *Fixed* (always YES or always NO)
  ▪ *Stochastic decision* (flip a weighted coin)
  ▪ *Social conformity* (start with one inclination, and move toward equilibrium within social network)
  ▪ *Health Belief Model*
  ▪ *Trans-theoretical Model*, ...

• Individual heterogeneity among agents and behaviors
  ▪ may depend on demographic or socio-economic factors
Behavior Change Theories

• Health Belief Model
• Trans-Theoretical Model
• Social Cognitive Theory
• Theory of Planned Behavior
• Social Ecological Model
Health Belief Model Constructs and Sample implementations

**Perceived susceptibility:**
agent's estimate of prevalence

**Perceived severity:**
agent's estimate of case-fatality ratio

**Perceived benefits:**
agent's estimates of health care cost savings

**Perceived barriers:**
- cost of vaccine
- standing in line
- taking time off from work

Note that all these perceptions are strongly influenced by friends and family!
Modeling vaccine logistics  eg supply chains

“Highly Extensible Resource for Modeling Epidemic Supplies”
• Opportunity 1: Better equipment
• Opportunity 2: Better designed vaccines
• Opportunity 3: Better designed systems
• Opportunity 4: Better information
**HERMES VISION**

Create a *freely available and user-friendly software tool* for decision makers to generate an *interactive simulation model of any supply chain (= a virtual laboratory)*.
Health Service Delivery Location

Health care worker:
1. opens vaccine vial and reconstitutes with diluent (if required)
2. administers vaccine to client

Client arrival based on health system or census/birth data

Available = successful immunization
Not available = missed immunization opportunity

Example of outputs
Open vial wastage = unused doses in opened vials
Medical Waste

Vaccine availability = clients successfully immunized all clients arriving

Hermes
HERMES Can Address...

- Impact of introducing new technology
  - e.g., vaccines, storage, and monitoring
- Characteristics of vaccines and other technologies
  - e.g., vaccine vial size, vaccine thermostability, cold device capacity
- Configuration and operations of the supply chain
  - e.g., storage, shipping frequency, personnel, ordering policy
- Effects of differing conditions/circumstances
  - e.g., power outages, delays, inclement weather, limited access
- Investment or allocation of resources
  - e.g., adding refrigerators vs. increasing transport frequency
- Optimizing vaccine delivery
  - e.g., minimize cost, cost per outcome, maximize immunizations
Vaccine supply chains

• Currently, little visibility on stock, capacity, storage conditions.
  – E.g.: overstock and stock-outs at the same store, same time.
  – Reporting systems don’t always expose this.

• Transactional systems can help:
  – Acting on real-time information
  – Learning from actual consumption rates to forecast demand better
  – Improve accountability

• Facilitated by mobile networks, POS devices, barcodes.
Introducing new Rotavirus and Pneumococcal vaccines

- **Niger:** $\uparrow$ cost/dose administered largely because bottlenecks worsened
  - *Regional level removal can $\uparrow$ vaccine availability*
  - *Relieving bottlenecks requires $\uparrow$ capacity at multiple locations and junctures*

- **Vietnam:** $\downarrow$ cost/dose administered because supply chain can readily accommodate new vaccines (i.e., more doses administered)

- More efficient supply chain (e.g., Vietnam) may be more vulnerable to shipping delay effects
- Removing regional level can $\uparrow$ vulnerability to power outage effects
- Power outages at Niger periphery $\downarrow$ impact because many cold devices not dependent on electricity
The Pitt Public Health Dynamics Lab

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Modeling of Interventions
Modeling of Pragmatics
Cost Benefit Analyses
Decision
Modeling Steps

Software

Academic Disciplines

Systems Thinking
Data mining
Time series decomposition
Social networks
GIS
Game theory
Remote sensing
Machine learning & A.I.
High-performance computing

Info Sci
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Biostat
Math
Comp Sci
Indust Engin
Enviro Engin
Behavior
Law
Econ
Policy
Philos

Disciplines

Benter Foundation

CDC
Bill & Melinda Gates Foundation

National Institutes of Health

The Pitt Public Health Dynamics Lab

Clara
Francis
FRED
Tycho

Equation Based Models

Support / Clients

Modeling Steps

Software

Academic Disciplines
PHILOSOPHIZING ABOUT MODELS
Ceci n’est pas une pipe.
Ceci n’est pas une épidémie
Conclusions

Public Health Dynamics is the future of Public Health:
• Increasing data sources
• Increasing computational power
• New methodologies
  (many from physics, math, computer science)

Allows non-computationalist public health experts to conduct better research, provide better teaching, and give improved applied decision support

=> We are looking for collaborators to build the Vaccine Decision Support Meta-Model (and other public health dynamics models)
Vaccine Meta-Modeling: Hot topics

(1) Data Access

How to make Public Health Data conveniently accessible
USA data, Global data
Efficient digitization
Centralized or cloud storage?
Barriers to sharing

(2) Pattern Detection

How detect relationships in large data sets
How to discover patterns among multiple variables

(3) Equation-Based Models

How to build and parameterize equation-based models
How to fit models to real world data data
Vaccine Meta-Modeling : Hot topics (continued)

(4) Individual-based models

How to create modular, flexible, extensible, robust, efficient IBMs

How to build multi-scale agent based models

How to build mixed equation-based and individual based models

How to know when enough detail is enough

(5) Evaluation of interventions

How to sweep efficiently intervention decision space and optimize

How to store, manage, retrieve code and data

How to publish data, code, methods, and results for reproducibility
Vaccine Meta-Modeling: Hot topics (continued)

(6) “Pragmatics”

How to turn theoretical models into approximations of reality

How to model human behavior including choices, changes

(7) Cost benefit

What to optimize against: deaths, dollars, votes

How to determine “cost to whom”

(8) Decision

How to build a truly integrated “Meta-Model” of steps 1-7

How to give psychological ownership of the model to the decision-maker

How to calculate the value of extra information upstream for better decisions downstream
Core Members

John J. Grefenstette, PhD
Director and Member, PHDL
Professor, Department of Biostatistics

Willem G. van Panhuis, MD, PhD
Member, PHDL
Research Assistant Professor, Department of Epidemiology

Shawn T. Brown, PhD
Member, PHDL
Assistant Professor, Department of Biostatistics
Research Fellow, Pittsburgh Supercomputing Center

Hasan Guclu, PhD
Member, PHDL
Assistant Professor, Department of Biostatistics

Bruce Y. Lee, MD, MBA
Member, PHDL
Assistant Professor, Department of Medicine and Department of Biomedical Informatics

Eunha Shim, PhD
Member, PHDL
Assistant Professor, Department of Epidemiology
UNIVERSITY OF PITTSBURGH PUBLIC HEALTH DYNAMICS LABORATORY

Associate Members

Bryan A. Norman, PhD
Associate Member, PHDL
Associate Professor,
Department of Industrial Engineering

Gregory Cooper, MD, PhD
Associate Member, PHDL
Associate Professor,
Department of Biomedical Informatics

Ralph Roskies, PhD
Associate Member, PHDL
Professor, School of Arts and Sciences
Department of Physics and Astronomy
Scientific Co-Director,
Pittsburgh Supercomputing Center

Jayant Rajgopal, PhD
Associate Member, PHDL
Professor,
Department of Industrial Engineering

Michael M. Wagner, MD, PhD
Associate Member, PHDL
Associate Professor,
Department of Biomedical Informatics

Ty Ridenour, PhD
Associate Member, PHDL
Research Associate Professor,
Department of Pharmaceutical Sciences

Kim F. Wong, PhD
Associate Member, PHDL
University of Pittsburgh Center for
Simulation and Modeling

Levent Yilmaz, PhD
Associate Member, PHDL
University of Pittsburgh Center for
Simulation and Modeling
External Affiliates

Derek Cummings, PhD  
Affiliate Member, PHDL  
Johns Hopkins University

Josh Epstein, PhD  
Affiliate Member, PHDL  
Johns Hopkins University

Patrick Grim, PhD  
Affiliate Member, PHDL  
SUNY, Stony Brook

Roni Rosenfeld, PhD  
Affiliate Member, PHDL  
Carnegie Mellon University

Nathan Stone, PhD  
Affiliate Member, PHDL  
Pittsburgh Supercomputing Center

Chad Vizino  
Affiliate Member, PHDL  
Pittsburgh Supercomputing Center

Joel Welling, PhD  
Affiliate Member, PHDL  
Pittsburgh Supercomputing Center
END
Epidemic from Greek *epidemia*:

\[ epi = "upon" + demos = "the people" \]

Epidemiology

epidemic + *logy* “the study of”

Related word: democracy
HURRICANE IRENE (AL09)
Early-cycle track guidance valid 0600 UTC, 23 August 2011
$10^8$ m   Earth

$10^6$ m   Country

$10^4$ m   City

$10^2$ m   Village

$10^0$ m   Human

$10^{-2}$ Tonsil

$10^{-4}$ Lymph follicle

$10^{-6}$ Cell

$10^{-8}$ DNA

$10^{-10}$ Nucleotide

$10^{-12}$ X ray

$10^{-14}$ Atomic nucleus

“Systems Public Health”

Systems Biology
THE GRAND SCHEME OF THINGS:

YOU ARE HERE
PATTERN DETECTION
What is the Public Health Dynamics Laboratory?

A “collaboratorium” designed to catalyze systems thinking and computational modeling and simulation at the Graduate School of Public Health

And to facilitate interdisciplinary collaborations across other academic units:

The University of Pittsburgh
  • School of Medicine
  • School of Engineering
  • School of Information Sciences
  • Center for Simulation and Modeling

Pittsburgh Supercomputing Center
Carnegie Mellon University
and other institutions
Jay Forrester (1918- )
MIT Professor of Computer Science and Management
Founder of the field of System Dynamics

• "All decisions are made on the basis of models. Most models are in our heads. Mental models are not true and accurate images of our surroundings, but are only sets of assumptions and observations gained from experiences ... Computer simulation models can compensate for weaknesses in mental models" (Forrester, 1994).
CLARA is named after:

- Clara Southmayd Ludlow (1852-1924)
  - Entomologist
  - 1st female member of the American Society of Tropical Medicine