Goal2 Realization of ultra-early disease prediction and intervention by 2050.
Challenge for Eradication of Diabetes and Comorbidities through Understanding and Manipulating Homeostatic Systems

Here begins our new MIRAI
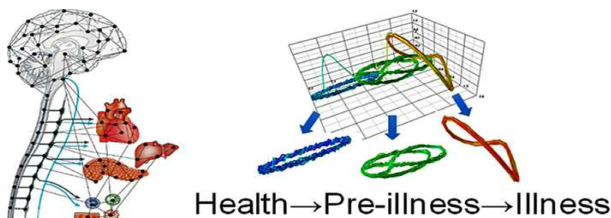MOONSHOT
RESEARCH & DEVELOPMENT PROGRAM

R&D Theme

Understanding homeostasis through mathematical model analysis and its applications, Understanding the pre-symptomatic stage of diabetes and its complications and building a database

Progress until FY2022

1. Outline of the project

The two R&D themes (Themes 4 and 5) play two roles in the project: (i) to collect various data over time on the transition from the normal or pre-symptomatic stage to the diseased state, focusing on type 2 diabetes and its concomitant disease, heart failure (Theme 5), and (ii) to use these animal experimental data and human biological data to advance mathematical model analysis to extract key elements for a comprehensive understanding (Theme 4, see figure below).

Health→Pre-illness→Illness

https://www.moonshot-katagiri.proj.med.tohoku.ac.jp/research-e.html

To achieve this, close collaboration between mathematical scientists and medical biologists is a challenge, and we are working on this as a challenging theme. We are working on the concept of linking experiments/data acquisition with model analysis, which is completely different from the conventional approach, using various methods such as biochemistry, gene expression analysis, epigenomics, metabolomics, organ-specific functional analysis, and mathematical model analysis.

2. Outcome so far

(1) Proceed with mathematical model analysis using glucose tolerance test data from healthy subjects, and estimate half-lives of insulin and C-peptide using a 9-organ compartment model
(2) Implementation of a glucose tolerance test simulator (see figure below)
(3) Construction of a circulatory system model using time series data of flow rate obtained as a result of blood circulation simulation (right figure)
(4) Start of mouse data acquisition for time-series analysis of pre-symptomatic states

In (2), we were able to visualize changes in blood glucose and insulin concentrations and the metabolic state of the whole body by changing various parameters. In (3), we constructed a 1D + 0D coupled model of the whole-body circulatory system and completed a prototype of a whole-body circulatory network model (upper right figure). (4) will lead to the clarification of key phenomena through the refinement of mathematical models and simulators.
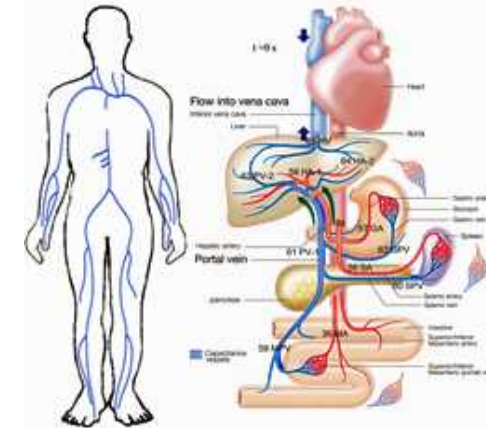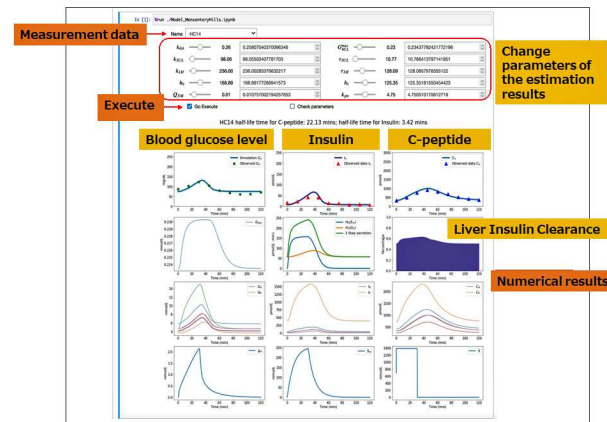
3. Future plans

In the future, to extend the inter-organ network model (compartment model) to a mathematical model corresponding to a normal diet, we will construct a mathematical model that enables us to understand the dynamic homeostasis of glucose metabolism. By applying the 9-compartment model to the same individual mouse data that transitions from healthy to diabetic, we will identify the parameters that change specifically for diabetes and clarify the mechanism of diabetes onset from a mathematical science perspective.

In addition, we will select effective time points for analysis from the pre-symptomatic stage to the diabetic state as an analysis in order to consider building a database by adding the effects of aging and sex differences. In this way, we will construct a pre-symptomatic disease database and share the obtained data with mathematical scientists from time to time to combine the estimation of mechanisms obtained from mathematical model analysis with molecular analysis in experiments.