Model Based Design of an Artificial Pancreas

Lane Desborough
Chief Engineer

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Model Based Design of an ~~Artificial Pancreas~~ Automated Insulin Delivery System

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Top 10 Reasons Bigfoot Doesn't Call Its Automated System an "Artificial Pancreas"

10 The pancreas does more than just make insulin.
9 "Artificial Pancreas" sounds like an implant...
8 ...or a transplant...
7 ...or a cure.
6 Our company's journey will have many solutions, each better than the last.
5 Our system will be part of a broader service, reducing your burden, your decision fatigue.
4 Automating insulin doesn't make us bionic; we're fully human & need to trust we have control.
3 "Artificial" means fake when the benefit our system provides will be real.
2 T1DExchange & FDA use "automated insulin delivery" to describe what it actually *does* - insulin in the right amounts at the right times.
1 The plural of "artificial pancreas" is "artificial pancrea"? Sorry. We just can't.

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Living with Diabetes (~9%)

30 million people in the United States

415 million people around the World

	Insulin Production	Commonly Afflicted Groups	Common physical attributes	Onset	Occurrence	Cure	Treatment
Type 1	Broken (autoimmune)	Children / teens	Normal or Thin	Rapid (weeks)	5% -10%	None	Insulin
Type 2	Tired (diet)	Adults, elderly, ethnic groups	Overweight or Obese	Slow (years)	90% - 95%	None*	Pills, Insulin

2-3 million Americans are dependent on insulin

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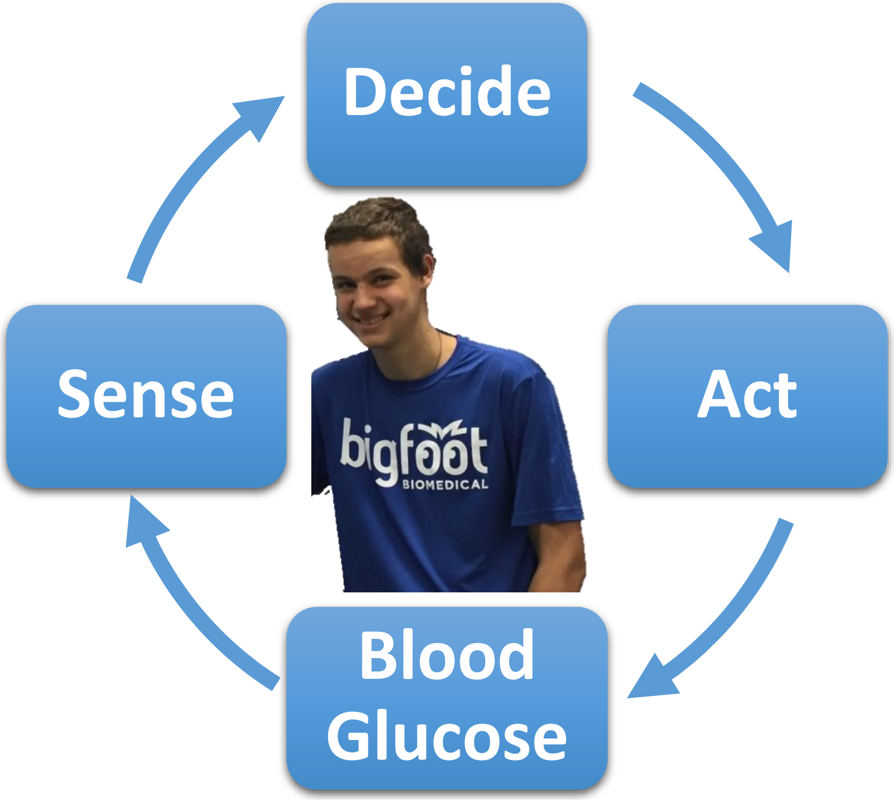
2-3 million Americans

Sense-Decide-Act



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Managing diabetes takes about an hour a day

Treatment burden and health-related quality of life of children with diabetes, cystic fibrosis and asthma

Tahereh Ziaian,[1] Michael G Sawyer,[2,3] Katherine E Reynolds,[2,3] Josephine A Carbone,[2,3] Jennifer J Clark,[2,3] Peter A Baghurst,[4] Jennifer J Couper,[3] Declan Kennedy,[3] A James Martin,[5] Rima Em Staugas[5] and Davina J French[6]

[1]School of Nursing and Midwifery, University of South Australia, [2]Research and Evaluation Unit, [4]Public Health Research Unit, [5]Department of Pulmonary Medicine, Women's and Children's Hospital, [3]Department of Paediatrics, The University of Adelaide, Adelaide, South Australia and [6]School of Psychology, University of Western Australia, Crawley, Western Australia, Australia

Aim: To identify the time required by children with cystic fibrosis (CF), diabetes or asthma to complete daily treatment tasks and the hassle they experienced when completing these tasks. To compare parent and child reports of daily treatment time and hassle. To investigate the relationship between treatment time and hassle, and (i) children's health-related quality of life (HRQL); and (ii) disease severity.

Methods: 160 children aged 10–16 years with CF, type 1 diabetes, or asthma were followed over a 2-year period. Information about children's treatment time and hassle, and their HRQL was obtained from parents and children at baseline, 1-year and 2-year follow-up assessments.

Results: On average, children with CF reported spending 74.6 ± 57.0 min completing treatment tasks, children with diabetes spent 56.9 ± 27.8 min and children with asthma spent 6.4 ± 9.3 min. Parents reported that children spent less time that was reported by their children. Over the two years, parent and child reports describing treatment time for children with CF did not vary significantly ($P = 0.3$). Treatment time for children with diabetes increased ($P = 0.02$) whereas that for children with asthma reduced ($P = 0.001$). The level of hassle experienced by children when completing individual treatment tasks was low for all three conditions. There was no significant relationship between treatment time and children's HRQL.

Conclusion: Children with CF or diabetes spent a substantial amount of time each day completing the treatment tasks. Although this was not related to HRQL, it could impact the ability to comply with complex and all home-based-therapies for some children.

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Managing diabetes involves ~750 tasks

Magnitude of Type 1 Diabetes Self-management in Youth:

Health Care Needs Diabetes Educators

Diabetes Educ. 2009 Mar-Apr;35(2):302-8

Ronald D. Coffen, Lynnda M. Dahlquist,

Abstract

The purpose of this article is to demonstrate the complexity of the type 1 diabetes regimen and to highlight the essential role of the diabetes educator in safely training and implementing the myriad skills in a developmentally appropriate manner for children and adolescents. A review of literature and a task analysis were preformed and suggest that the complexity of the regimen is often not adequately addressed. Reviewed research assessed the regimen using measures with on average about 25 items while the task analysis contains over 600 tasks.

www.andrews.edu/~coffen/Full_Table.pdf

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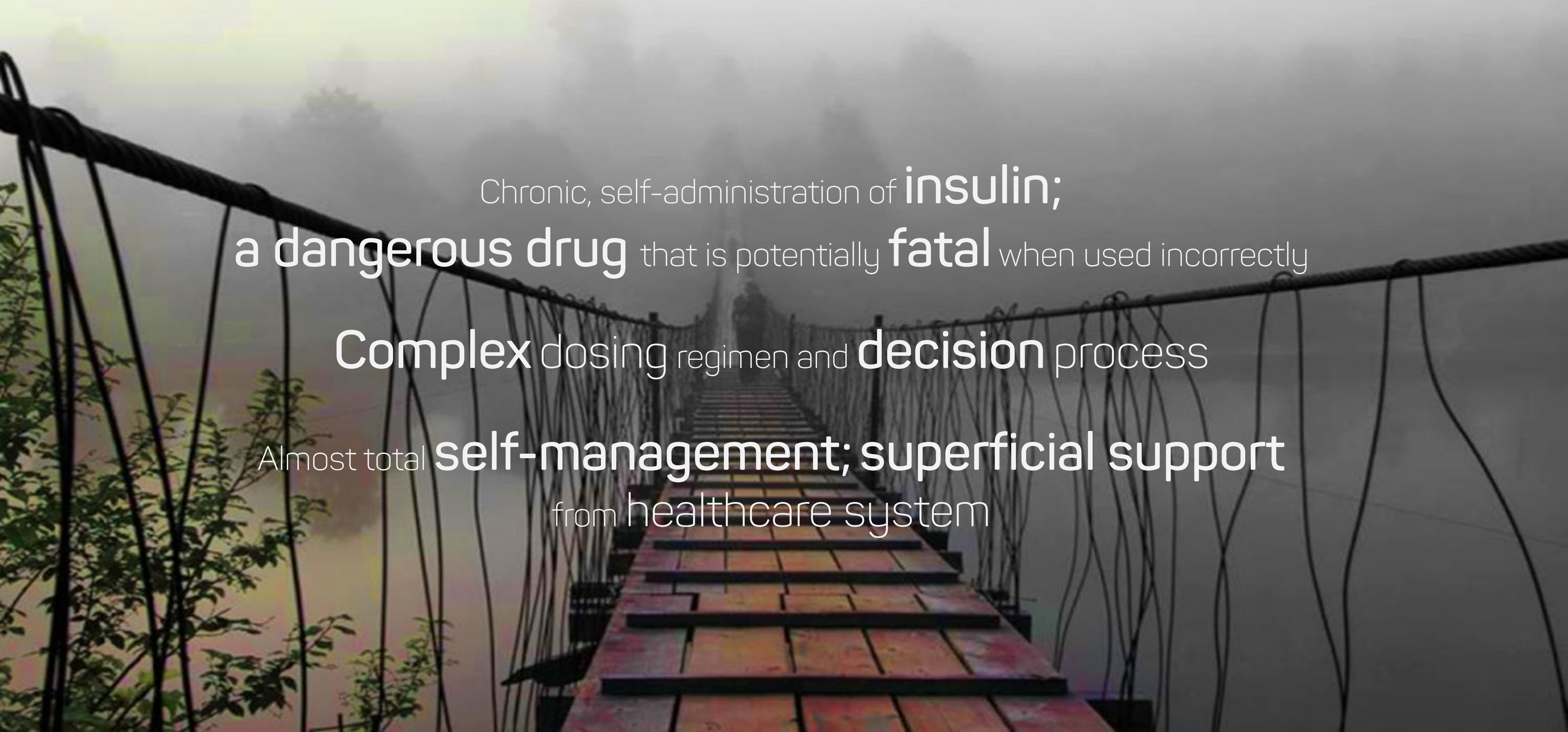
The Reality of Insulin Dependent Diabetes



Chronic, self-administration of **insulin;**
a dangerous drug that is potentially **fatal** when used incorrectly

Complex dosing regimen and **decision** process

Almost total **self-management; superficial support**
from healthcare system

The Founders

Jeffrey Brewer, CEO

- Former CEO of JDRF
- Successful dotcom Entrepreneur

Bryan Mazlish, CTO

- Inventor of the Bigfoot System
- Founder of fully automated Wall Street trading company

Jon Brilliant, CFO

- Founding board member and former CFO of WellDoc
- Successful VC and Advisor

Lane Desborough, Chief Engineer

- Former Chief Engineer at Medtronic
- Co-developer of Nightscout CGM in the Cloud

Our Mission

To improve the lives of people with insulin-dependent diabetes through the application of smart technology.

Bigfoot: founded December 2014

Today: ~40 employees, ~32 million dollars raised

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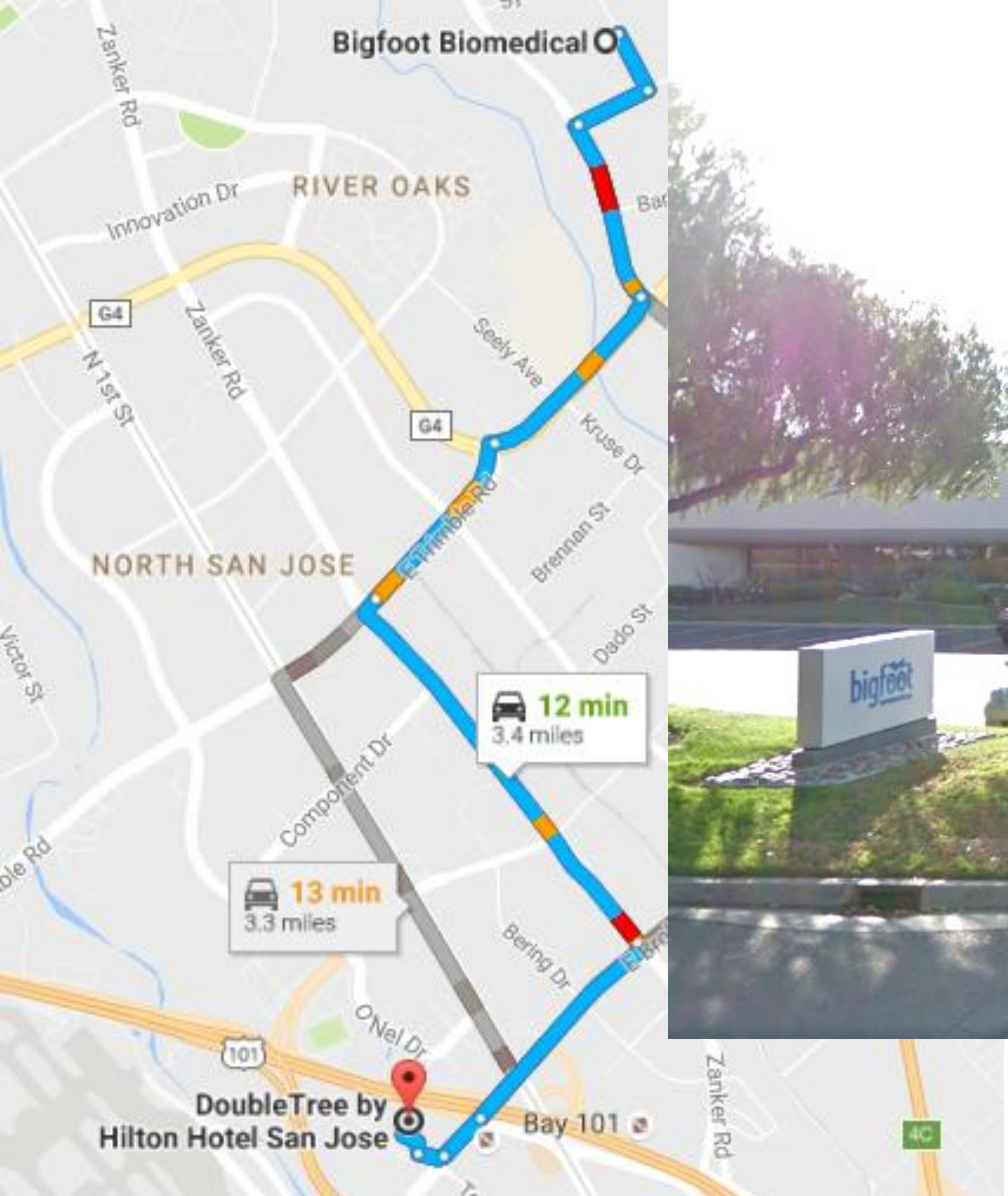

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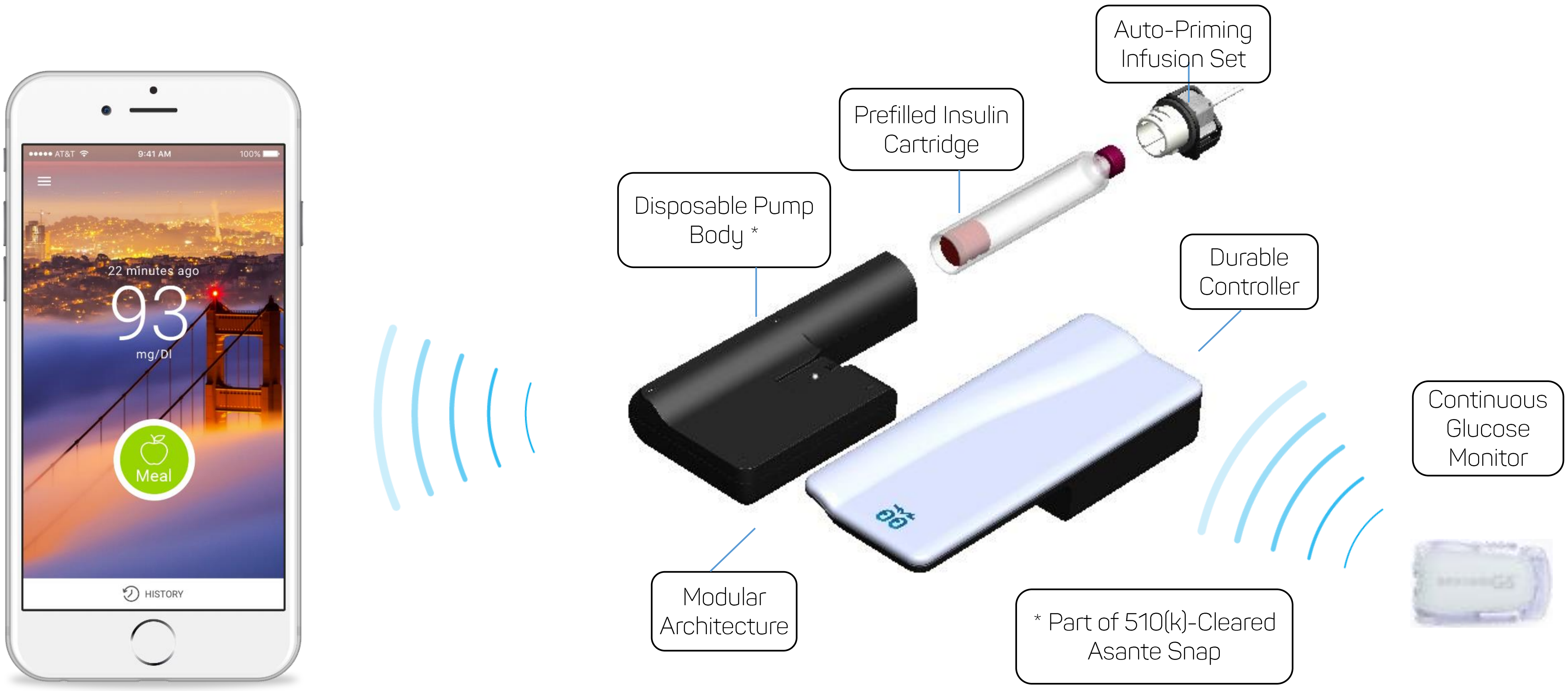
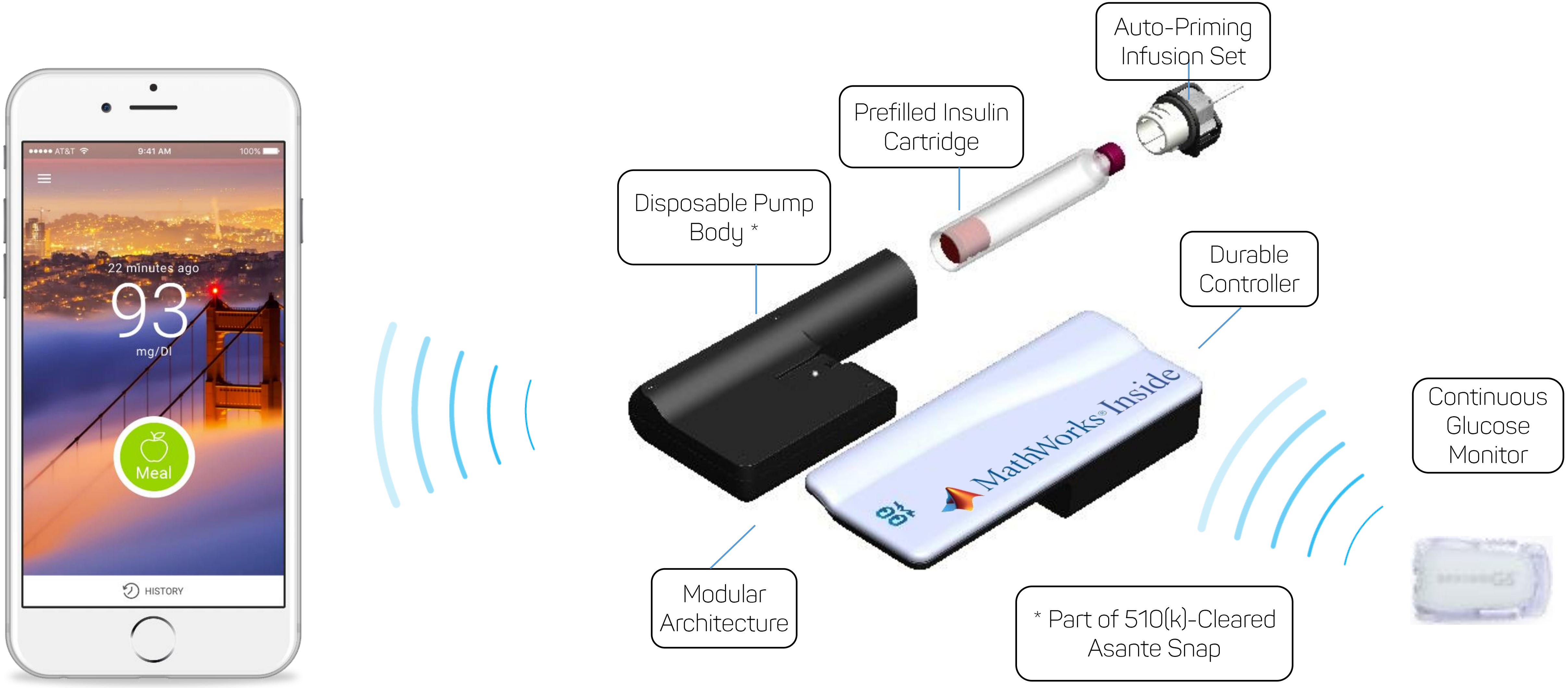
AUTOMATED INSULIN DELIVERY

- Access all system features via smartphone
- Combines simplest insulin infusion pump & most accurate continuous glucose monitor
- Secure wireless on-body network
- Proprietary algorithms for closed loop automation
- Metabolic individualization & cloud-based remote safety monitoring
- Accessed w/ single prescription & reimbursed as a service for a monthly fee

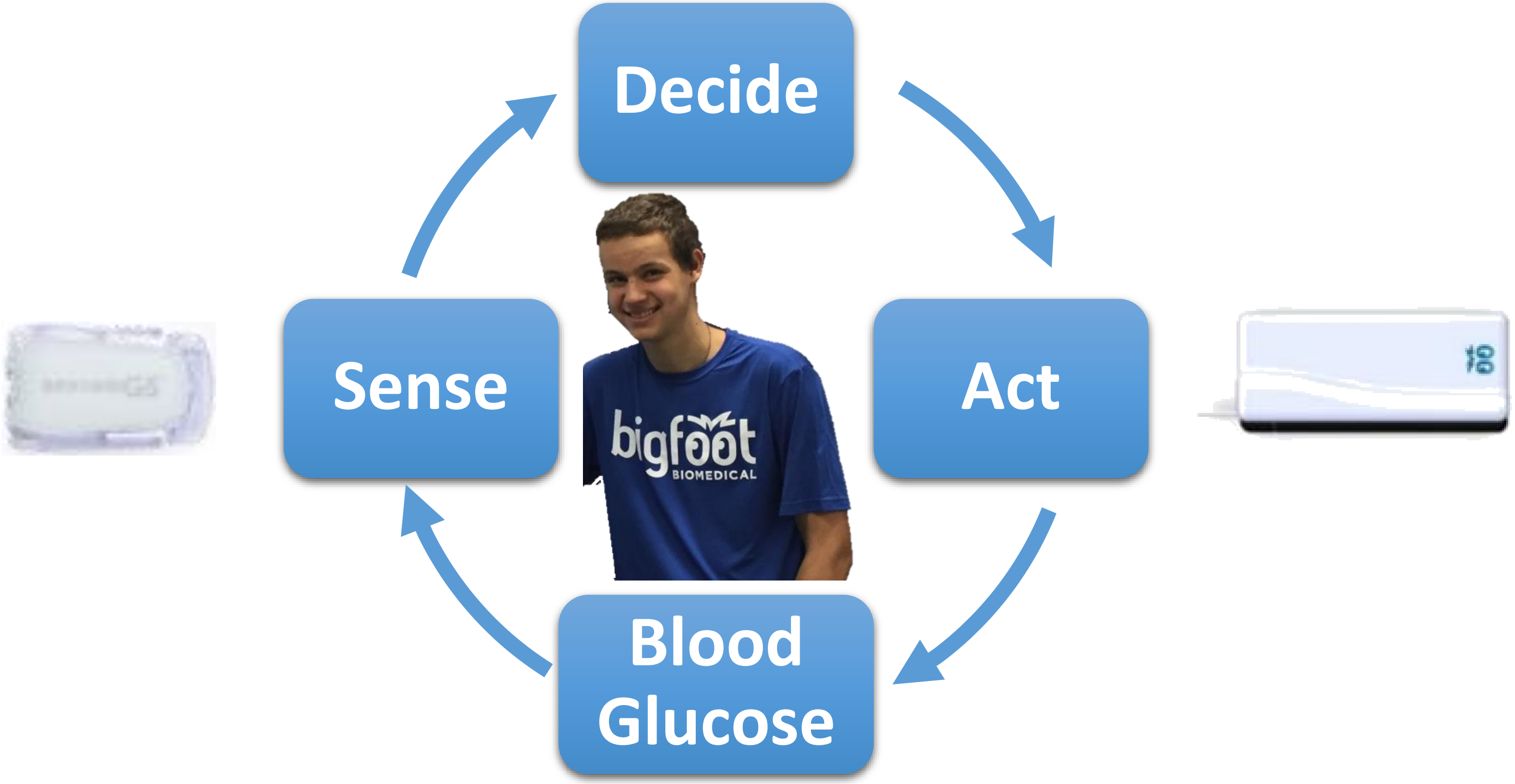
Components of the Bigfoot System

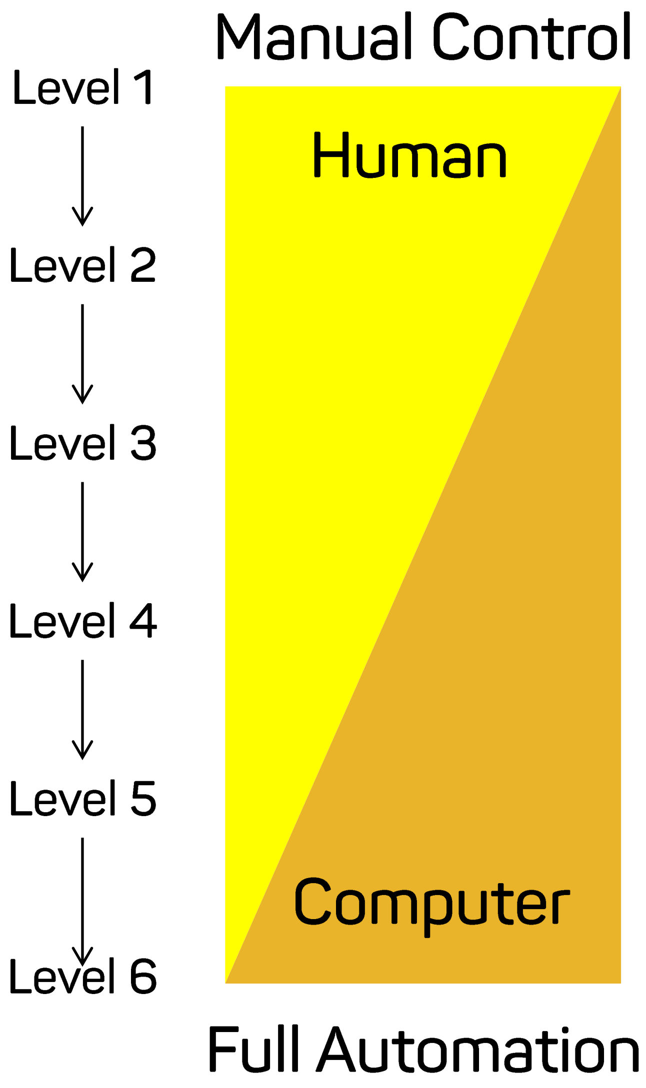


Components of the Bigfoot System

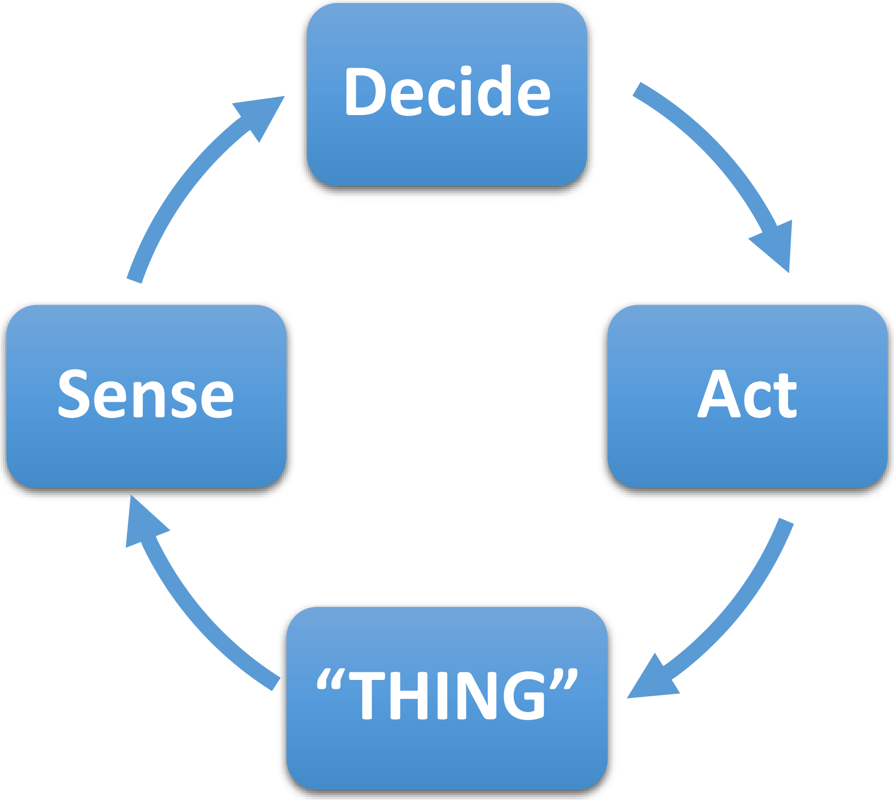


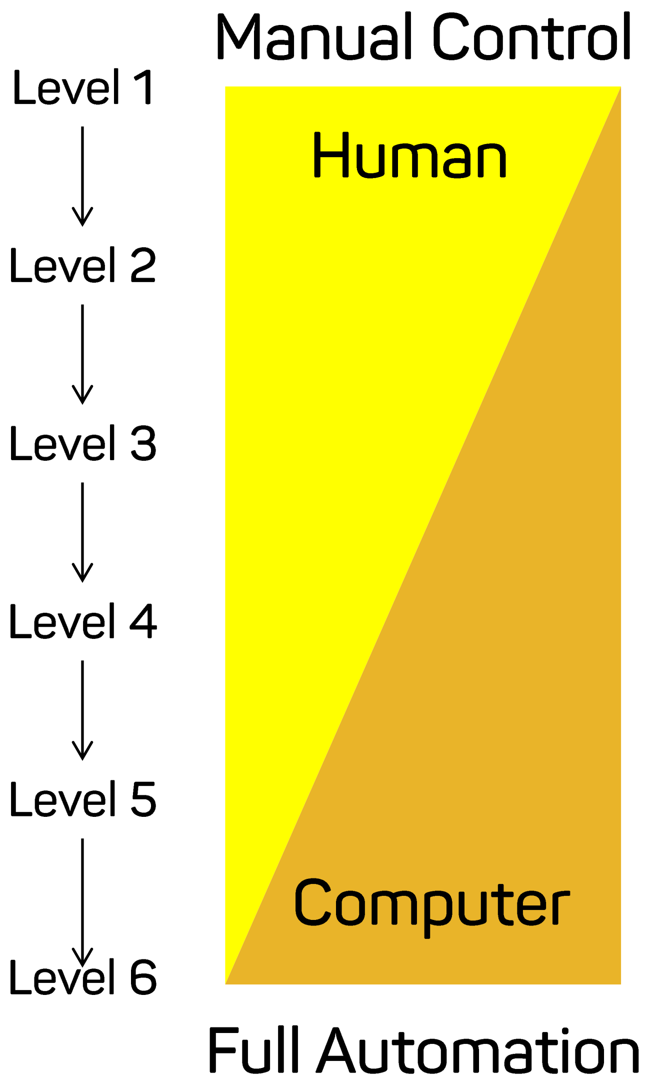
Automated Insulin Delivery





Automation of Tasks





The purpose of control is to safely transfer variability … so that we don't have to do as much work

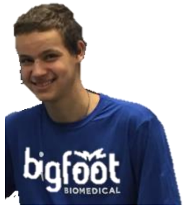
From: **To:**

Cruise control:

Thermostat:

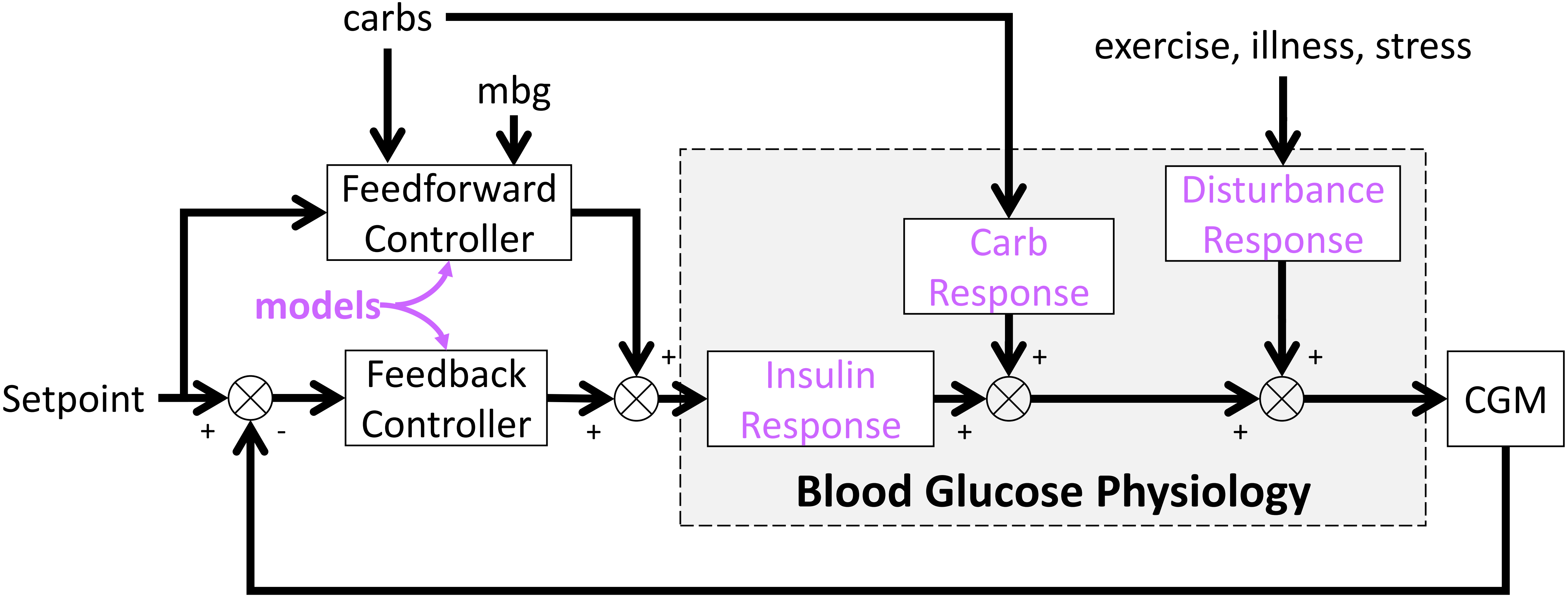
Control System:


Autopilot

Automated Insulin Delivery


Automated Insulin Delivery



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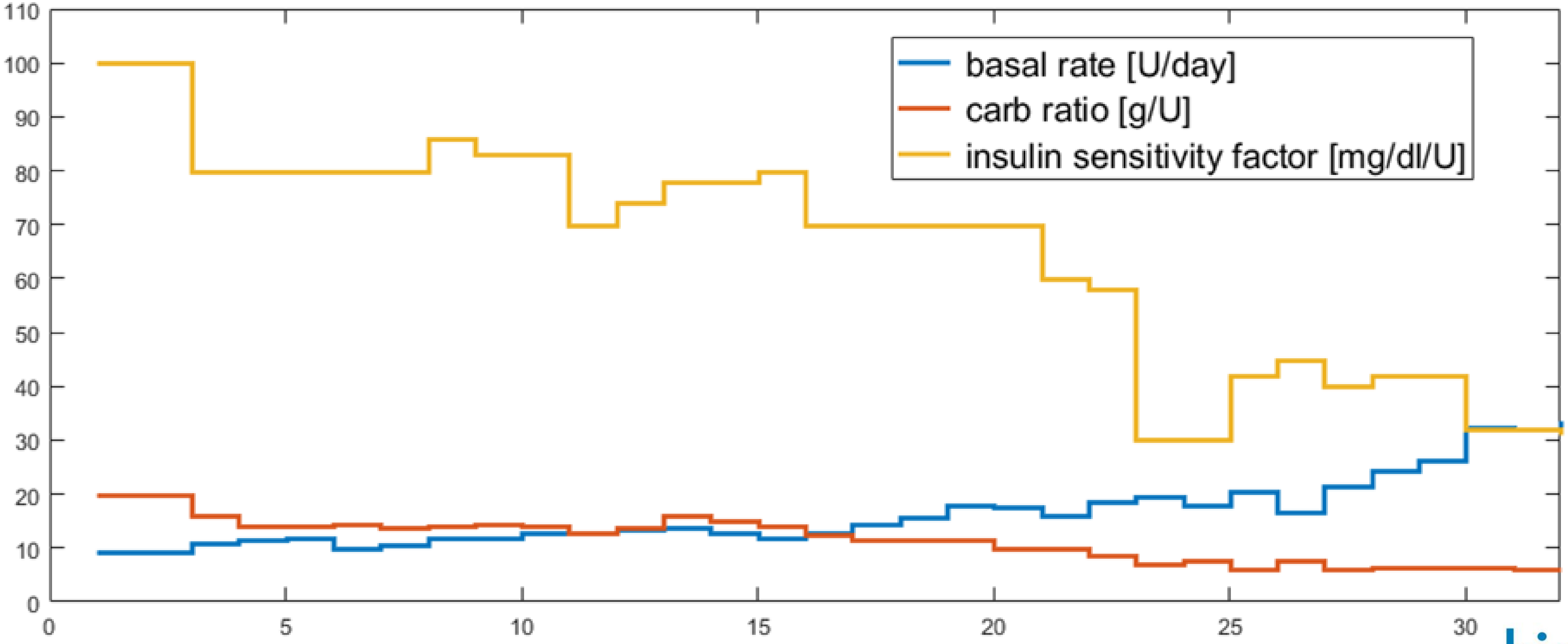
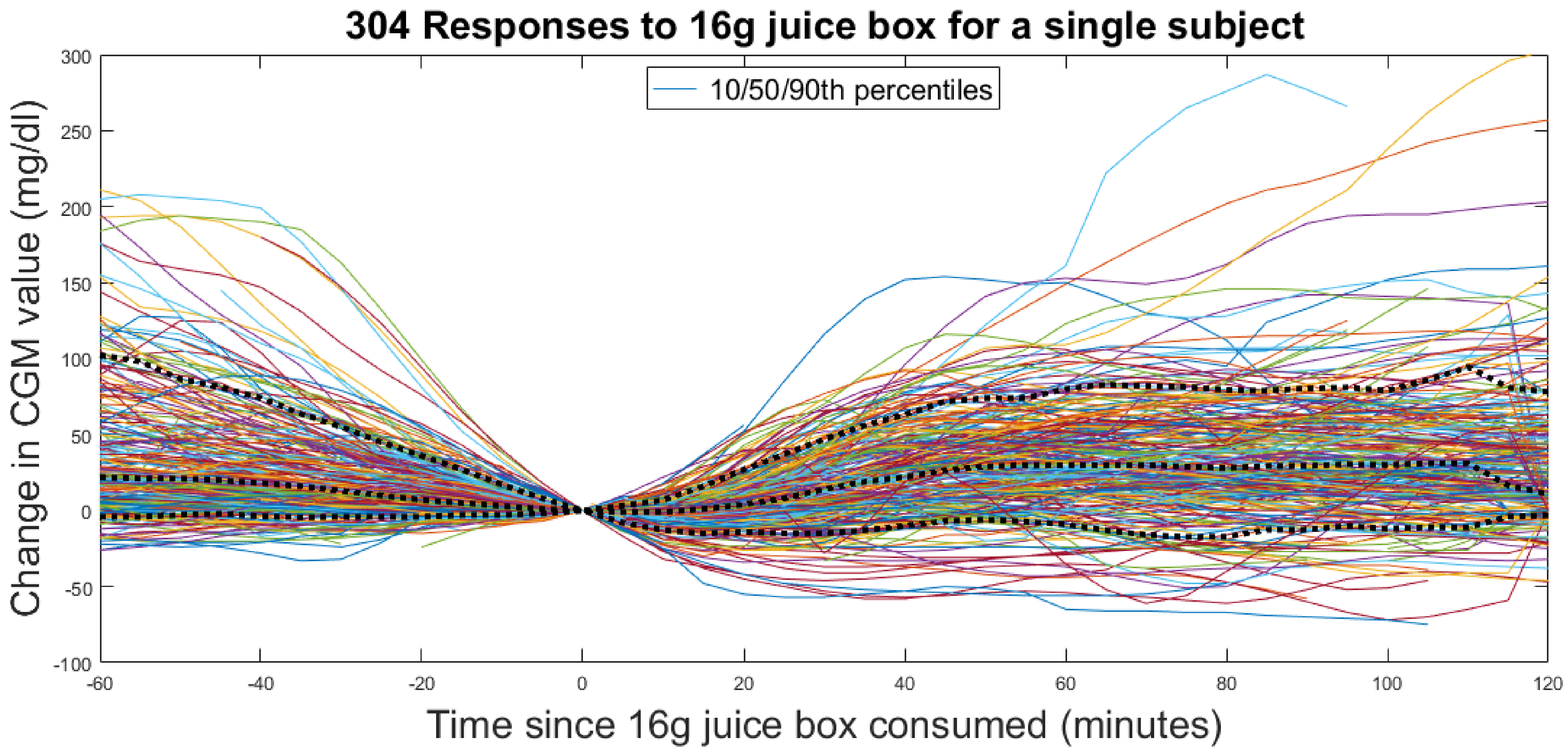
Physiology and behavior change over time



Same stimulus, different responses



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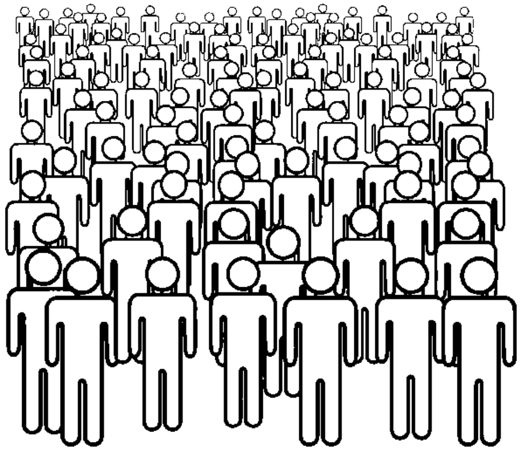
One system needs to work across a wide range of users and use conditions

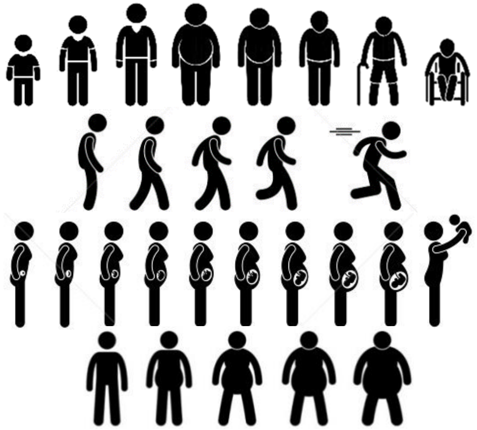
change
across
population



change
throughout
the day

change
with activities
and events

change
over
time



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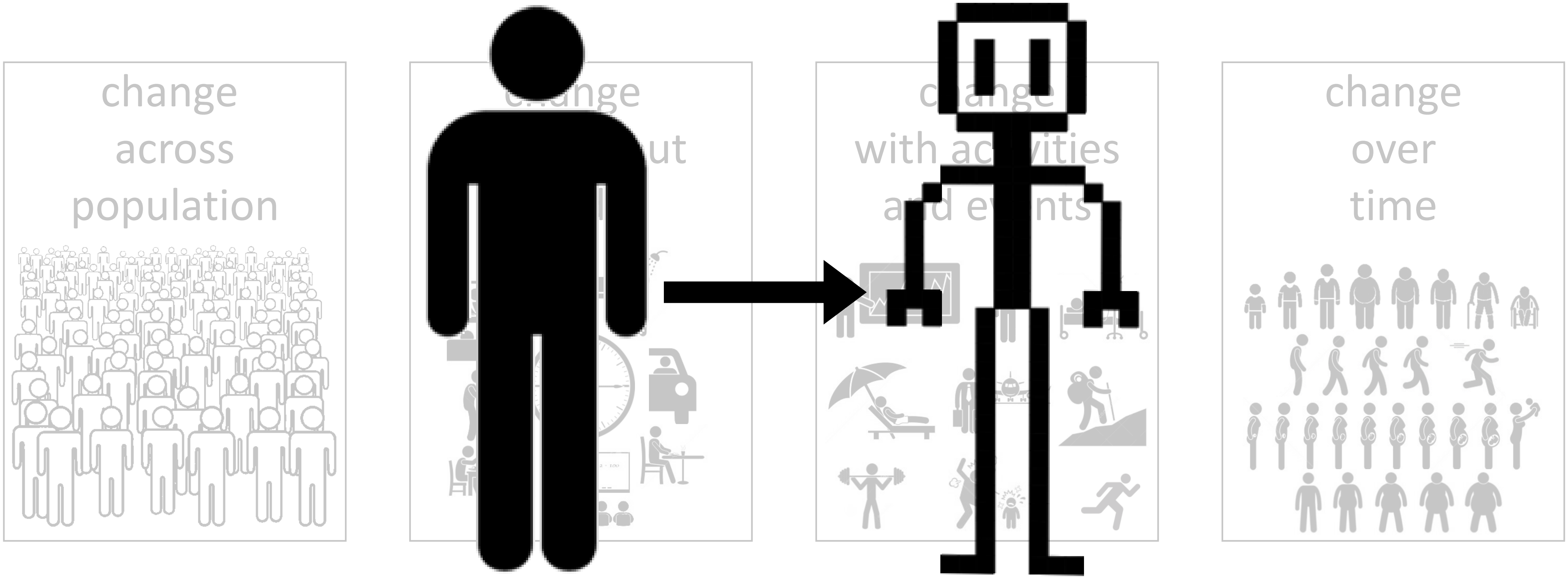
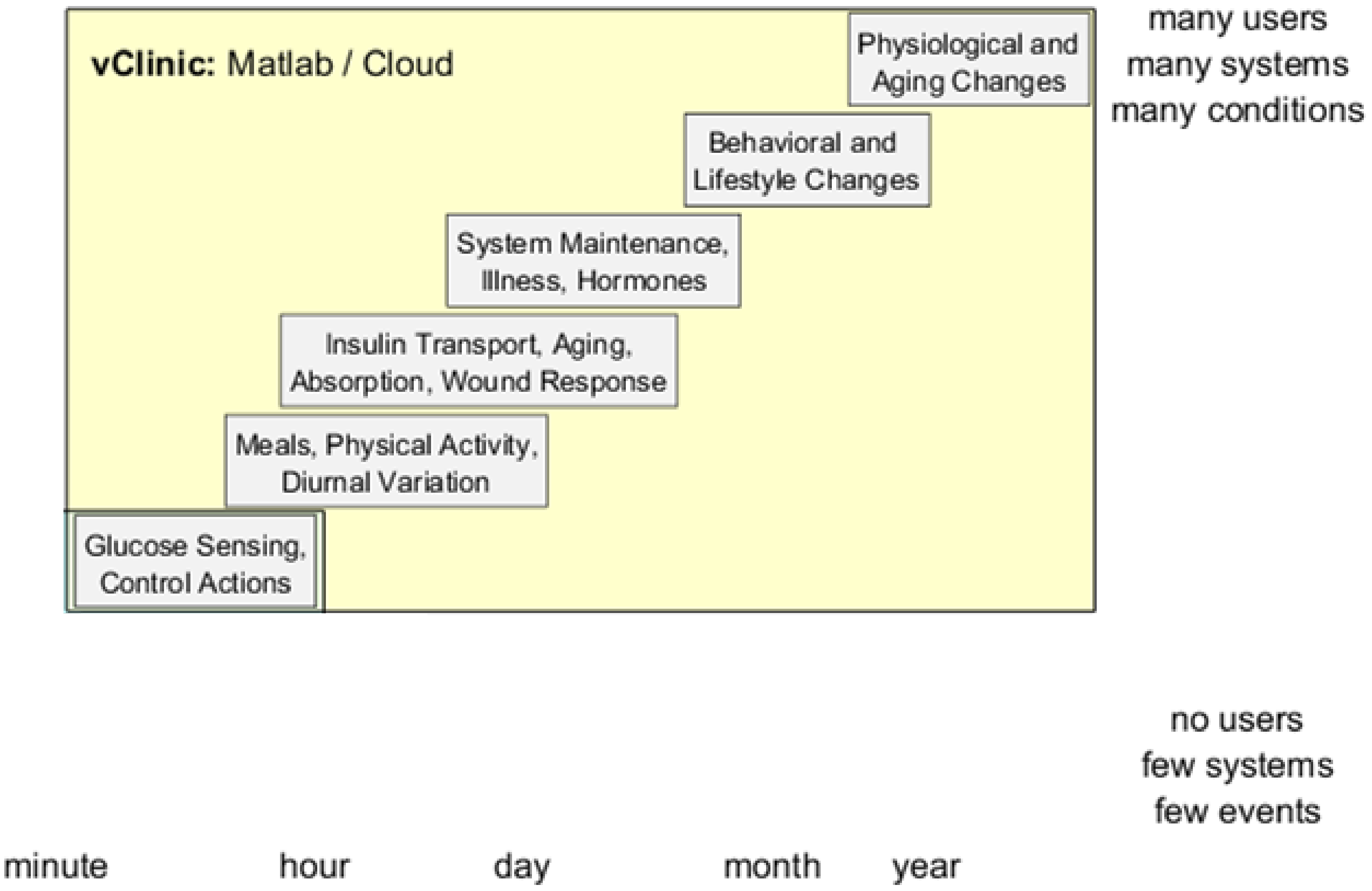
Replace Actual with Model:
physiology, behavior, events, activities



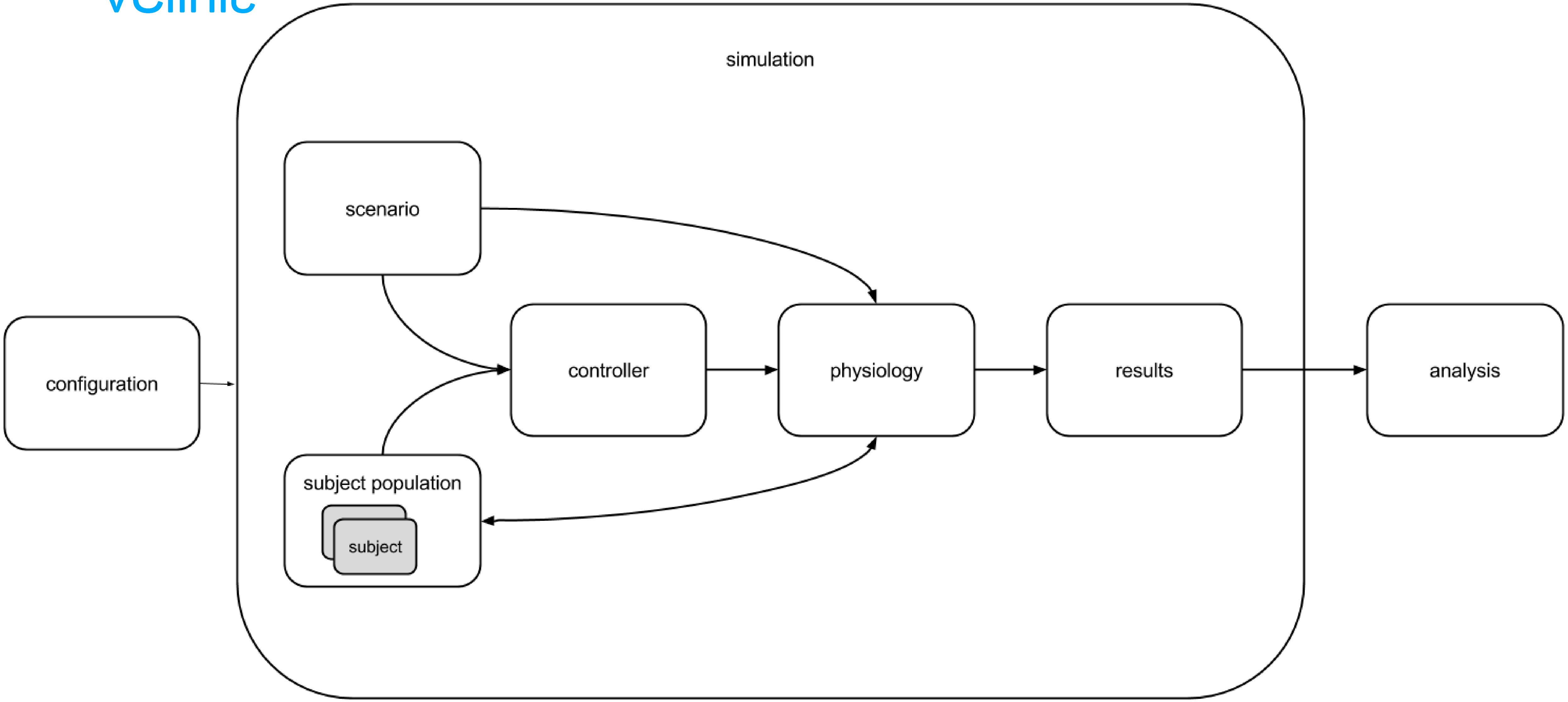
vClinic

- Very fast simulation (AWS)
- MATLAB / object oriented
- Large simulations (100's of subjects, 100's of days)

- Physiology
- Exercise, meals, carb counting error, missed meals, missed insulin, illness
- Different controllers
- Sensor behavior / misbehavior



vClinic



simulation
scenario
configuration
controller
physiology
results
analysis
subject population
subject

BigfootBiomedical/vClinic

GitHub, Inc. [US] | https://github.com/BigfootBiomedical/vClinic

Each simulation is configured via a .yml config file which allows multiple different parameters to be configured to customize an experiment as needed.

Once a configuration file has been completed, a simulation by using the vClinic class Simulation. Here is a example work flow inside the MATLAB terminal:

```
cd ~/vClinic/core
addpath('.');
import com.bigfoot.vclinic.simulation.*;
import com.bigfoot.vclinic.results.*;
s = Simulation('+com/+bigfoot/+vclinic/config/template.yml');
s.startSim();
```

The simulation will start and you can see the status via the progress bar that is printed to the screen. The total time to complete the simulation is depended on how many subjects and how many days that are trying to be simulated. Simulations that take a long time (i.e. a 90 day simulation) the project has been configured to be able to use MATLAB Distributed Computing Server; which allows the simulation to run with up to 256 cores. See the Setting up MATLAB Cloud Center for more information.

analyzing the data

Each simulation saves a .mat file of all the data from the experiment ran. See the output scheme for more details.

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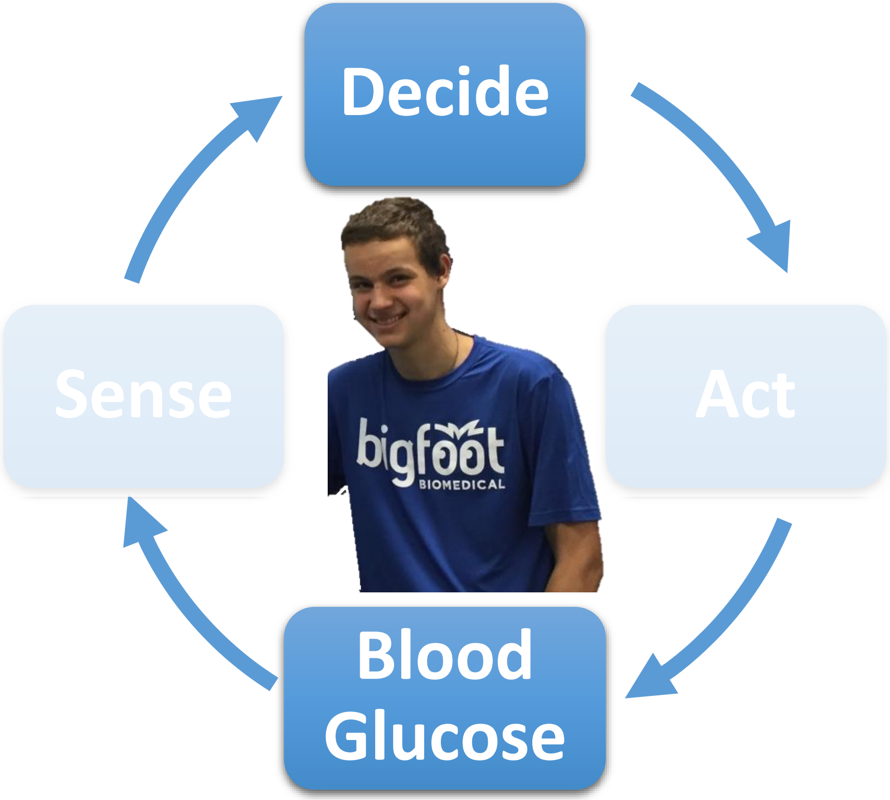
vClinic: physiology, behavior, control algorithm



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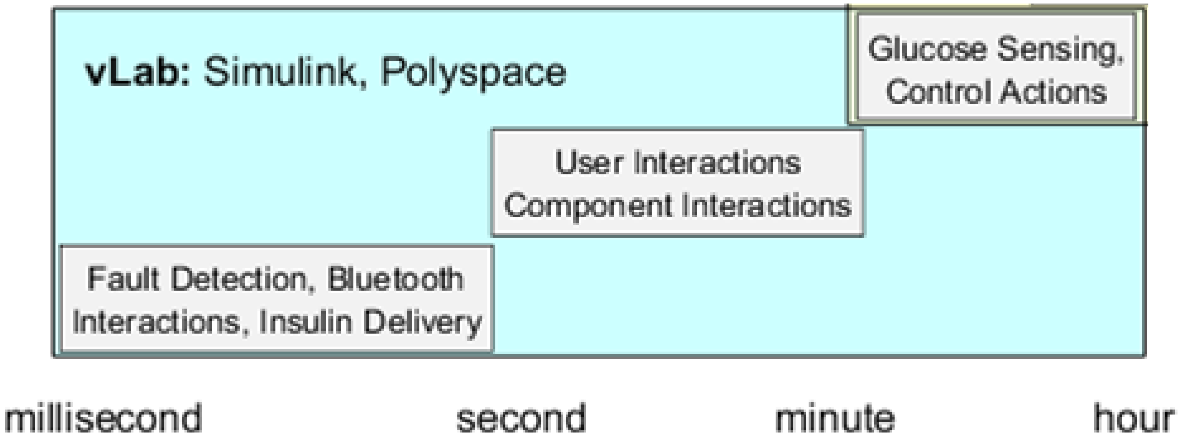
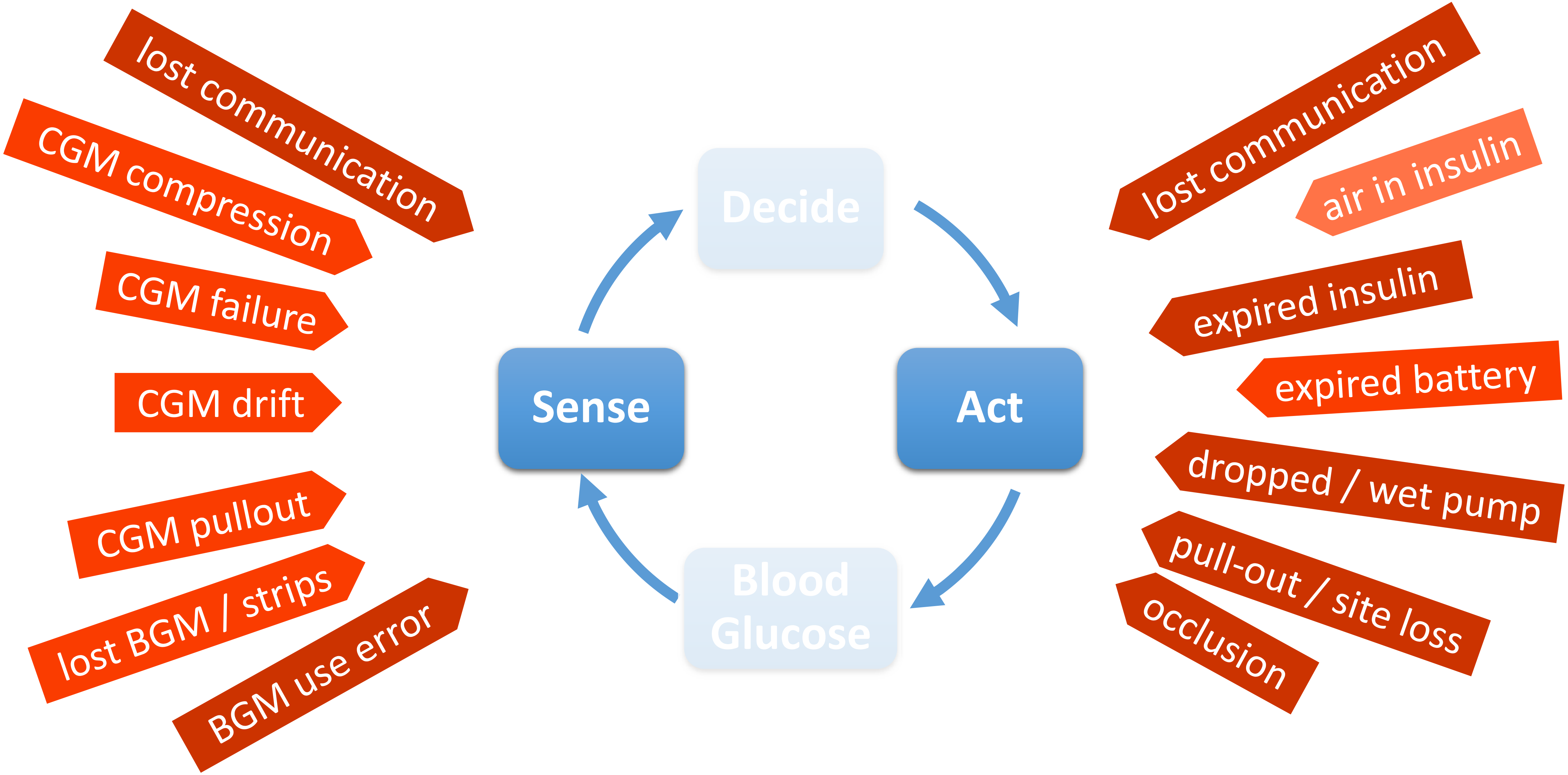
vLab

- Narrow but deep simulation
- Simulink, Stateflow, Polyspace

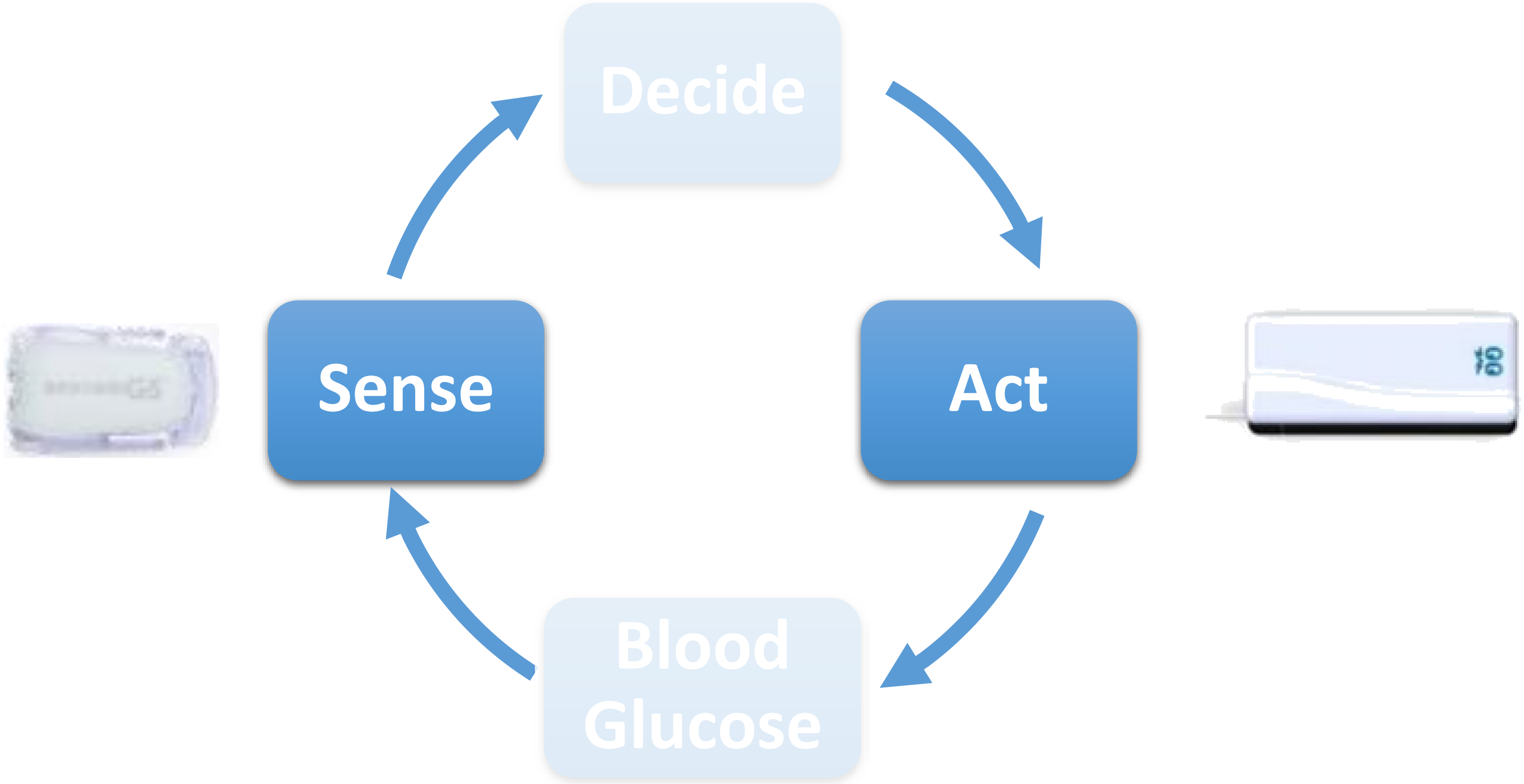
- Characterizes interactions with other system components



System Events: Component Interactions, Faults



vLab: system behavior



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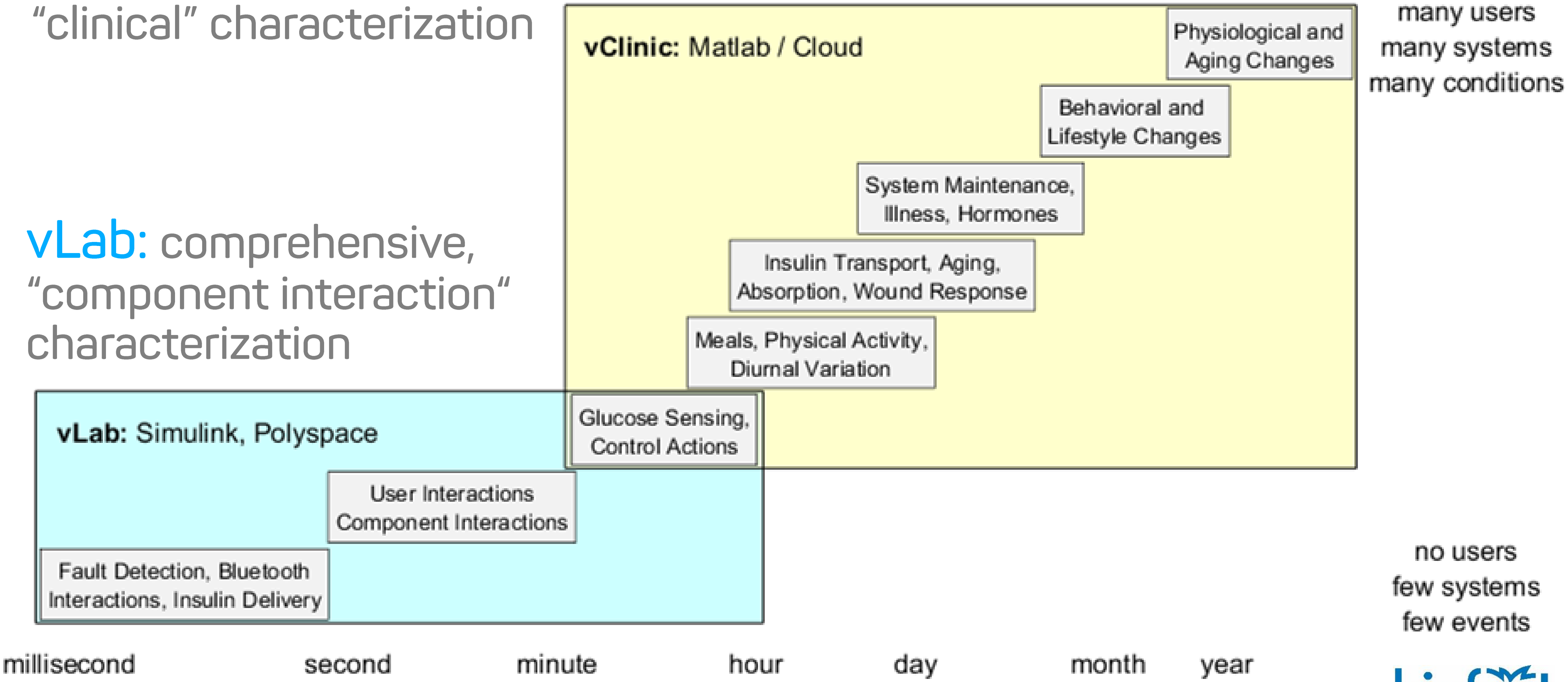
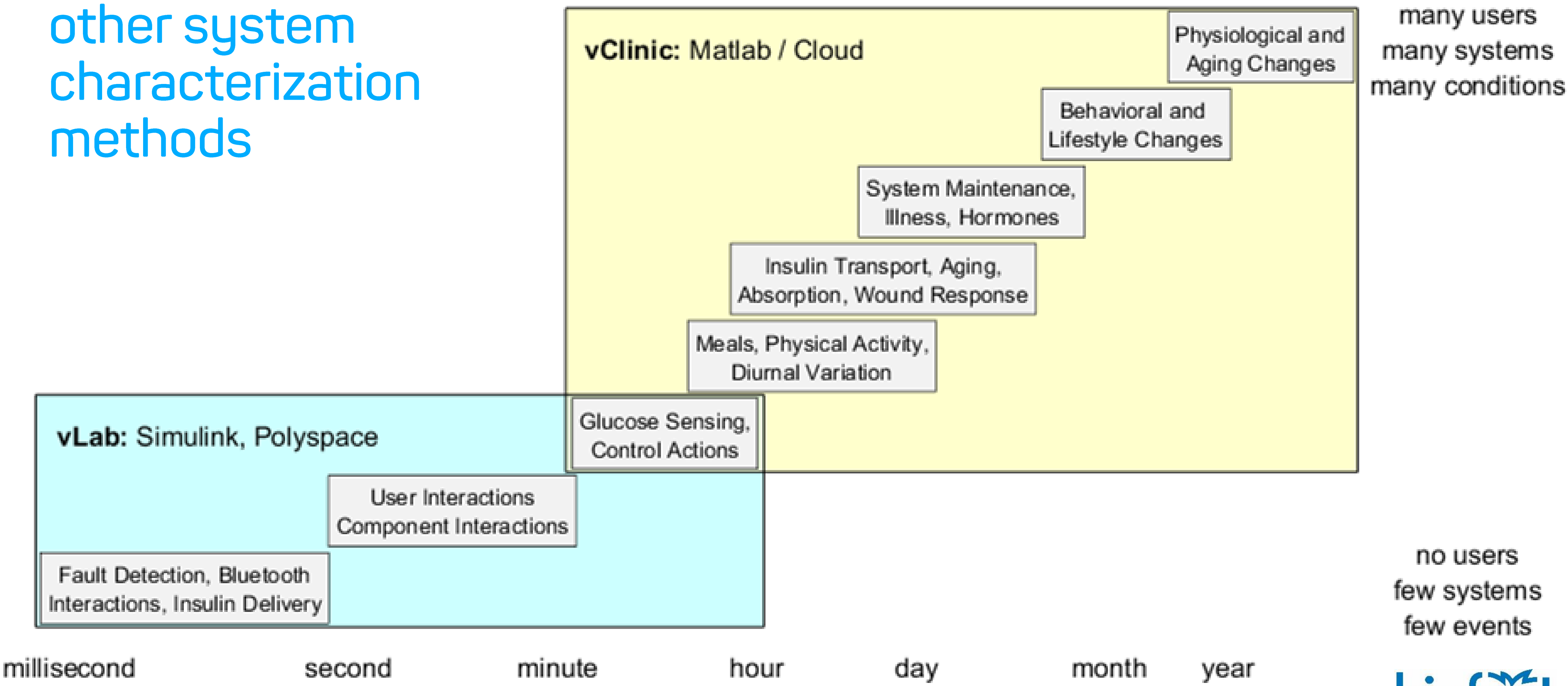
vClinic: fast, large "clinical" characterization

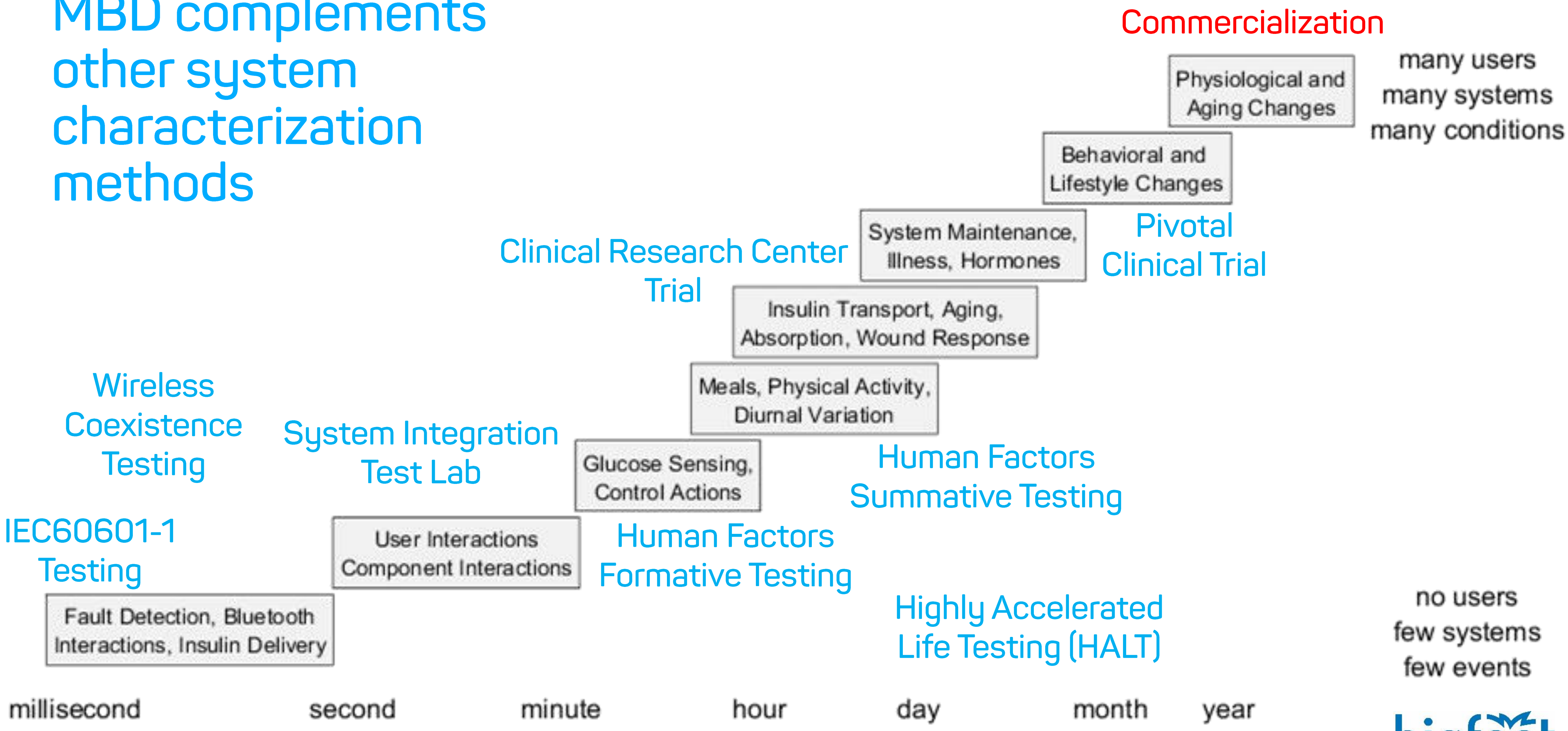
vLab: comprehensive, "component interaction" characterization



MBD complements other system characterization methods



MBD complements other system characterization methods



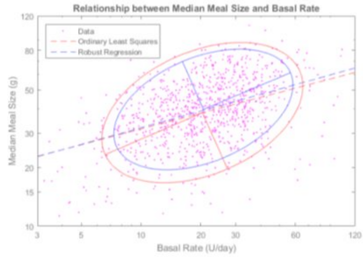
Applicability

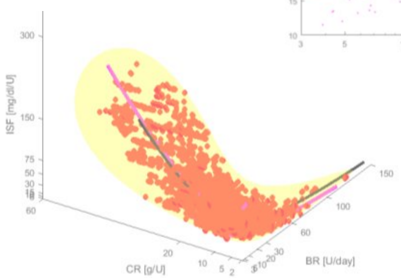
- Algorithm design
- Algorithm implementation
- System V&V
- Regulatory submissions
- Clinical trial design
- Reimbursement modeling
- Investor due diligence
- Interface design
- User Training
- Hazard Analysis

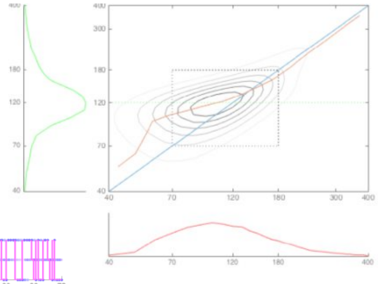
MBD for an Automated Insulin Delivery System

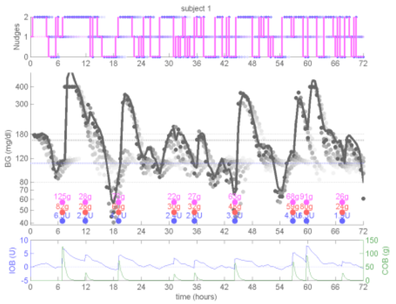
"Models"

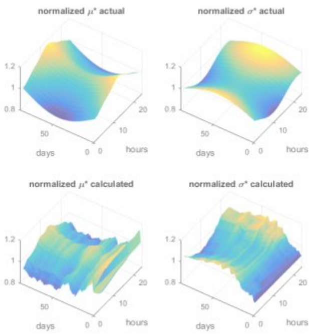
- Physiology
  - Macro, micro
  - Data-driven
  - Parsimonious
- Control Algorithms
- Device Behavior
  - CGM, pump
- Human Behavior

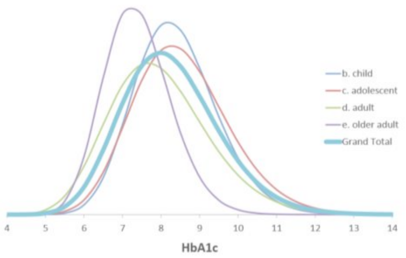












"Simulation Factory"

- Model-Based Design
  - vClinic
  - vLab
  - V&V
- Why? better decisions, faster
  - algorithm development
  - system V&V
  - clinical trial design
  - reimbursement / outcomes