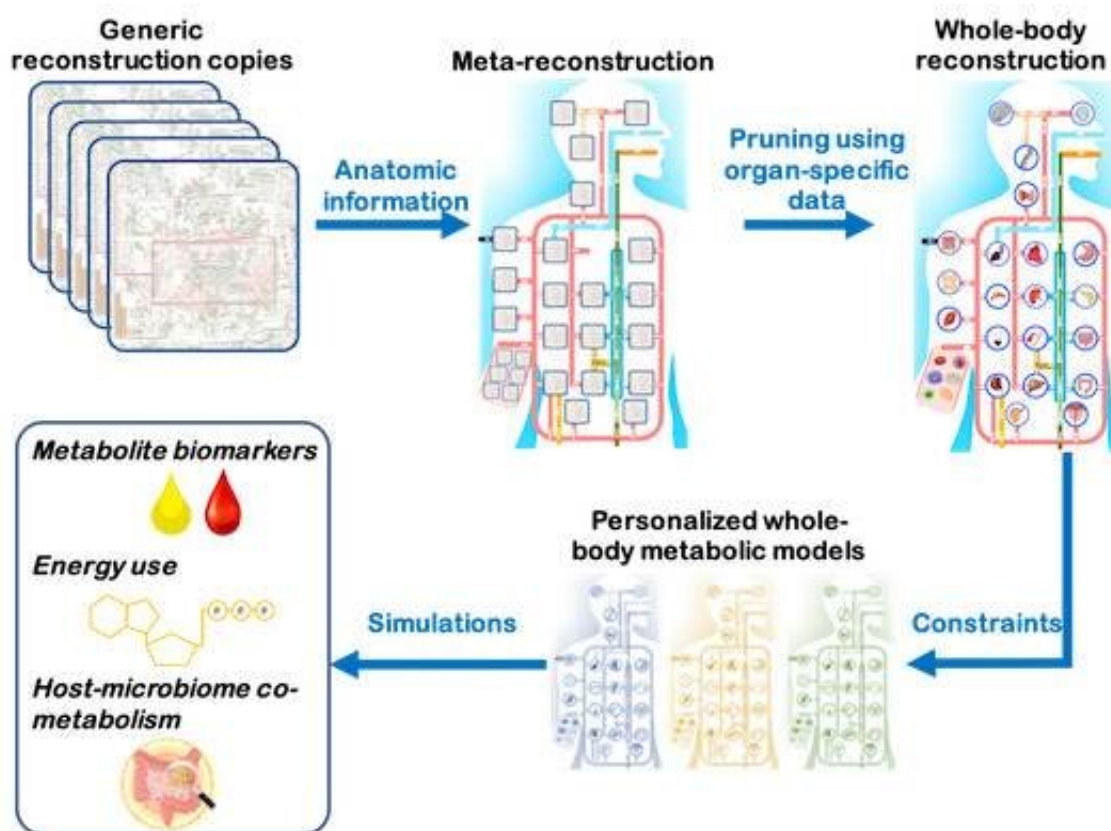


Virtual metabolic humans, Harvey and Harvetta, novel computational models for personalised medicine

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Credit: Science Foundation Ireland (SFI)

We are all unique. Our health is determined by our inherent genetic differences combined with our lifestyles and the environments in which we live. This unique identity means that a "one size fits all" approach is

no longer accepted as the best way to manage our individual health. There is a demand for new "personalised" approaches to better manage our health and to target therapies to achieve optimum health outcomes.

By combining and analysing information about our genome, with other clinical and diagnostic information, patterns can be identified that can help to determine our individual risk of developing disease, detect illness earlier and determine the most effective interventions to help improve health, be they medicines, lifestyle choices, or even simple changes in diet.

Researchers, led by Prof Ines Thiele, a Principal Investigator at APC Microbiome Ireland SFI Research Centre, who is based in National University of Ireland, Galway, have developed whole-body computational models—Harvey and Harvetta. These [virtual humans](#) represent whole-body metabolism, physiology, diet and the gut microbiome. These new models successfully predict known biomarkers of inherited [metabolic diseases](#) and enable exploration of potential metabolic interactions between humans and their gut microbiomes at a personal level.

Precision, or personalised, medicine requires realistic, mechanistic computational models that capture the complexity of the human representing each individual's physiology, [dietary habits](#), metabolism and microbiomes. Molecular biology has yielded great insight into the 'parts list' for [human cells](#), but it remains challenging to integrate these parts into a virtual whole human body. The Virtual Human Physiome project has generated comprehensive computational models about the anatomy and physiology of human organs but has yet to be connected with molecular level processes and their underlying networks of genes, proteins, and biochemical reactions.

Prof Thiele's team tackled this challenge to develop the first whole-body,

sex-specific, organ-resolved computational models of human metabolism, which mechanistically connect anatomy and physiology with molecular level [metabolic processes](#). Their study is published today in the prestigious journal *Molecular Systems Biology*.

Harvey and Harvetta are virtual male and female human metabolic models, respectively, built from literature and data on human metabolism, anatomy and physiology as well as biochemical, metabolomic and proteomic data. They are anatomically interconnected as whole-body metabolic models, comprised of more than 80,000 [biochemical reactions](#) distributed over 26 organs and 6 types of blood cell. Moreover, they can be expanded to include gut microbial metabolism. These unique models enable generation of personalised whole-body metabolic models using an individual's physiological, genomic, biochemical and microbiome data.

Whole-body metabolic model

Generating personalised whole-body metabolic models is an interdisciplinary effort. The development of whole-body models of metabolism required the development of novel algorithms and software for constraint-based modelling of high-dimensional biochemical networks. "A whole-body model is generated by starting with a set of anatomically interconnected generic reconstructions of human [metabolism](#)", says Assistant Prof Ronan Fleming, a co-author of the study from the Leiden Academic Centre for Drug Research, Leiden University. "This draft [model](#) had in excess of 300 thousand dimensions, which was then pared down to approximately 80 thousand organ-specific reactions using efficient algorithms and high-performance computing facilities."

"Harvey and Harvetta will usher in a new era for research into causal host-microbiome relationships and greatly accelerate the development of

targeted dietary and microbial intervention strategies" said Prof Ines Thiele, who lead the research. "These models could accelerate insights into pathways involved in sex-specific disease development and progression. Moreover, thanks to the ability to personalize the [whole-body](#) metabolic models with clinical, physiological, and omics data, they represent a significant step towards personalised, predictive modelling of dietary and drug interventions and drug toxicity, which lies at the heart of precision medicine."

More information: Ines Thiele et al. Personalized whole-body models integrate metabolism, physiology, and the gut microbiome, *Molecular Systems Biology* (2020). [DOI: 10.15252/msb.20198982](https://doi.org/10.15252/msb.20198982)

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