An ecosystem for digital twins in healthcare

Liesbet Geris
Executive Director @ VPH Institute
PI @ University of Liège & KU Leuven, Belgium
DTH = community effort

- Policies
- Incentives
- Community
- User experience
- Technical implementation
Adapted from NUVIUM
From data to action

Data → Information → Knowledge → Actionable knowledge
From data to action

Data → Information → Predictive model → Credibility assessment
DT = wide spectrum of technologies

- Black box
  - Driven by data
  - Artificial Intelligence, machine learning
- White box
  - Driven by knowledge
  - Physics-based models, Mechanistic models

- Turn data into actionable knowledge
- The problem determines the appropriate technology!
the Human Digital Twin can be a distributed digital infrastructure, made of data and model standards, standard operative procedures (SOPs), and standardised application programming interfaces (APIs), that will allow our community to accrue all the predictive models it develops, and all experimental and clinical data employed in building and validating the model, into a shared facility for reuse and collaboration.
EDITH

- Ecosystem
- Roadmap HDT
- Federated cloud-based repository
- Simulation platform
Roadmap towards HDT

• Personal Health Forecasting
  – for the patient/citizen; subject specific real-time simulations using data from wearable sensors

• The Digital Patient (CSA)
  – for the doctor; patient specific modelling for decision support

• In Silico Clinical Trials (CSA)
  – for the biomedical R&D; patient specific models to support industry value chain
Simulation platform

• Cfr presentation Yannis Ioannidis
Ecosystem

Regulators

In silico medicine

Repositories

Wearables

HPC

AI

Policy makers

Users

Health data

Infrastructures
Barriers to adoption of in silico medicine

• New technologies
• Validation collections (data)
• Policies
• Regulatory pathways
• Scalable services
• Commercial services
• Better informed stakeholders
• Properly trained workforce
• Sustainability
C⁴ Bio

Community Challenge towards Consensus on Characterization of Biological tissue

Nele Famaey
KU Leuven
Achieve community consensus regarding the testing protocols for material characterization of biological tissue and disseminate this consensus to the relevant standards bodies (i.a. ISO & ASME).

Initial focus: mechanical properties
Test campaign: 4 steps

1. Quantify the **variability** among different research groups: testing using participants’ own methodology

2. Standardize the **approach** by defining consensus methodology between participants

3. Evaluate standardized **approach** by retesting using consensus methodology

4. Make the outcome publicly **available** in a white paper with results & consensus methodology
Barriers to adoption of in silico medicine

• New technologies
• Validation collections (data)
• **Policies**
• Regulatory pathways
• Scalable services
• Commercial services
• Better informed stakeholders
• Properly trained workforce
• Sustainability
US policy makers

In Silico Clinical Trials.—In Silico clinical trials use computer models and simulations to develop and assess devices and drugs, including their potential risk to the public, before being tested in live clinical trials. Advanced computer modeling can also be used to predict how a drug or device will behave when deployed in the general population, thereby protecting the public from the unintended consequences of side effects and drug interactions. In Silico trials protect public health, advance personalized treatment, and can be executed quickly and for a fraction of the cost of a full scale live trial. By understanding the impact a drug or device will have on the human body immediately and over time, as well as within different populations, millions of dollars in development costs can be saved. A mere ten percent improvement in predicting failures before a clinical trial could save $100,000,000 in development costs per drug. As such, the Committee directs the FDA to expand its use of in silico clinical models through a pilot project aimed at creation of a full human in silico model able to test drugs and devices across the entire body, including long-term effects and among distinct populations. If necessary to enact this project, the FDA shall issue a unified guidance to allow the model to be used to test both drugs and devices. The Committee requests a written report outlining the FDA’s plans for development of the model within 120 days of enactment of this act.

“... the committee directs the FDA to expand its use of in silico models ...”
Communication on building a European Health Union

- “The rapidly evolving technological environment and digital solutions (AI, High Performance Computing, computational models and simulation system) provides an opportunity to update surveillance systems, integrating data from new and different sources, and to create sensitive systems that detect early signals”

- “In order to facilitate the work and the exchange of information under this Regulation, provision should be made for the establishment and management of IT infrastructures and synergies with other existing IT systems or systems under development, including the EUDAMED IT platform for medical devices. That work should also be facilitated by, where appropriate, emerging digital technologies such as computational models and simulations for clinical trials, as well as data...”
Barriers to adoption of in silico medicine

• New technologies
• Validation collections (data)
• Policies
• **Regulatory pathways**
• Scalable services
• Commercial services
• Better informed stakeholders
• Properly trained workforce
• Sustainability
“Develop computational modeling technologies to support regulatory decision-making”
COMMENTARY

Verifying and Validating Quantitative Systems Pharmacology and In Silico Models in Drug Development: Current Needs, Gaps, and Challenges

Flora T. Musuamba1,3,4, Roberta Bursi1, Ethymios Manolis1,6, Kristin Karlsson1,8, Ali Al-Abed1, Jean-Pierre Boissel7, Raphaëlle Lesage5, Cécile Crozatier6, Emmanuelle M. Voisin1, Rossana Alessandrello11 and Liesbet Geris8,12

The added value of in silico models (including quantitative systems pharmacology models) for drug development is now unanimously recognized. It is, therefore, important that the standards used are commonly acknowledged in the case, the incomplete and low standards reporting to ensure a form an adequate regulatory evaluation of mechanistic in silico drug and disease models in drug development: building model credibility

Flora T. Musuamba, Ine Skottheim Rusten, Raphaëlle Lesage, Giulia Russo, Roberta Bursi, Luca Emili, Gaby Wangorsch, Ethymios Manolis, Kristin E. Karlsson, Alexander Kulesza, Fualie Courcelles, Jean-Pierre Boissel, Cécile F. Rousseau, Emmanuelle M. Voisin, Rossana Alessandrello, Nuno Curado, Enrico Dall’ara, Blanca Rodriguez, Francesco Pappalardo, Liesbet Geris... See fewer authors

First published: 08 June 2021 | https://doi.org/10.1002/psp4.12669

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi:10.1002/psp4.12669
Barriers to adoption of in silico medicine

- New technologies
- Validation collections (data)
- Policies
- Regulatory pathways
- Scalable services
- **Commercial services**
- Better informed stakeholders
- Properly trained workforce
- Sustainability
Business model

• EDITH aims to determine how to regulate, incentivise, and support the DTH ecosystem to eventually turn it into a thriving, economically profitable sector of the European technology landscape
  – Lean start-up & customer discovery business modeling methodologies
Barriers to adoption of in silico medicine

- New technologies
- Validation collections (data)
- Policies
- Regulatory pathways
- Scalable services
- Commercial services
- Better informed stakeholders
- Properly trained workforce
- Sustainability
User community

<table>
<thead>
<tr>
<th>STRENGTHS</th>
<th>WEAKENESSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>AWARENESS</td>
<td>REQUIRED TECHNICAL EXPERTISE</td>
</tr>
<tr>
<td>CONFIDENCE</td>
<td>ACCESS TO COMPUTING RESOURCES</td>
</tr>
<tr>
<td>ACCURACY</td>
<td>CM&amp;S IS SLOW</td>
</tr>
<tr>
<td>TRUST</td>
<td>STILL LIMITED TO A FEW FIELDS</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>OPPORTUNITIES</td>
<td></td>
</tr>
<tr>
<td>TRUST</td>
<td>REGULATORY APPROVAL</td>
</tr>
<tr>
<td>GROWTH OF CASES; METHODS AND DATA</td>
<td>LEVEL OF AWARENESS IN CERTAIN TERMS</td>
</tr>
<tr>
<td>APPLICATIONS IN TEACHING</td>
<td>MISTRUST/OVER EXPECTATIONS</td>
</tr>
<tr>
<td>DIGITAL GENERATION OF HEALTHCARE PROVIDERS</td>
<td>DATA</td>
</tr>
</tbody>
</table>

© 2022 VPH Institute
Barriers to adoption of in silico medicine

- New technologies
- Validation collections (data)
- Policies
- Regulatory pathways
- Scalable services
- Commercial services
- Better informed stakeholders
- Properly trained workforce
- Sustainability
Sustainability

• Sustainability plan
  – Survey of providers & user communities
  – Internal assessment of costs
  – Conceptualisation of the marketplace mechanism
  – Proof-of-concept software architecture
Good Simulation Practice

• Good Simulation Practice is defined as a set of rules and criteria for a quality system related to
  • the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of in silico studies …
  • aimed to complement / reduce, refine, or replace in vitro & in vivo testing

• In silico world grassroots initiative
• Supported by international stakeholders (FDA, EMA, DIN, …)

Join In Silico World Community of Practice on slack
Policies
Incentives
Community
User experience
Technical implementation
In silico medicine will be the future
Help us to make it happen!

Thank you

http://www.vph-institute.org
http://insilico.world