Model Based Design of an Artificial Pancreas

Lane Desborough
Chief Engineer
Model Based Design of an Automated Insulin Delivery System

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Chief Engineer
Living with Diabetes (~9%)
30 million people in the United States
415 million people around the World

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

2-3 million Americans are dependent on insulin

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2-3 million Americans
Sense-Decide-Act
Managing diabetes takes about an hour a day

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

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1School of Nursing and Midwifery, University of South Australia, 2Research and Evaluation Unit, 4Public Health Research Unit, 5Department of Pulmonary Medicine, Women’s and Children’s Hospital, 3Department of Paediatrics, The University of Adelaide, Adelaide, South Australia and 6School 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.
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 performed 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](http://www.andrews.edu/~coffen/Full_Table.pdf)
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
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

- Prefilled Insulin Cartridge
- Disposable Pump Body *
- Modular Architecture
- Auto-Priming Infusion Set
- Durable Controller
- Continuous Glucose Monitor
- * Part of 510(k)-Cleared Asante Snap
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* Part of 510(k)-Cleared Asante Snap
Automated Insulin Delivery

Sense → Decide → Act

Blood Glucose

Manual Control

Level 1
Level 2
Level 3
Level 4
Level 5
Level 6

Full Automation

Human

Computer
Automation of Tasks

- Decide
- Act
- Sense
- “THING”

Level 1
Level 2
Level 3
Level 4
Level 5
Level 6

Manual Control

Human

Computer

Full Automation
The purpose of control is to safely transfer variability ... so that we don’t have to do as much work

Cruise control:

Thermostat:

Control System:

Autopilot

Automated Insulin Delivery
Automated Insulin Delivery

Blood Glucose Physiology

- Feedforward Controller
- Feedback Controller
- Carb Response
- Insulin Response
- Disturbance Response
- CGM

Models

Setpoint

Carbs

mbg

exercise, illness, stress
Physiology and behavior change over time
Same stimulus, different responses

304 Responses to 16g juice box for a single subject

Change in CGM value (mg/dl)

Time since 16g juice box consumed (minutes)
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
Replace Actual with Model: physiology, behavior, events, activities

change across population

change throughout

can change with activities and events

change over time
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
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 an example workflow inside the MATLAB terminal:

```matlab
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.
vClinic: physiology, behavior, control algorithm
vLab

- Narrow but deep simulation
- Simulink, Stateflow, Polyspace
- Characterizes interactions with other system components
System Events: Component Interactions, Faults

- CGM compression
- CGM failure
- CGM drift
- CGM pullout
- Lost BGM / strips
- BGM use error
- Lost communication
- Air in insulin
- Expired insulin
- Expired battery
- Dropped / wet pump
- Pull-out / site loss
- Occlusion
vLab: system behavior
**vClinic:** fast, large “clinical” characterization

**vLab:** comprehensive, “component interaction” characterization
MBD complements other system characterization methods.
MBD complements other system characterization methods.

- Clinical Research Center Trial
  - System Maintenance, Illness, Hormones
  - Insulin Transport, Aging, Absorption, Wound Response
  - Meals, Physical Activity, Diurnal Variation
- Pivotal Clinical Trial
  - Behavioral and Lifestyle Changes
  - Physiological and Aging Changes
- Summative Testing
  - Human Factors Testing
  - Highly Accelerated Life Testing (HALT)
- Formative Testing
  - Glucose Sensing, Control Actions
- Test Lab
  - System Integration
  - Wireless Coexistence Testing
  - User Interactions, Component Interactions
- Testing
  - Fault Detection, Bluetooth Interactions, Insulin Delivery

Time Scales:
- millisecond
- second
- minute
- hour
- day
- month
- year

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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

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