Applied Mathematics and Informatics In Drug Discovery

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Copy of the original laboratory notebook record showing 100% inhibition of malaria parasites by the Qinghao neutral extract when tested on a rodent malaria model.

Artemisinin — A Gift from Traditional Chinese Medicine to the World, Youyou Tu, Nobel Lecture 2015.

Dr. Jitao David Zhang, Computational Biologist

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Contact the author



Disclaimer



 Teaching is my personal engagement. My opinions and views do not necessarily reflect those by F. Hoffmann-La Roche, my employer.

• Please be aware of my biases and limitations.

- I am neither a mathematician nor a computer scientist by training. I am a computational biologist working in drug discovery.
- I see my task is to share with you the mathematical concepts and computational approaches used in drug discovery that I find beautiful and useful.
- I look forward to learning from you mathematics and other expertise that I did not know.









- Now is the best time in human history to fight diseases
- Applied mathematics and informatics approaches are indispensable to modern drug discovery
- Applied mathematics and informatics will join interdisciplinary efforts to transform drug discovery in the coming decades

The history of *Homo sapiens* is a history of living with, understanding, and fighting diseases



Trypanosomes

Plasmodium

Tropical diseases

~500,000 years ago



A young patient of smallpox, the first eradicated infectious disease

Hygiene, vaccination, and antibiotics

~250 years ago

Chloral hydrate, the first synthesized drug

OH

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OH

Pharmaceutical drugs

~150 years ago

Nobel prize laureates 2018, immune checkpoints, and drugs targeting the pathways

Personalized precise healthcare

~20 years ago

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Now is the best time in human history to fight diseases



and imaging

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How Do You Make A Drug?

It sounds simple, but...





Increasing cost and decreasing return of investment in drug discovery



Modified from Smietana *et al.* "Improving R&D Productivity." Nature Reviews Drug Discovery, 2015

Finding new drugs has become more challenging and expensive

U N I B A S E L







Danger + Opportunity

Introduction to Applied Mathematics and Informatics in Drug Discovery (*iAMIDD*)

A new course series at DMI, Uni Basel

- Introduction to drug discovery
- Bioinformatics and computational biology
 - Biological sequence analysis
 - Omics data analysis
 - Protein sequence and structure
- Cheminformatics and computer-aided drug design
 - Chemical structure representation and search
 - Molecular modelling
 - Molecular descriptors and QSAR

- Mathematical modelling
 - Principles and applications of modelling in pharmacology
 - Pharmacokinetics (PK) and pharmacodynamics (PD) modelling
 - Clinical pharmacology and pharmacometrics
- Statistics and machine learning
 - Emerging biomarkers: imaging and digital biomarker
 - Clinical trials
 - From real-world data to causal analysis and inference

It is hoped that iAMIDD builds a bridge between students and quantitative aspects of drug discovery



Applied mathematics empowers drug discovery by many ways

Applied mathematics *in drug discovery* is not a definable scientific field but a human attitude.









I am glad to share my expertise in drug discovery, and to learn from you!

Course information

- Lecturer: Jitao David Zhang
 - jitao-david.zhang@unibas.ch (Email)
- Website: amidd.ch
- Thirteen lectures this semester
 - Introduction to drug discovery (1 session)
 - Molecular level modelling (2 sessions)
 - Omics- and cellular level modelling (2 sessions)
 - Organ- and system-level modelling (1.5 sessions)
 - Populational level modelling (1.5 sessions)
 - Case studies (1 session)
 - Invited guest speakers (2 sessions)
 - Dies Academicus
 - Near-end-term presentations (2 sessions)

- Fridays 12:15–14:00, two sessions of \sim 45 min each.
- No exercise hour yet; pre-reading and post-reading articles, as well as videos, are shared and recommended.
- We focus on interdisciplinary research with mathematics as the language and informatics as the tool.
- Both slides and board are used. Slides and notes are shared.
- The final note is given by participation (20%), presentation (30%), and an oral examination (50%).
- The oral examination will be about concepts that we learned together, and about explaining mathematical concepts (or concepts in your domain of experts) to a layman.
- Questions?





Questions on the video on Herceptin by Susan Desmond-Hellmann

- 1. What is the indication of *Herceptin*? What is its generic (USAN, or United States Adopted Name) name?
- 2. What is the **gene target** of Herceptin?
- 3. In which year was the target of Herceptin described? When was Herceptin approved?
- 4. What was the improvement of Herceptin compared with earlier antibodies?
- 5. Why does a **biomarker** matter besides developing drugs?
- 6. In the clinical trial of *Herceptin* for **metastatic breast cancer**, how much improvement in the **median survival** did Herceptin achieve? And how much improvement is in the **adjuvant setting** (Herceptin applied directly after operation)?

Questions for further thinking

- Susan Desmond-Hellmann summarizes great drug development in four key concepts: (1) Having a deep understanding of the basic science and the characteristics of the drug. (2) Target the right patients. (3) Set a high bar in the clinic. (4) Work effectively with key regulatory decision markers. Where do you think mathematics and informatics play a crucial role?
- She emphasized the importance of collaboration. What skillsets do we need for that?
- How do you like her presentation? Anything that you can learn from her about presentation and story telling?

Please introduce yourself!



- Name?
- Background?
- Which part of mathematics (or other background) are you mostly interested in? Why?
- What do you want to take away from this course?

Questions on the package insert info



- 1. What is the **indication** of *ZYRTEC*? What is its generic name?
- 2. What is the gene target of ZYRTEC?
- 3. How much time does ZYRTEC reaches **maximum concentration** following oral administration?
- 4. How long do normal vonlunteers have to **wait** until the skin wheal and flare caused by the intradermal injection of histamine is inhibited after taking 10mg ZYRTEC?
- 5. What types of **adverse reactions** are observed in volunteers taking ZYRTEC?
- 6. Is there a **biomarker** for ZYRTEC?

Questions for further thinking

• What are the commonalities between Herceptin and Zyrtec, and what are the differences?

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Summary and Q&A



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