



Department of
Biomedical Informatics

BMI 500: Introduction to Ethical Data Science and Informatics

Lecture 11. An introduction to model-based machine learning

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November 7, 2025

Overview

- 1 The art of modeling
- 2 Model-based machine learning
- 3 Case study I: Model-based ML for bias removal and ethical AI
- 4 Case study II: epidemic disease spread modeling
 - Compartmental models
 - Agent-based models
- 5 Case study III: electrocardiogram modeling
- 6 The lab session

Outline

- 1 The art of modeling
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What is a model?

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An entity that resembles a system or object in certain aspects; but is easier to operate as compared to the original system.

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Forms of models

- Mathematical equations
- Software
- Synthetic time-series generators
- A firmware or hardware
- Another physical system
- etc.

or a combination of multiple forms....

Where to use models?

Where to use models?

Modeling applications

- ① Identification and better understanding of systems
- ② Simulation of a system's behavior; generating synthetic data resembling scarce or hardly achievable real data
- ③ Prediction of a system's future behavior
- ④ Problem solving and control, as the ultimate goal of modeling (but not always possible)

 From top to bottom the problem becomes more difficult.

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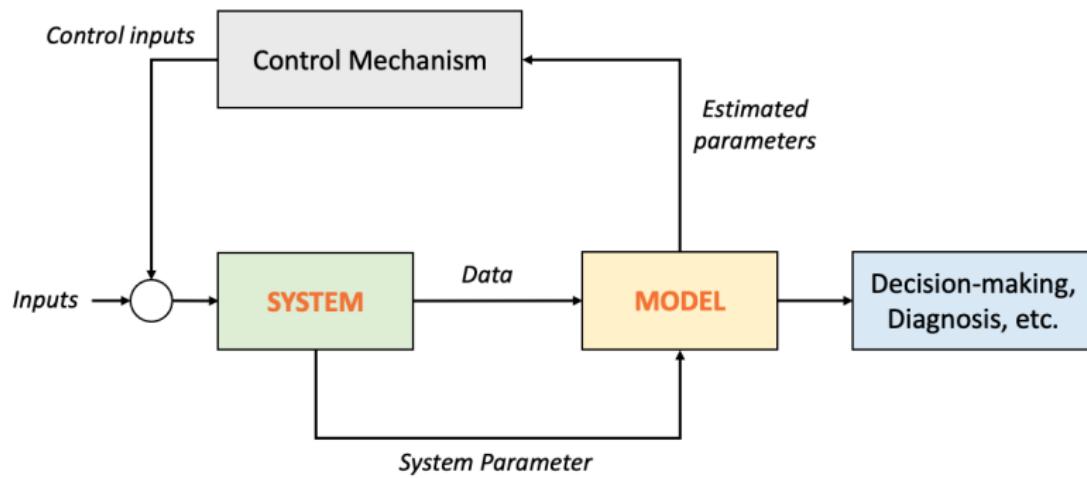
Disclaimer:

"All models are wrong; some are useful!"

— George Box

Modeling in practice

The big picture



Why use a model?

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Working with real systems is not always possible, for example:

- ① Optimizing the parameters of under-construction systems by trial and error (time-taking, expensive and impractical without a model)
- ② Testing drugs and new technologies on human/animal species (unethical)
- ③ Chemical and biological reactions (dangerous without a model)
- ④ Studying the formation of galaxies or natural species (impossible without a model)

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How to model and how to use models in machine learning?

Is the subject of this lecture.

Model types

Note

- Mental, lingual, physical, mathematical, etc.
- In our context, we are interested in mathematical models, or models that can be implemented as an algorithm or software for machine learning.

Introduction to modeling

(continued)

Modeling limitations

- Models are **not unique**; different models can co-exist for a single system;

Introduction to modeling

(continued)

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Introduction to modeling

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Introduction to modeling

(continued)

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Some models are only valid in certain levels of abstraction. Example:
The **diffusion law** is a macroscopic-level model, not a microscopic one.

Introduction to modeling

(continued)

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Modeling doctrine

A model should be ***as simple as possible, as complex as necessary***.

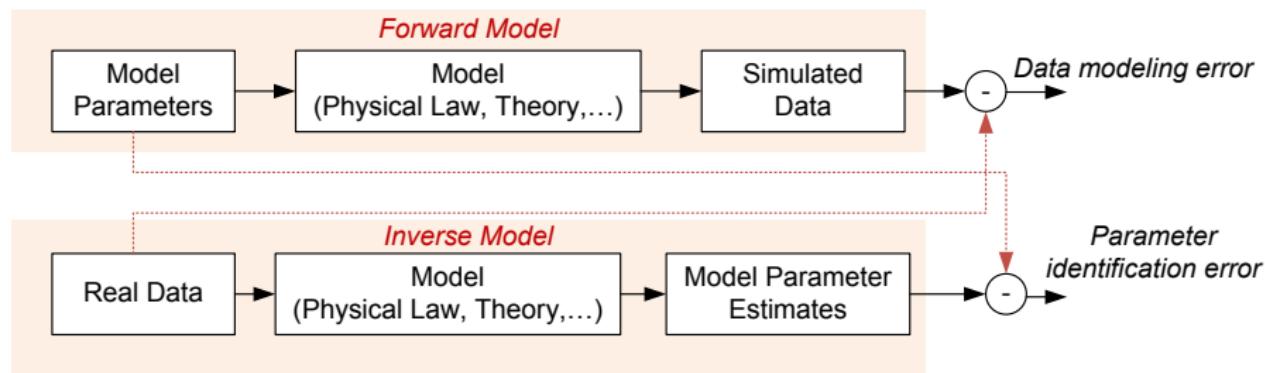
Introduction to modeling

(continued)

Modeling approaches

- **Forward:** from modeling to measurements/observations
 - **Inverse:** from measurements/observations to model parameters

 These approaches are not distinct; we iterate between forward and backward modeling to develop, tune and validate models



Introduction to modeling

(continued)

Example: Forward versus inverse modeling

Low-resolution brain electromagnetic tomography (LORETA) and its extensions:
sLORETA, eLORETA, etc. (Pascual-Marqui et al., 1994, 2002)

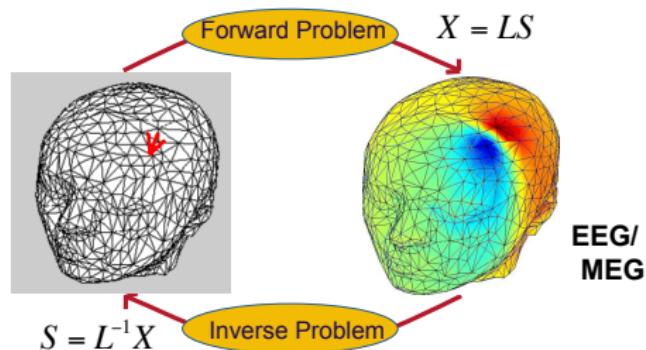


Figure: Adopted from: http://cfmriweb.ucsd.edu/ttliu/be280a_12/BE280A12_eeg5.pdf

Introduction to modeling

(continued)

Mathematical model types

- **Deterministic:** all the model elements (rules, equations and parameters) are deterministic, e.g., $x(t) = a \sin(\omega t + \phi)$ with deterministic parameters
- **Stochastic:** have some stochastic elements, e.g., $x(t) \sim \mathcal{N}(0, 1)$
- **Hybrid:** Partially deterministic and stochastic, e.g., $x(t) = a \sin(\omega t) + n(t)$

Introduction to modeling

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 Complex deterministic models are sometimes approximated by simple stochastic models

Example

The model

$x(t) = \sin(\omega t) + 0.01 \sin(2\omega t)^2 + 0.03 \sqrt{0.2 \sin(3\omega t) + 1} + \exp(-80.0t^2)$ can be approximated by $\tilde{x}(t) = \sin(\omega t) + n(t)$, where $n(t)$ is considered a stochastic term with a bounded variance used for modeling the minor terms of $x(t)$

Model construction

How to construct a mathematical model?

- **Evidence-based:** using existing models based on physical, biological or empirical laws (“*physics-informed*” modeling)
- **Data fitting:** fit a parametric model over observed data points
- **Hybrid:** combination of evidence-based and data fitting

Example: Evidence-based

Intramuscular injection of drugs and its diffusion in the body

Example: Data fitting

Training deep neural networks on biomedical data

Introduction to modeling

(continued)

Discussion

- All **physical laws** are in fact models for physical systems, for which counter examples have not yet been found, within a certain level of abstraction. **Examples:** 1) Kirchhoff voltage and current laws in lumped circuits vs. Maxwell's equations; 2) Newtonian mechanics vs. relativistic mechanics.

Introduction to modeling

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- Name a few well-known biologic and physiologic models. Which types of models are they?
- Name a few well-known economics laws. Which types of models are they?

Introduction to modeling

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Model-based machine learning

What is model-based machine learning?

Model-based (also known as **physics-informed**) machine learning integrates contextual knowledge of systems' properties/behaviors (physical, physiological, etc.) in forming machine learning models and their training on real-world data (Karniadakis et al., 2021).

REVIEWS



Physics-informed machine learning

George Em Karniadakis^{1,2✉}, Ioannis G. Kevrekidis^{3,4}, Lu Lu⁵, Paris Perdikaris⁶, Sifan Wang⁷ and Liu Yang^{8,1}

Abstract | Despite great progress in simulating multiphysics problems using the numerical discretization of partial differential equations (PDEs), one still cannot seamlessly incorporate noisy data into existing algorithms, mesh generation remains complex, and high-dimensional problems governed by parameterized PDEs cannot be tackled. Moreover, solving inverse problems with hidden physics is often prohibitively expensive and requires different formulations and elaborate computer codes. Machine learning has emerged as a promising alternative, but training deep neural networks requires big data, not always available for scientific problems. Instead, such networks can be trained from additional information obtained by enforcing the physical laws (for example, at

DOI: 10.1038/s42254-021-00314-5



Model-based machine learning

(continued)

Applications of model-based ML

- Ethical AI; acquiring data from living species should always be justified (and avoided as much as possible)

Model-based machine learning

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Model-based machine learning

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- Enforcing physical constraints in ML models

Model-based machine learning

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- Generating synthetic data for data augmentation: deep learning models, generative adversarial networks (GANs), etc.

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- Artificial patients and digital twins with applications in personal health information protection
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- Generating synthetic data for data augmentation: deep learning models, generative adversarial networks (GANs), etc.
- Data imbalance: generating synthetic data for abnormal and rare border cases that are not available or abundant in real-world datasets
- Hybrid physical-ML models: model what is known with maths, model the unknown (or complex) ones with machine and/or deep learning

How to use modeling in ML?

- We can get creative on where and how we use modeling in ML;
beyond skills, modeling is an art!
- We will study the a few use cases:
 - Incorporating models in ML training
 - Modeling for synthetic data generation and data augmentation
 - Modeling for prediction and control

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Bias in machine learning and AI

Research questions

- Do certain algorithms perform differently by age/sex/race?
- Do these biases differ by algorithm/model design metric?
- Can we mitigate algorithm biases?

Approaches

- ① Data imbalance correction techniques: resampling, class weighting, ensemble methods, cost-sensitive learning, etc.
- ② Optimizing ML models subject to health equity and reduced bias objective functions
- ③ Data augmentation with synthetic samples of the minority class

Case study

Journal of Electrocardiology 74 (2022) 5–9

Contents lists available at ScienceDirect

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journal homepage: www.jecgonline.com







Age, sex and race bias in automated arrhythmia detectors

Erick A. Perez Alday^{a,*}, Ali B. Rad^a, Matthew A. Reyna^a, Nadi Sadr^a, Annie Gu^a, Qiao Li^a, Mircea Dumitru^a, Joel Xue^{a,b}, Dave Albert^b, Reza Sameni^a, Gari D. Clifford^{a,c}

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ARTICLE INFO

Keywords:
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 Healthcare

ABSTRACT

Despite the recent explosion of machine learning applied to medical data, very few studies have examined algorithmic bias in any meaningful manner, comparing across algorithms, databases, and assessment metrics. In this study, we compared the biases in sex, age, and race of 56 algorithms on over 130,000 electrocardiograms (ECGs) using several metrics and propose a machine learning model design to reduce bias. Participants of the 2021 PhysioNet Challenge designed and implemented working, open-source algorithms to identify clinical diagnosis from 2- lead ECG recordings. We grouped the data from the training, validation, and test datasets by sex (male vs female), age (blinded by decade), and race (Asian, Black, White, and Other) whenever possible. We computed recording-wise accuracy, area under the receiver operating characteristic curve (AUROC), area under the precision recall curve (AUPRC), F-measure, and the Challenge Score for each of the 56 algorithms. The Mann-Whitney U and the Kruskal-Wallis tests assessed the performance differences of algorithms across these demographic groups. Group trends revealed similar values for the AUROC, AUPRC, and F-measure for both male and female groups across the training, validation, and test sets. However, recording-wise accuracies were 20% higher ($p < 0.01$) and the Challenge Score 12% lower ($p = 0.02$) for female subjects on the test set. AUPRC, F-measure, and the Challenge Score increased with age, while recording-wise accuracy and AUROC decreased with age. The results were similar for the training and test sets, but only recording-wise accuracy (12% decrease per decade, $p < 0.01$), Challenge Score (1% increase per decade, $p < 0.01$), and AUROC (1% decrease per decade, $p < 0.01$) were statistically different on the test set. We observed similar AUROC, AUPRC, Challenge Score, and F-

DOI: [10.1016/j.jelectrocard.2022.01.014](https://doi.org/10.1016/j.jelectrocard.2022.01.014)

Case study

(continued)

2021 PhysioNet Challenge

- The teams implemented open-source algorithms to identify 26 clinical diagnoses from 2-lead ECG recordings
- **Data:** 131,155 recordings from 9 databases, 4 countries, and 3 continents.
- 88,253 public for training, 6,630 hidden for validation, and 36,272 hidden for test

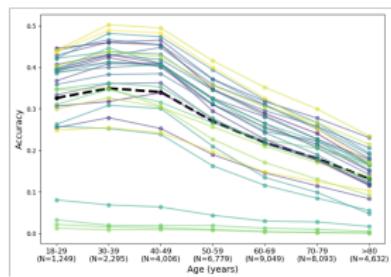
Method

- Grouped the datasets by sex (male vs female), age (binned by decade), and race (Asian, Black, White, and Other) whenever possible
- Reported standard ML metrics and the Challenge Score (a metric designed to account for misdiagnosis severity) per algorithm
- The Mann-Whitney U and the Kruskal-Wallis tests assessed the performance differences of algorithms across these demographic groups

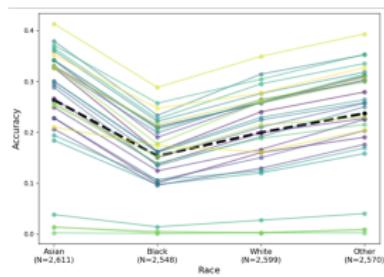
Case study

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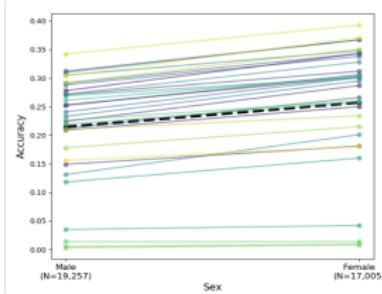
Results



(a) Age; ~12% decrease/decade, $p<0.01$



(b) Race; 39% difference, $p<0.01$



(c) Sex, 20% difference, $p<0.01$

Figure: Performance biases in the 2021 PhysioNet Challenge algorithms

Reduced-bias ML model design

Proposed scheme: For a parametric model/algorithm θ , we propose a regularized (or “bias-penalized”) optimization loss function:

$$C(\theta) = f(\theta) + \lambda\phi(\theta)$$

- $C(\theta)$: loss function
- $f(\theta)$: conventional machine-learning loss functions
- $\phi(\theta)$: bias metric
- λ : regularization (penalization) factor

For example:

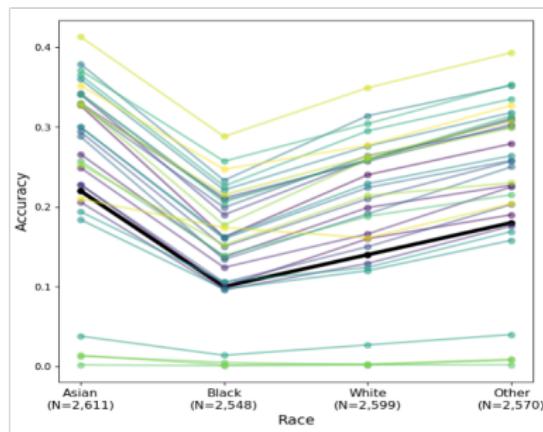
$$C = \text{Accuracy} + \lambda|\text{difference in accuracy between Black \& Asian subjects}|$$

Note: Constrained optimization generally degrades the optimization cost in favor of satisfying the additional constraint (a **reduced-bias** in this study)

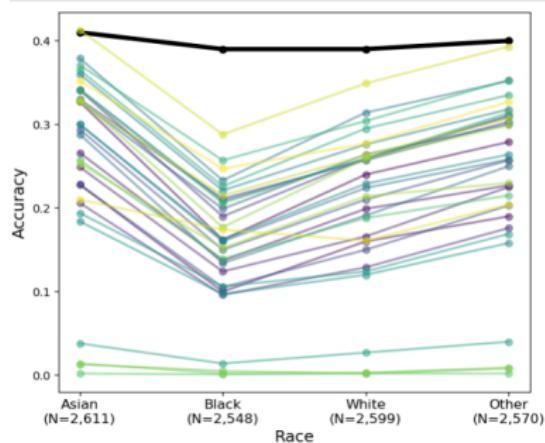
Reduced-bias ML model design

(continued)

Model accuracy before vs after bias reduction



(a) Before bias correction



(b) After bias correction

Figure: Performance biases of an ensemble model from the 2021 PhysioNet Challenge algorithms before (left) and after (right) bias correction

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Mathematical modeling of epidemic and pandemic diseases

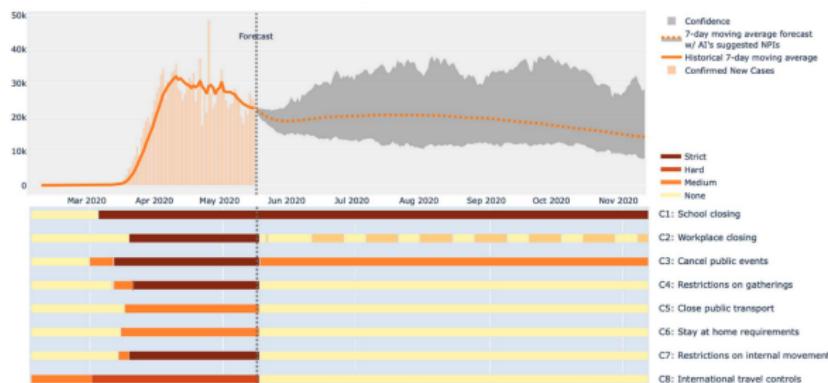
Pandemic modeling

- **Objective:** To model the outbreak and spread of pandemic diseases and to estimate the effectiveness of pandemic containing policies
- **Context:** Mathematical epidemiology; biological systems modeling; applied mathematics; computer simulation; optimal control theory

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Miikkulainen, et al. (2021). From Prediction to Prescription: Evolutionary Optimization of Nonpharmaceutical Interventions in the COVID-19 Pandemic. IEEE Tran. Evol. Comp. DOI: 10.1109/tevc.2021.3063217

Mathematical modeling of epidemic and pandemic diseases

(continued)

Major approaches

- Top-down (macro-level modeling): compartmental models and spatio-temporal compartmental models
 - **Tools:** ordinary differential equations, partial differential equations, dynamic systems, estimation theory

Mathematical modeling of epidemic and pandemic diseases

(continued)

Major approaches

- Top-down (macro-level modeling): compartmental models and spatio-temporal compartmental models
 - **Tools:** ordinary differential equations, partial differential equations, dynamic systems, estimation theory
- Bottom-up (micro-level modeling): modeling the activity of a population of individuals
 - **Tools:** agent-based methods, cellular automata and computerized simulations

The two methods can be combined in a hybrid model

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Case study

IEEE JOURNAL OF SELECTED TOPICS IN SIGNAL PROCESSING, VOL. 16, NO. 2, FEBRUARY 2022

307

Model-Based Prediction and Optimal Control of Pandemics by Non-Pharmaceutical Interventions

Reza Sameni , Senior Member, IEEE

Abstract—A model-based signal processing framework is proposed for pandemic trend forecasting and control, by using non-pharmaceutical interventions (NPI) at regional and country levels worldwide. The control objective is to prescribe quantifiable NPI strategies at different levels of stringency, which balance between human factors (such as new cases and death rates) and cost of intervention per region/country. Due to infrastructural disparities and differences in priorities of regions and countries, strategists are given the flexibility to weight between different NPIs and to select the desired balance between the human factor and overall NPI cost. The proposed framework is based on a *finite-horizon optimal control* (FHOC) formulation of the bi-objective problem and the FHOC is numerically solved by using an ad hoc *extended Kalman filtering/smoothing* framework for optimal NPI estimation and pandemic trend forecasting. The algorithm enables strategists to select the desired balance between the human factor and NPI cost with a set of weights and parameters. The parameters of the model are partially selected by epidemiological facts from COVID-19

identifying quantifiable *non-pharmaceutical intervention* (NPI) plans, with fact-based estimates of the impact and cost of each NPI [1], and 3) simulated multi-objective pandemic response strategies, which balance between NPI cost and effectiveness, to help governments and policymakers in resource allocation and fact-based decision making to control new pandemic waves.

In this context, NPIs refer to actions and policies adopted by individuals, authorities or governments that help slowing down the spread of epidemic diseases. Enforcement of social distancing, face covering, restrictions on social events and public transportation, etc. were among the NPIs that were experienced during the COVID-19 pandemic. NPIs are among the best ways of controlling pandemic diseases when vaccines or medications are not yet available.¹

During the COVID-19 pandemic, several attempts were made

DOI: 10.1109/JSTSP.2021.3129118

Compartmental modeling

Definition

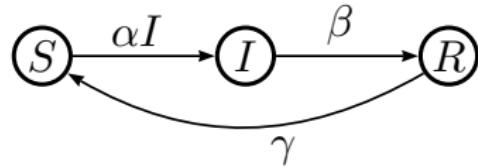
A **compartmental model** is a **weighted directed graph** representation of a linear or nonlinear **dynamic system**

Compartmental modeling

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A **compartmental model** is a **weighted directed graph** representation of a linear or nonlinear **dynamic system**

Example: An epidemic without life-time immunity



$$\begin{aligned}\frac{dS(t)}{dt} &= -\alpha S(t)I(t) + \gamma R(t) \\ \frac{dI(t)}{dt} &= \alpha S(t)I(t) - \beta I(t) \\ \frac{dR(t)}{dt} &= \beta I(t) - \gamma R(t)\end{aligned}$$

Compartmental modeling of epidemic diseased

Compartmental modeling steps

- ① Define the compartments: **homogeneous** non-overlapping partitions of the population with common properties (up to level of abstraction).
Ex: susceptible vs infected; benign vs malignant cells.

Compartmental modeling of epidemic diseased

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Ex: susceptible vs infected; benign vs malignant cells.
- ② Assign time variables of interest to the compartments
- ③ Write flow equations between the compartments (how individuals move between compartments)
- ④ Parameter selection: 1) fact-based, or 2) model fitting on real data

Compartmental modeling of epidemic diseased

Epidemic disease spread in large populations

A population of N individuals can be partitioned into **population fractions**:

- **Susceptibles**: $s(t)$
- **Exposed** (without symptoms): $e(t)$
- **Infected** (with symptom): $i(t)$
- **Recovered**: $r(t)$
- **Deceased**: $p(t)$

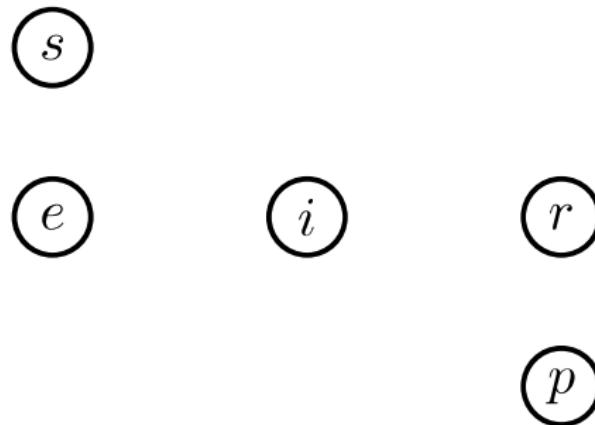
subject to $s(t) + e(t) + i(t) + r(t) + p(t) = 1$

Compartmental modeling of epidemic diseased

(Continued)

Example: A mortal non-immunizing susceptible-exposed-infected-recovered (SEIR) model

Draw the compartments:

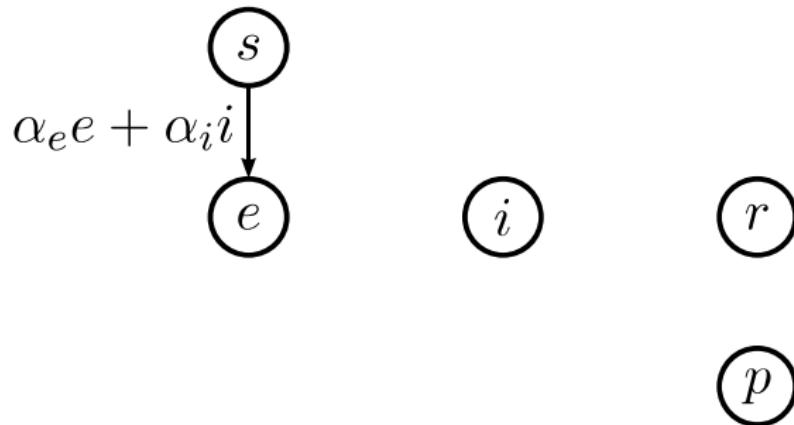


Compartmental modeling of epidemic diseased

(Continued)

Example: A mortal non-immunizing susceptible-exposed-infected-recovered (SEIR) model

Individuals are infected as they contact infected or exposed subjects.

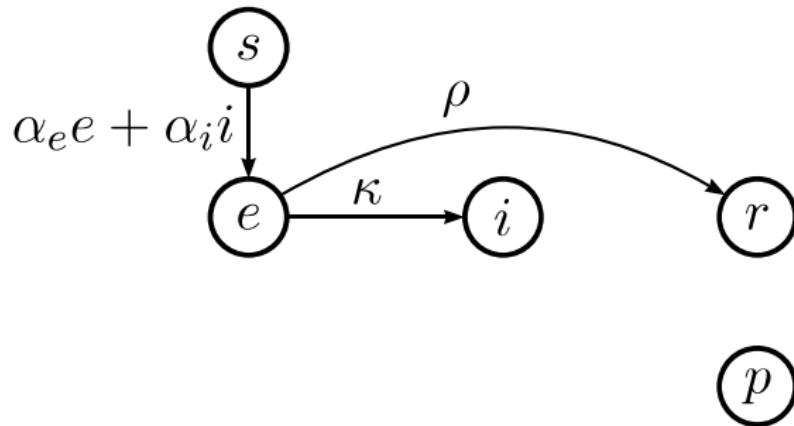


Compartmental modeling of epidemic diseased

(Continued)

Example: A mortal non-immunizing susceptible-exposed-infected-recovered (SEIR) model

The exposed either recover or become infected with symptoms.

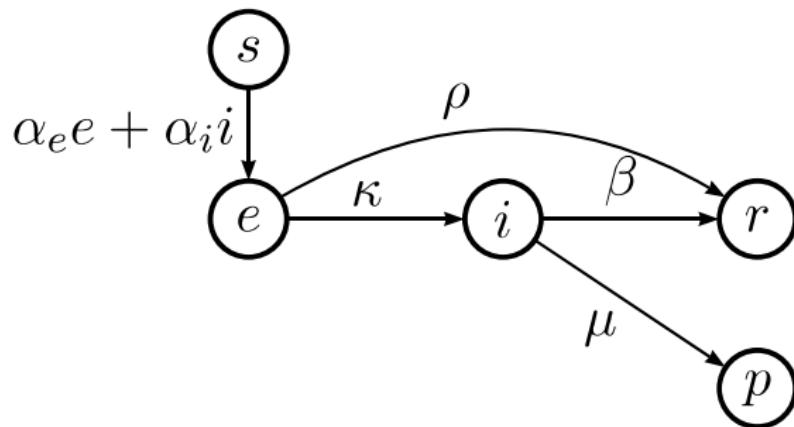


Compartmental modeling of epidemic diseased

(Continued)

Example: A mortal non-immunizing susceptible-exposed-infected-recovered (SEIR) model

The infected either recover or pass away.

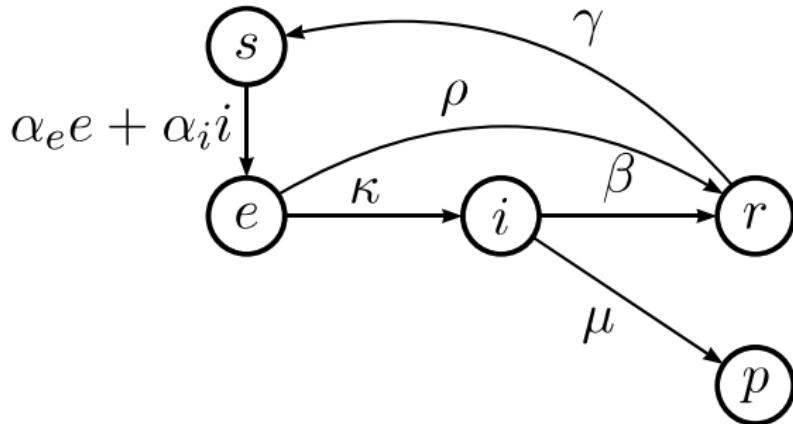


Compartmental modeling of epidemic diseased

(Continued)

Example: A mortal non-immunizing susceptible-exposed-infected-recovered (SEIR) model

The recovered may again become susceptible.

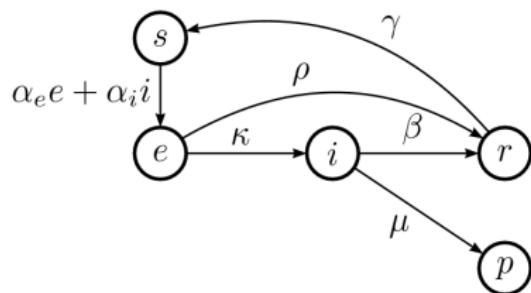


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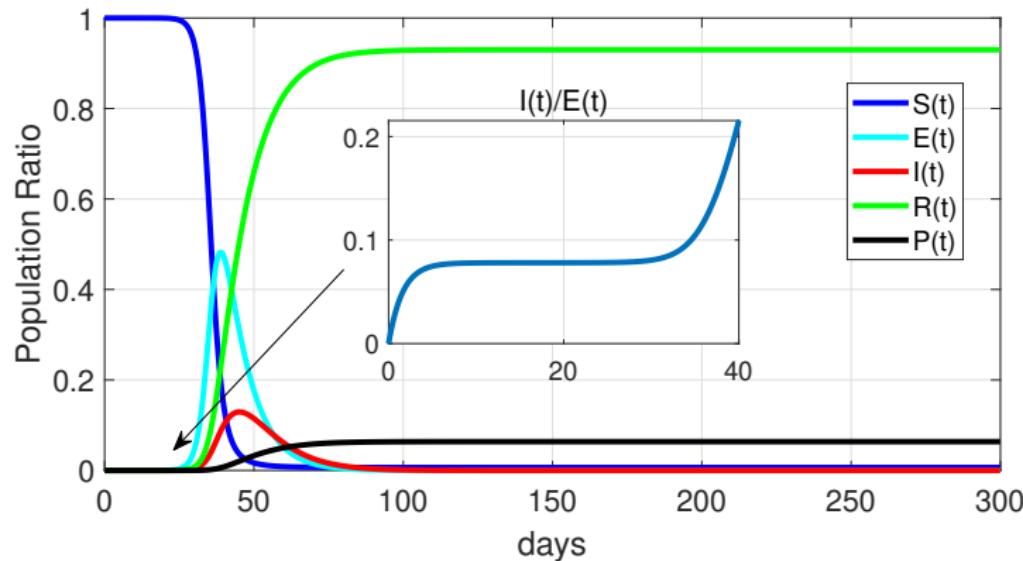
The full model and its corresponding dynamic equations, which can be numerically solved from **initial conditions** $[s(t_0), e(t_0), i(t_0), r(t_0), p(t_0)]$:



$$\begin{aligned}\frac{ds(t)}{dt} &= -\alpha_e s(t)e(t) - \alpha_i s(t)i(t) + \gamma r(t) \\ \frac{de(t)}{dt} &= \alpha_e s(t)e(t) + \alpha_i s(t)i(t) - \kappa e(t) - \rho e(t) \\ \frac{di(t)}{dt} &= \kappa e(t) - \beta i(t) - \mu i(t) \\ \frac{dr(t)}{dt} &= \beta i(t) + \rho e(t) - \gamma r(t) \\ \frac{dp(t)}{dt} &= \mu i(t)\end{aligned}$$

Typical solutions

The life-time immune case ($\gamma = 0$)



Compartmental modeling of epidemic diseased

(Continued)

What can we learn from compartmental models of the pandemic?

Compartmental modeling of epidemic diseased

(Continued)

What can we learn from compartmental models of the pandemic?

- ① The future trend of the pandemic can be estimated with quantitative confidence intervals

Compartmental modeling of epidemic diseased

(Continued)

What can we learn from compartmental models of the pandemic?

- ① The future trend of the pandemic can be estimated with quantitative confidence intervals
- ② The peak of the infected population can be estimated to avoid reaching the healthcare system break-point

Compartmental modeling of epidemic diseased

(Continued)

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Compartmental modeling of epidemic diseased

(Continued)

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- ④ Potential future outbreaks of the pandemic

Compartmental modeling of epidemic diseased

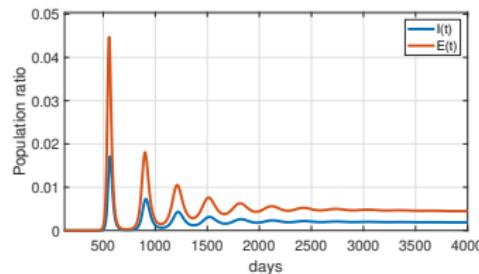
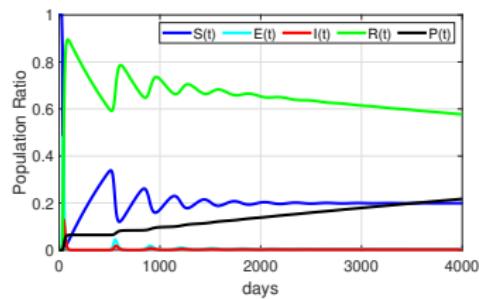
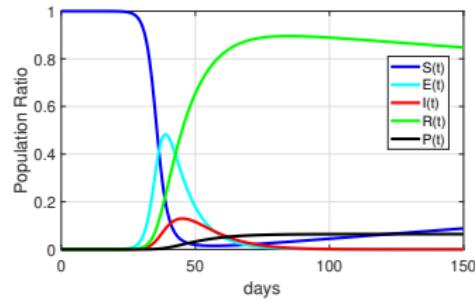
(Continued)

What can we learn from compartmental models of the pandemic?

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- ② The peak of the infected population can be estimated to avoid reaching the healthcare system break-point
- ③ The effect of quarantine, social distancing, lockdown, and reopening can be studied
- ④ Potential future outbreaks of the pandemic
- ⑤ The model accuracy and its consistency with real-world data

Typical solutions

Repeated pandemic waves ($\gamma \neq 0$)

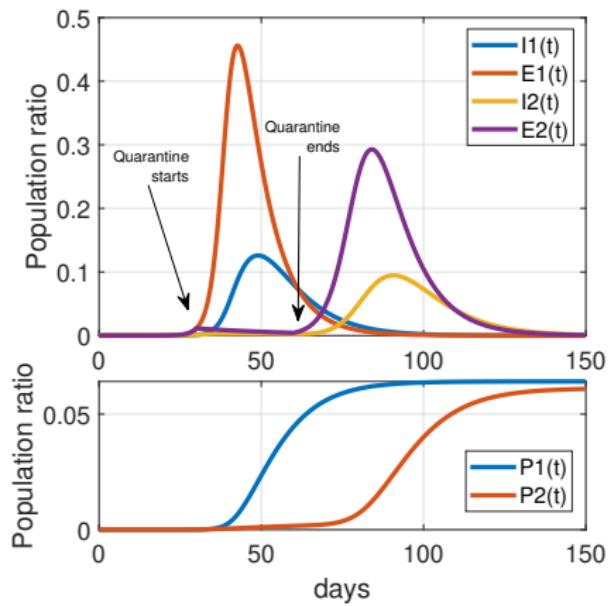


Sameni, R. (2020). Mathematical Modeling of Epidemic Diseases; A Case Study of the COVID-19 Coronavirus (Version 4). DOI: 10.48550/ARXIV.2003.11371

Typical solutions

(continued)

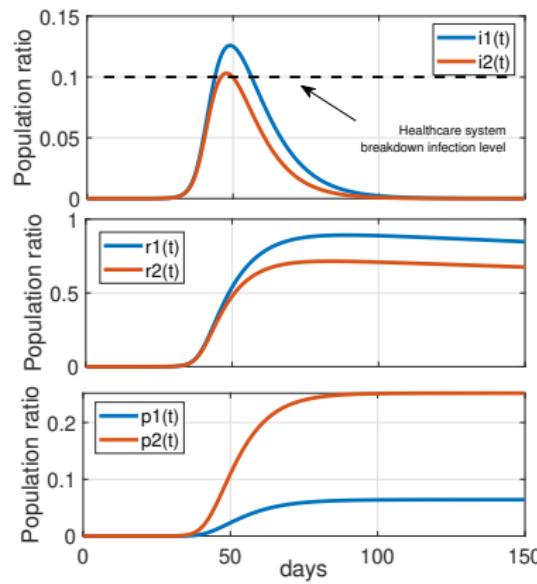
Insufficient lockdown periods



Typical solutions

(continued)

Healthcare system saturation and breakdown



Time-variant model parameters:

$$\beta(t) = (\beta_s - \beta_0)h(i(t)) + \beta_0$$

$$\mu(t) = (\mu_s - \mu_0)h(i(t)) + \mu_0$$

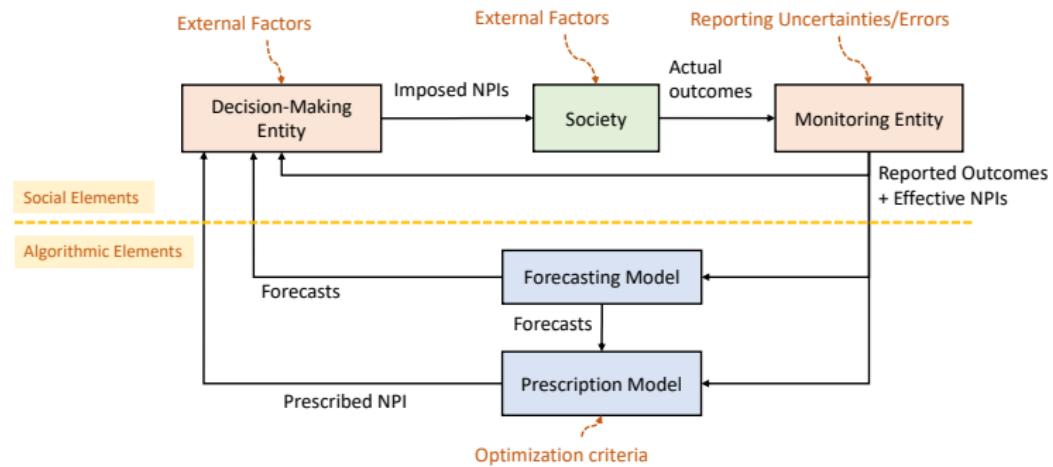
where

$$h(i) = \frac{1}{2}[1 + \tanh(\frac{i - i_0}{\sigma})]$$

Compartmental modeling of epidemic diseased

(Continued)

Application: Pandemic control by nonpharmaceutical interventions



Sameni, R. (2022). Model-Based Prediction and Optimal Control of Pandemics by Non-Pharmaceutical Interventions. In IEEE Journal of Selected Topics in Signal Processing. DOI: 10.1109/jstsp.2021.3129118

Compartmental modeling of epidemic diseased

(Continued)

Shortcomings of macro-level compartmental models

- ① Explicit modeling of individual behaviors. For example: “will I get COVID-19 if I go to a party?”

Compartmental modeling of epidemic diseased

(Continued)

Shortcomings of macro-level compartmental models

- ① Explicit modeling of individual behaviors. For example: “will I get COVID-19 if I go to a party?”
- ② Modeling family-level or community-level behavior

Compartmental modeling of epidemic diseased

(Continued)

Shortcomings of macro-level compartmental models

- ① Explicit modeling of individual behaviors. For example: “will I get COVID-19 if I go to a party?”
- ② Modeling family-level or community-level behavior
- ③ Modeling individual background diseases

Outline

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- 6 The lab session

Case study

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IEEE TRANSACTIONS ON EVOLUTIONARY COMPUTATION, VOL. 25, NO. 2, APRIL 2021

From Prediction to Prescription: Evolutionary Optimization of Nonpharmaceutical Interventions in the COVID-19 Pandemic

Risto Miikkulainen[✉], Fellow, IEEE, Olivier Francon, Elliot Meyerson, Xin Qiu, Darren Sargent, Elisa Canzani, and Babak Hodjat

Abstract—Several models have been developed to predict how the COVID-19 pandemic spreads, and how it could be contained with nonpharmaceutical interventions, such as social distancing restrictions and school and business closures. This article demonstrates how evolutionary AI can be used to facilitate the next step, i.e., determining most effective intervention strategies automatically. Through evolutionary surrogate-assisted prescription, it is possible to generate a large number of candidate strategies and evaluate them with predictive models. In principle, strategies can be customized for different countries and locales, and balance the need to contain the pandemic and the need to minimize their economic impact. Early experiments suggest that workplace

Most of the modeling efforts so far have been based on traditional epidemiological methods, such as compartmental models [1]. Such models can be used to predict the spread of the disease, assuming a few parameters, such as the basic reproduction number R_0 can be estimated accurately. New ideas have also emerged, including using cell-phone data to measure social distancing [2]. These models have been extended with NPIs by modifying the transmission rates: each NPI is assumed to reduce the transmission rate by a certain amount [3]–[5]. Such models have received a lot of attention:

DOI: 10.1109/TEVC.2021.3063217

Micro-level modeling of epidemic diseases

Agent-based model steps

- ① Individuals (or particles in the broader context) are modeled as abstract entities with certain attributes.

Micro-level modeling of epidemic diseases

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Micro-level modeling of epidemic diseases

Agent-based model steps

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- ③ A large population of individuals are simulated, as they randomly interact with one another in the environment and their health condition switches (statistically)

Micro-level modeling of epidemic diseases

Agent-based model steps

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- ③ A large population of individuals are simulated, as they randomly interact with one another in the environment and their health condition switches (statistically)
- ④ Population-wised behavior is estimated through Monte Carlo simulation and the marginalized behavior of the agents (individuals, particles, etc.)
- ⑤ Marginal statistics (e.g. the number of exposed, infected, recovered, etc.) are calculated over the entire population

Micro-level modeling of epidemic diseases

Agent-based model elements for pandemic modeling

- **Attributes:** age, gender, nationality, infection status, background illness, social group, environment density, chance of illness, etc.
- **Behaviors:** going to work/school, shaking hands, traveling with public transport, going to markets, etc.
- **Environment:** school, office, market, bus, train, etc.

Micro-level modeling of epidemic diseases

(continued)

Example: Implementation of agent-based models; an object-oriented approach

The screenshot shows a code editor window with three tabs at the top: "Environment.h", "Individual.h", and "Epidemiology.cpp". The "Epidemiology.cpp" tab is active. The code is as follows:

```
Environment.h    Individual.h  x  Epidemiology.cpp
Epidemiology      (Global Scope)

class Individual
{
    friend class Environment;
private:
    Gender gender;
    double age;
    double height;
    double weight;

    Nationality nationality;
    Country country;
    Location location_initial;
    Location location;
    DisplacementMatrix displacement_matrix;

    HealthRecord healthrecord;
    InfectionStatus healthstatus;
    InfectionLevels healthlevel;
public:

    int Move();
    friend int InteractBilateral(Individual indv1, Individual indv2);
    friend int ImpactUnilateral(Individual indv_source, Individual indv_destination);
    int ImpactEnvironment(Environment env);
    int GetImpactedByEnvironment(Environment env);
}
```

The status bar at the bottom indicates "83 %", "No issues found", "Ln: 40", and "Ch: 1". Below the status bar is a toolbar with various icons.

Micro-level modeling of epidemic diseases

(continued)

Illustration of an agent-based environment

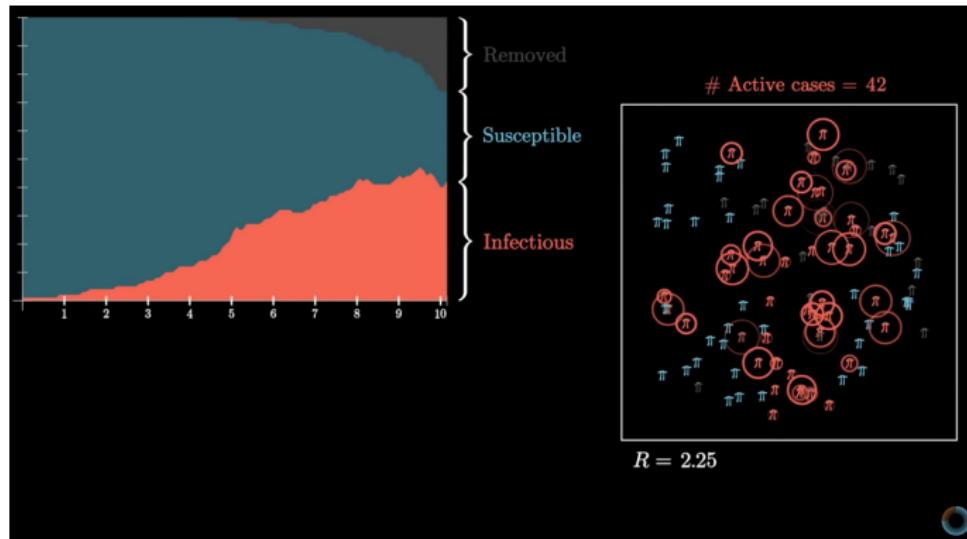


Figure: adopted from <https://youtu.be/gxAa02rsdIs>

Micro-level modeling of epidemic diseases

(continued)

Pros

- ① The provided information is low-level and higher in resolution (at individual, family, and community-level)
- ② Can result in guidelines for individuals, families, policymakers, etc.
- ③ Is more graphical and more convincing for decision-makers!

Micro-level modeling of epidemic diseases

(continued)

Pros

- ① The provided information is low-level and higher in resolution (at individual, family, and community-level)
- ② Can result in guidelines for individuals, families, policymakers, etc.
- ③ Is more graphical and more convincing for decision-makers!

Cons

- ① There are more parameters; selection and tuning of individual parameters is more difficult than in macro-level models
- ② Mathematical proofs for identifiability, stability, and confidence intervals are no longer achievable
- ③ The simulations can be very susceptible to initial conditions and simulation **seeds**

Resources and further reading

Resources

- 1 The theoretical details of this research: <https://arxiv.org/abs/2003.11371>
- 2 The source codes of this research: <https://github.com/rsameni/EpidemicModeling.git>
- 3 COVID-19 real-time data: <https://www.worldometers.info/coronavirus/>
- 4 Johns Hopkins University's CSSE Git repository: <https://github.com/CSSEGISandData/COVID-19>

Further reading

- 1 Epidemic models: Brauer et al. (2012)
- 2 Biological systems modeling: Haefner (2005); de Vries et al. (2006)
- 3 The stochastic aspects of mathematical epidemiology: Britton (2010); Pellis et al. (2012); Brauer et al. (2012); Miller (2019)
- 4 Optimal estimation and Kalman filtering: Grewal & Andrews (2001)
- 5 Linear systems theory: Kailath (1980)
- 6 An interesting video on agent-based methods (the micro-modeling approach): <https://youtu.be/gxAa02rsdIs>

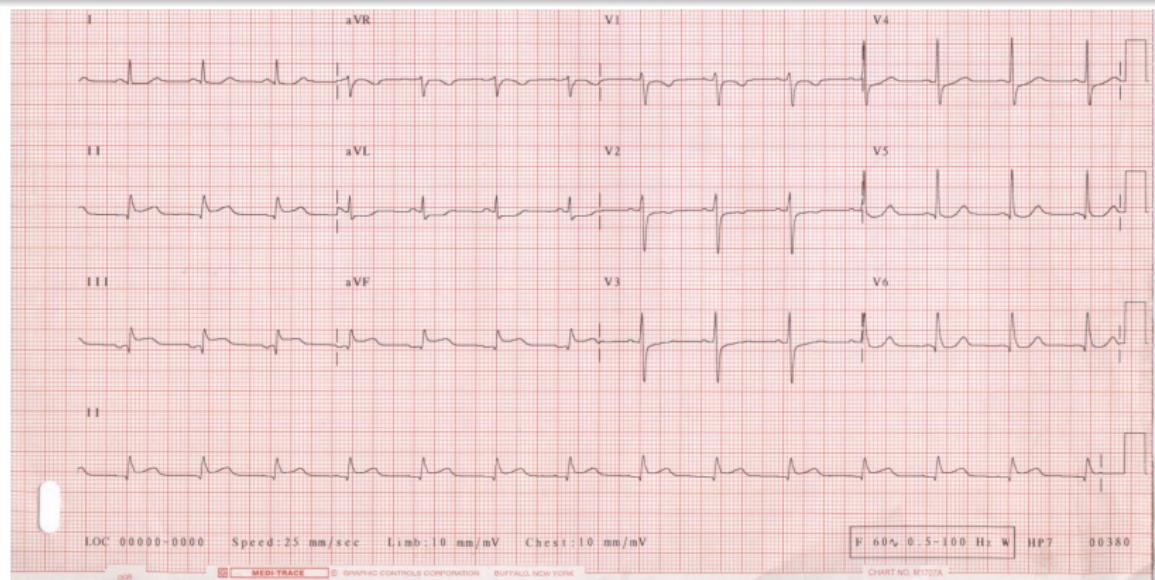
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Electrocardiogram modeling

Objective

Model the temporal waveform of cardiac signals to produce normal and abnormal electrocardiogram (ECG) data with realistic morphology, heart rates and noises.



Glenlarson, CC BY-SA 3.0



Electrocardiogram modeling

Motivation

- Better understanding of the electrical cardiac function
- Generate synthetic ECG for evaluating biomedical signal processing and machine learning algorithms
- Generating typical and extreme ECG cases for testing ECG devices
- Generating ECG for training data greedy deep learning models
- Dynamic models can be used to develop filtering and forecasting algorithms, e.g. *Kalman filters*

Electrocardiogram modeling

(continued)

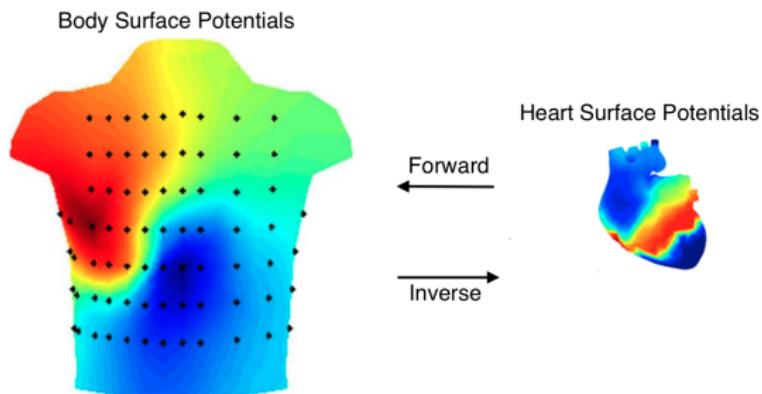
How to model the ECG

- ① ECG modeling can be studied in various levels of abstraction, ranging from low-level neural models to high-level body surface potential models.
- ② In many applications, macroscopic models that mimic the cardiac signal morphology and heart-rate are required
- ③ Similar models can be used for adult and fetal ECG and magnetocardiogram (MCG), in normal and abnormal cases
- ④ The model should also be linked to system-level physiological models of cardiac signals, which consider physiological factors that influence the heart rate and ECG morphology

Forward-backward body potential modeling

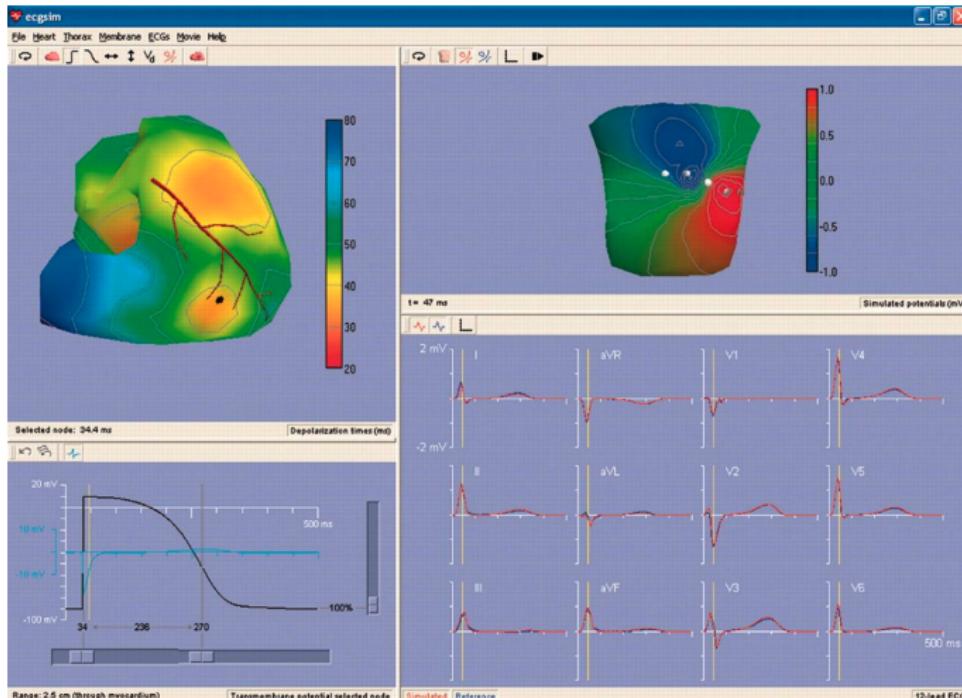
Body/heart surface potential modeling

The forward and inverse problems of body surface and myocardial surface potential estimation is ill-posed, but may be solved by **finite and boundary element** methods subject to regularity constraints.



Adapted from: Yao, B., & Yang, H. (2016). Physics-driven Spatiotemporal Regularization for High-dimensional Predictive Modeling: A Novel Approach to Solve the Inverse ECG Problem. *Scientific Reports*. DOI: 10.1038/srep39012

Body surface and myocardial surface potential models



Adopted from: van Oosterom, A. and Oostendorp T.F (2004). ECGSIM: an interactive tool for studying the genesis of QRST waveforms. Heart. BMJ. DOI: 10.1136/heart.2003.014662

Morphological ECG waveform modeling

Motivation

- Finite and boundary element methods for ECG modeling and simulation are computationally intense and are over-parameterized.
- Alternatively, one may model the body surface ECG as a pseudo-periodic waveform using mathematical functions
- The limited model parameters can be identified by data fitting

A dynamic model for ECG generation

IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 50, NO. 3, MARCH 2003

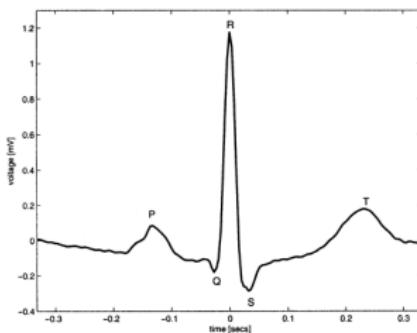
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A Dynamical Model for Generating Synthetic Electrocardiogram Signals

Patrick E. McSharry*, Gari D. Clifford, Lionel Tarassenko, and Leonard A. Smith

Abstract—A dynamical model based on three coupled ordinary differential equations is introduced which is capable of generating realistic synthetic electrocardiogram (ECG) signals. The operator can specify the mean and standard deviation of the heart rate, the morphology of the PQRST cycle, and the power spectrum of the RR tachogram. In particular, both respiratory sinus arrhythmia at the high frequencies (HFs) and Mayer waves at the low frequencies (LFs) together with the LF/HF ratio are incorporated in the model. Much of the beat-to-beat variation in morphology and timing of the human ECG, including QT dispersion and R-peak amplitude modulation are shown to result. This model may be employed to assess biomedical signal processing techniques which are used to compute clinical statistics from the ECG.

Index Terms—Dynamical model, heart rate variability (HRV), Mayer waves, QRS morphology, QT-interval, respiratory sinus arrhythmia, RR-interval, RR tachogram, synthetic ECG.



McSharry, P. E., Clifford, G. D., Tarassenko, L., & Smith, L. A. (2003). A dynamical model for generating synthetic electrocardiogram signals. In IEEE Transactions on Biomedical Engineering. DOI: 10.1109/tbme.2003.808805

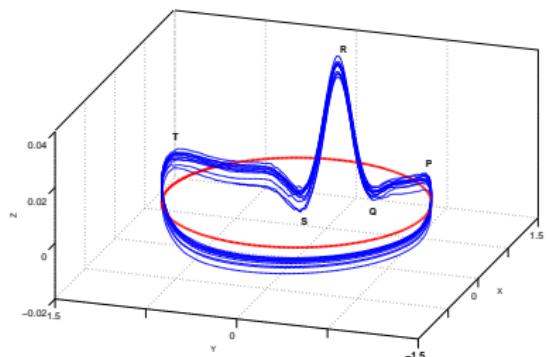
McSharry-Clifford's model (McSharry et al., 2003)

$$\begin{cases} \frac{dx}{dt} = \rho x - \omega y \\ \frac{dy}{dt} = \rho y + \omega x \\ \frac{dz}{dt} = -\sum_{i \in \{P, Q, R, S, T\}} a_i \Delta \theta_i \exp\left(-\frac{\Delta \theta_i^2}{2b_i^2}\right) - (z - z_0) \end{cases}$$

- x , y , and z are state variables, $\rho = 1 - \sqrt{x^2 + y^2}$, $\Delta \theta_i = (\theta - \theta_i) \bmod (2\pi)$, $\theta = \text{atan2}(y, x)$ is the four quadrant arctangent, and ω is the angular velocity of the trajectory as it moves around the limit cycle in the $x - y$ plane.
- a_i , b_i , and θ_i correspond to the amplitude, width, and center parameters of the Gaussian functions.
- The baseline wander of the ECG is modeled with the parameter z_0 , considered as a relatively low amplitude sinusoidal component coupled with the respiratory frequency.

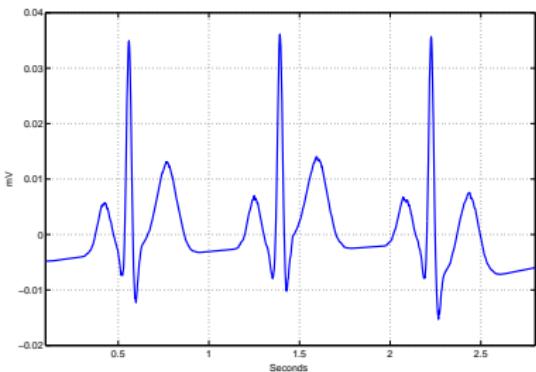
McSharry-Clifford's model (McSharry et al., 2003)

(continued)



(a) 3D trajectory of the ECG model.

The red line corresponds with the unit circle in the $x - y$ plane



(b) Projection of the 3D trajectory onto the z -axis

Figure: 3D representation and 1D ECG representation of the dynamic model by McSharry et al. (2003)

The simplified McSharry-Clifford's model in discrete form (Sameni et al., 2007b)

$$\begin{cases} \theta_{k+1} = (\theta_k + \omega\delta) \bmod (2\pi) \\ z_{k+1} = -\sum_i \delta \frac{\alpha_i \omega}{b_i^2} \Delta\theta_i \exp\left(-\frac{\Delta\theta_i^2}{2b_i^2}\right) + z_k + \eta \end{cases}$$

- $\Delta\theta_i = (\theta_k - \theta_i) \bmod (2\pi)$, η is a random additive noise that models the inaccuracies of the dynamic model (including the baseline wander)
- The summation is taken over the number of Gaussian functions used for modeling the shape of a desired ECG.
- Due to the *universal approximation* property of Gaussian functions, any smooth waveform can be approximated by using a sufficient number of Gaussians

Vectorcardiogram modeling (Sameni et al., 2007a) |

$$\dot{\theta} = \omega$$

$$\dot{x} = - \sum_i \frac{\alpha_i^x \omega}{(b_i^x)^2} \Delta\theta_i^x \exp\left[-\frac{(\Delta\theta_i^x)^2}{2(b_i^x)^2}\right]$$

$$\dot{y} = - \sum_i \frac{\alpha_i^y \omega}{(b_i^y)^2} \Delta\theta_i^y \exp\left[-\frac{(\Delta\theta_i^y)^2}{2(b_i^y)^2}\right]$$

$$\dot{z} = - \sum_i \frac{\alpha_i^z \omega}{(b_i^z)^2} \Delta\theta_i^z \exp\left[-\frac{(\Delta\theta_i^z)^2}{2(b_i^z)^2}\right]$$

$\Delta\theta_i^x = (\theta - \theta_i^x) \bmod (2\pi)$, $\Delta\theta_i^y = (\theta - \theta_i^y) \bmod (2\pi)$, $\Delta\theta_i^z = (\theta - \theta_i^z) \bmod (2\pi)$, and $\omega = 2\pi f$, f is the beat-to-beat heart rate in Hz.



By adding stochastic deviations to the parameters of McSharry-Clifford's model and its extensions, we can generate more realistic cardiac dipoles with inter-beat variations.

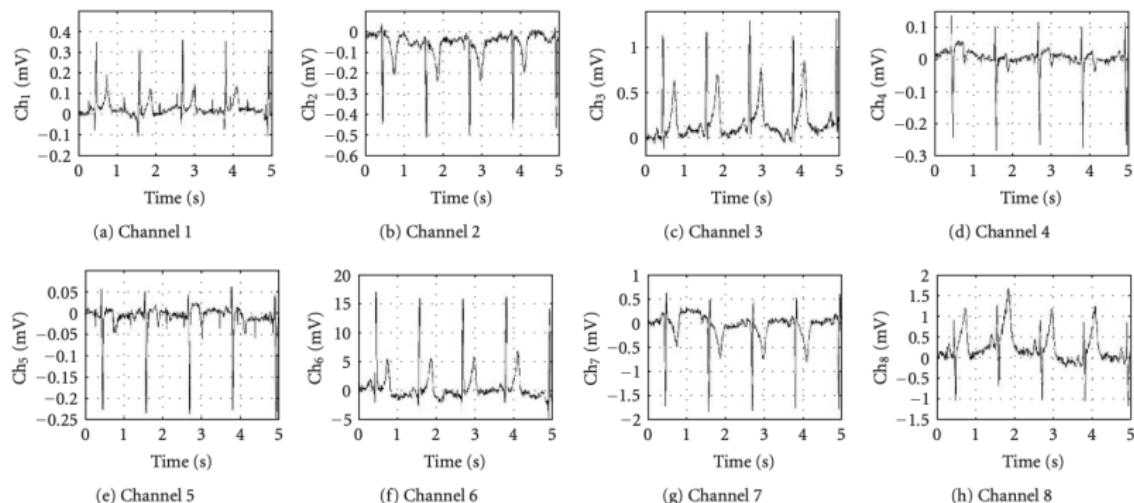
Multi-channel ECG generation with realistic noise (Sameni et al., 2007a)

$$ECG(t) = H \cdot R \cdot \Lambda \cdot s(t) + W(t)$$

- $ECG(t)_{N \times 1}$ is a vector of the ECG channels recorded from N leads, $s(t)_{3 \times 1} = [x(t), y(t), z(t)]^T$ contains the three components of the dipole vector $\mathbf{d}(t)$, $H_{N \times 3}$ corresponds to the body volume conductor model (as for the Dower transformation matrix), $\Lambda_{3 \times 3} = \text{diag}(\lambda_x, \lambda_y, \lambda_z)$ is a diagonal matrix corresponding to the scaling of the dipole in each of the x , y , and z directions, $R_{3 \times 3}$ is the rotation matrix for the dipole vector, and $W(t)_{N \times 1}$ is the noise in each of the N ECG channels.
- **Note:** H , R , and Λ are generally functions of time.

Multi-channel ECG generation with realistic noise (Sameni et al., 2007a)

(continued)



Sameni, R., Clifford, G. D., Jutten, C., & Shamsollahi, M. B. (2007). Multichannel ECG and Noise Modeling: Application to Maternal and Fetal ECG Signals. In EURASIP Journal on Advances in Signal Processing. DOI: 10.1155/2007/43407

Joint maternal and fetal ECG model (Sameni et al., 2007a):

$$X(t) = H_m \cdot R_m \cdot \Lambda_m \cdot s_m(t) + H_f \cdot R_f \cdot \Lambda_f \cdot s_f(t) + W(t)$$

- Subscripts m and f refer to the mother and the fetus, respectively.
- H_m , H_f , R_m , R_f , Λ_m and, Λ_f are body volume conduction, rotation and scaling matrices
- R_f models the relative position of the fetus with respect to the axes of the maternal body, enabling us to model the fetus in the different typical positions: *vertex* (fetal head-down) or *breech* (fetal head-up).
- $s_f(t) = [x_f(t), y_f(t), z_f(t)]^T$ is a canonical representation of the fetal dipole vector with respect to the fetal body axes.

Joint maternal and fetal ECG model (Sameni et al., 2007a):

II

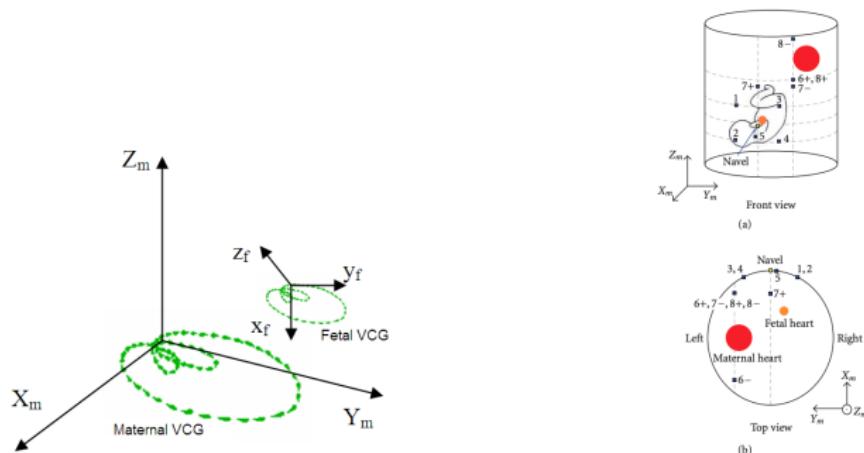


Figure: (left) Illustration of the fetal and maternal VCGs vs. their body coordinates; (right) Model of the maternal torso, with the locations of the maternal and fetal hearts and the simulated electrode configurations

Stochastic ECG models

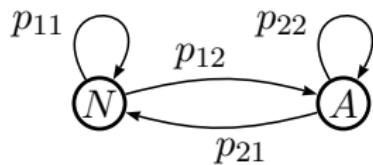
We can add stochastic aspects to the model:

- Beat-to-beat variations of the ECG morphology
- Natural beat-to-beat **heart rate variability** (HRV)
- Morphological variations due to occasional ectopic beats and arrhythmia
- Heart rate variability due to physical activity and cardiac abnormalities such as Tachycardia and Bradycardia

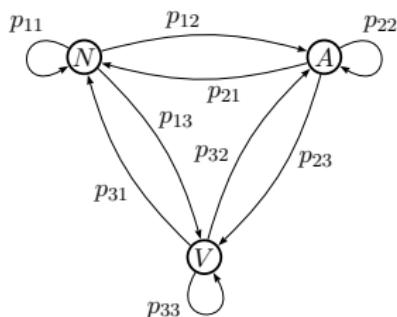


Markov models are useful tools for modeling beat-wise variation.

Abnormal ECG modeling with Markov models (Clifford et al., 2010): I



(a) State transition graph between normal (N) and abnormal (A) beats using a first-order Markov chain. The graph can be extended to more abnormal beat types.



(b) State transition graph between normal (A), abnormal (B), and ectopic (V) beats using a first-order Markov chain.

Figure: Using Markov chains to model the state transition between a) normal and abnormal, or b) normal, abnormal and ectopic beats

Abnormal ECG modeling with Markov models (Clifford et al., 2010): II

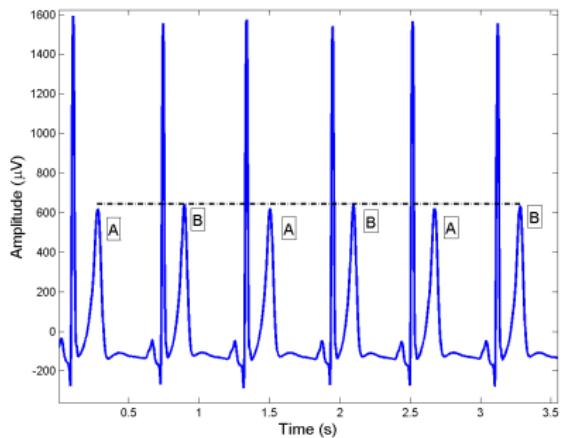


Figure: Typical alternating 'ABAB' TWA pattern generated from our model.

Abnormal ECG modeling with Markov models (Clifford et al., 2010): III

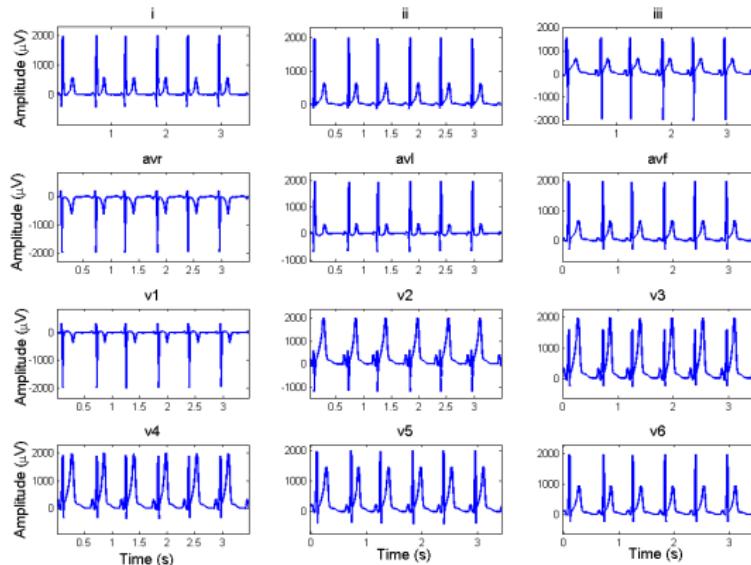


Figure: Example of 12 lead ECG with T-wave alternans.

Abnormal ECG modeling with Markov models (Clifford et al., 2010): IV

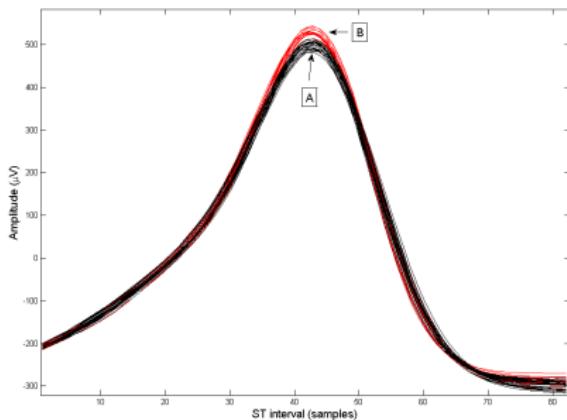
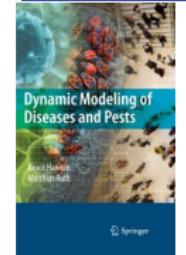
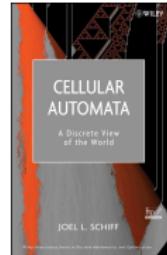
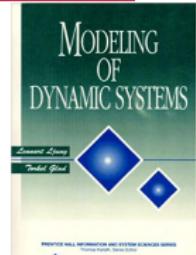
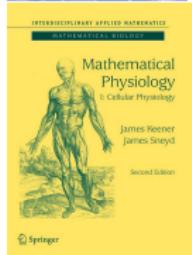
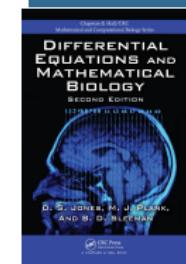
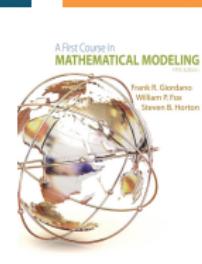
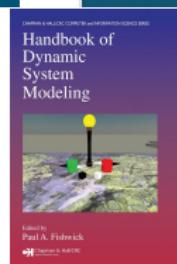
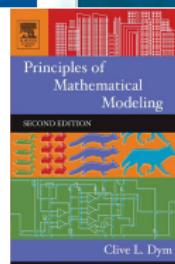
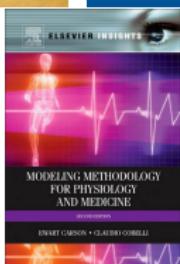
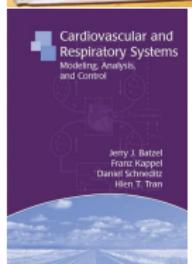
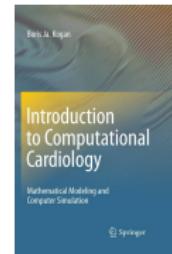
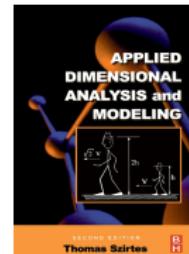
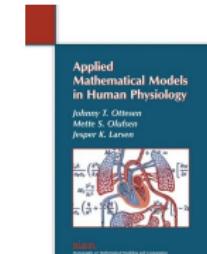
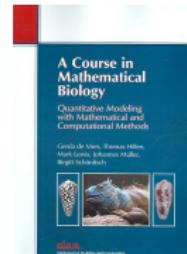
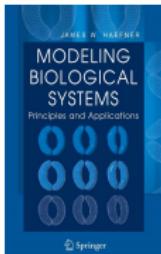
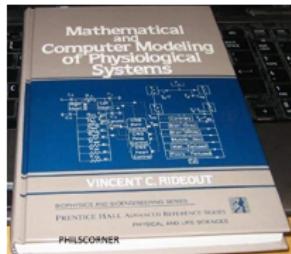


Figure: Multiple ST-T segments from two beat classes taken from one of the VCG projections. Class A beats are black and class B beats are red.

Text books on modeling



Outline

- 1 The art of modeling
- 2 Model-based machine learning
- 3 Case study I: Model-based ML for bias removal and ethical AI
- 4 Case study II: epidemic disease spread modeling
 - Compartmental models
 - Agent-based models
- 5 Case study III: electrocardiogram modeling
- 6 The lab session

Lab session source codes

Requirements

- Clone the **staging** branch of **the open-source electrophysiological toolbox (OSET)**:
<https://github.com/alphanumericslab/OSET.git>
- Clone the open-access repository for the mathematical modeling of epidemic diseases:
<https://github.com/alphanumericslab/EpidemicModeling>

Sample scripts on modeling with applications

Epidemic spread modeling and data for research

https://youtu.be/gxAaO2rsdIs	A video on agent-based methods (the micro-modeling approach)
https://www.worldometers.info/coronavirus/	COVID-19 real-time data
https://github.com/CSSEGISandData/COVID-19	Johns Hopkins University's CSSE Git repository
<code>testPrescribeXPRIIZE02.m</code>	Pandemic optimal control by non-pharmaceutical interventions
https://github.com/alphanumericslab/EpidemicModeling/	Epidemic modeling tools and sample codes

ECG and noise modeling with applications

OSET ECG generators	Generates synthetic ECG
AFib generators	Model for Simulating ECG and PPG Signals with Arrhythmia Episodes

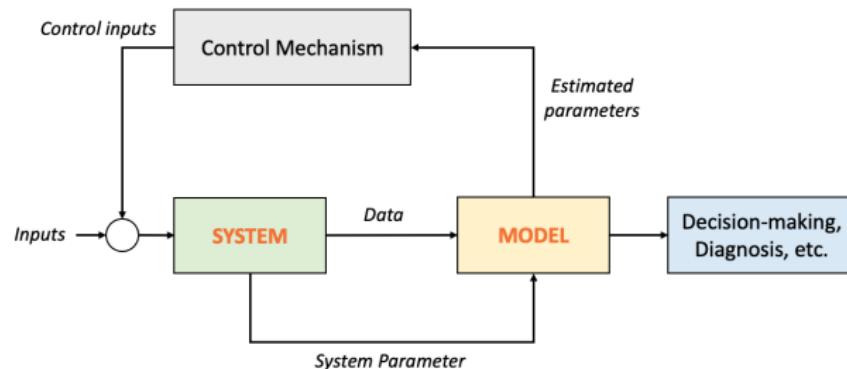
Thank you! Questions?

Part II

Appendices

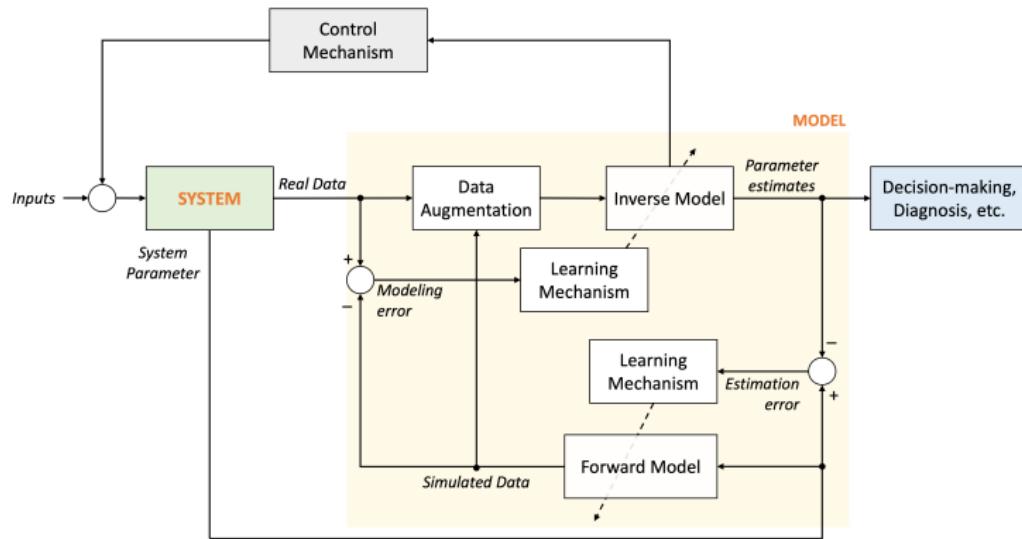
Modeling in machine learning

The big picture (from slide 6)



Modeling in machine learning

Inside a model



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