Algorithm for the Infusion Rate of Glucose During an Insulin Clamp

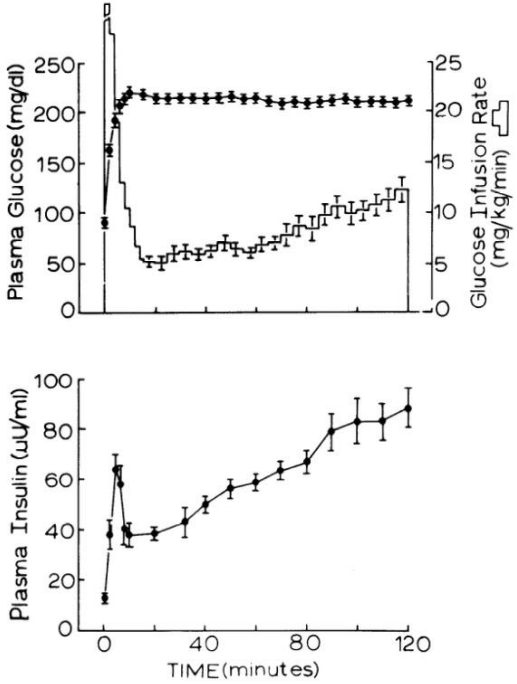
Jason Blohm, Nicholas Diehl, Joe Jeffrey, Sheng-Yau Lim

Background: Our advisor

- Matt Luther, M.D.
  - Nephrologist and endocrinologist at VUMC
  - Interested in pharmacological effects on insulin secretion and insulin sensitivity in vivo
  - Hyperglycemic and hyperinsulinemic clamp studies

Background: Hyperglycemic clamp

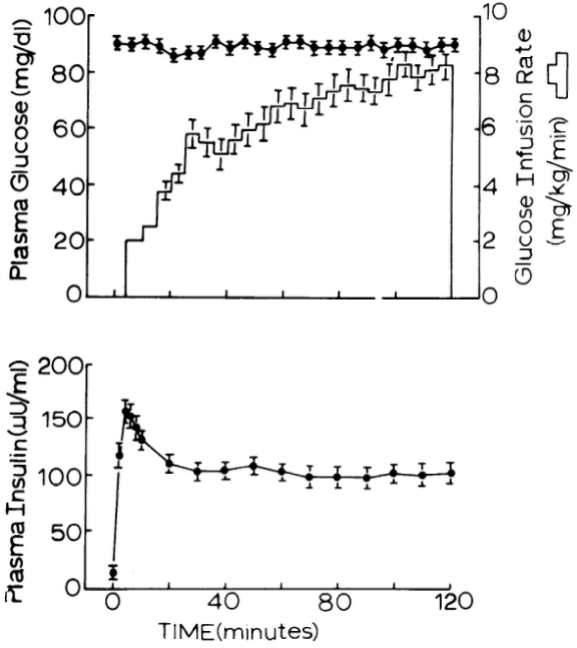
- Plasma glucose is raised and kept constant at 200 mg/dL
- Adjust glucose infusion rate (GIR) in order to maintain glucose levels
- Measures insulin secretion
- Duration: ~2 hours



Defronzo et al., 1979

Background: Hyperinsulinemic clamp

- Plasma insulin rate is raised and held at 120 μU/mL via constant insulin infusion
- Glucose is infused and blood glucose levels are measured; GIR adjusted
- Measures <u>insulin sensitivity</u> in patient
- Duration: ~2 hours



Defronzo et al., 1979

Problem Statement

- In hyperinsulinemic clamp studies, Dr. Luther adjusts GIR on the fly based on his clinical judgment
- This can lead to inaccurate adjustments which can affect subject safety and data validity
- Some people claim that an algorithmic approach works, but no one Dr. Luther has talked to has been successful
- We will develop an algorithm that allows researchers to perform these studies in a more controlled manner

Needs Assessment: Provider

Interface

1. Should be simple to understand
2. Should include inputs for all possible variables the physician may want to change: target glucose level, insulin clamp level, demographic data, time of experiment
3. Given patient demographics and history, should simulate the glucose level over time, prior to clinical testing

Needs Assessment: Provider

Algorithm

1. Should calculate the amount of glucose uptake based on the constant insulin infusion rate the physician specifies
2. Depends on accurate glucose infusion rate
3. Should output a recommended glucose infusion rate that accounts for the time delay in measuring glucose level from blood sample (t-1)

Needs Assessment: Provider

Timing

1. Runtime -- should provide physician with proper glucose infusion rate (GIR) within 10 seconds of inputting the current glucose level
2. Should include an easy to navigate UI for immediate data entry

Needs Assessment: Patient

Safety

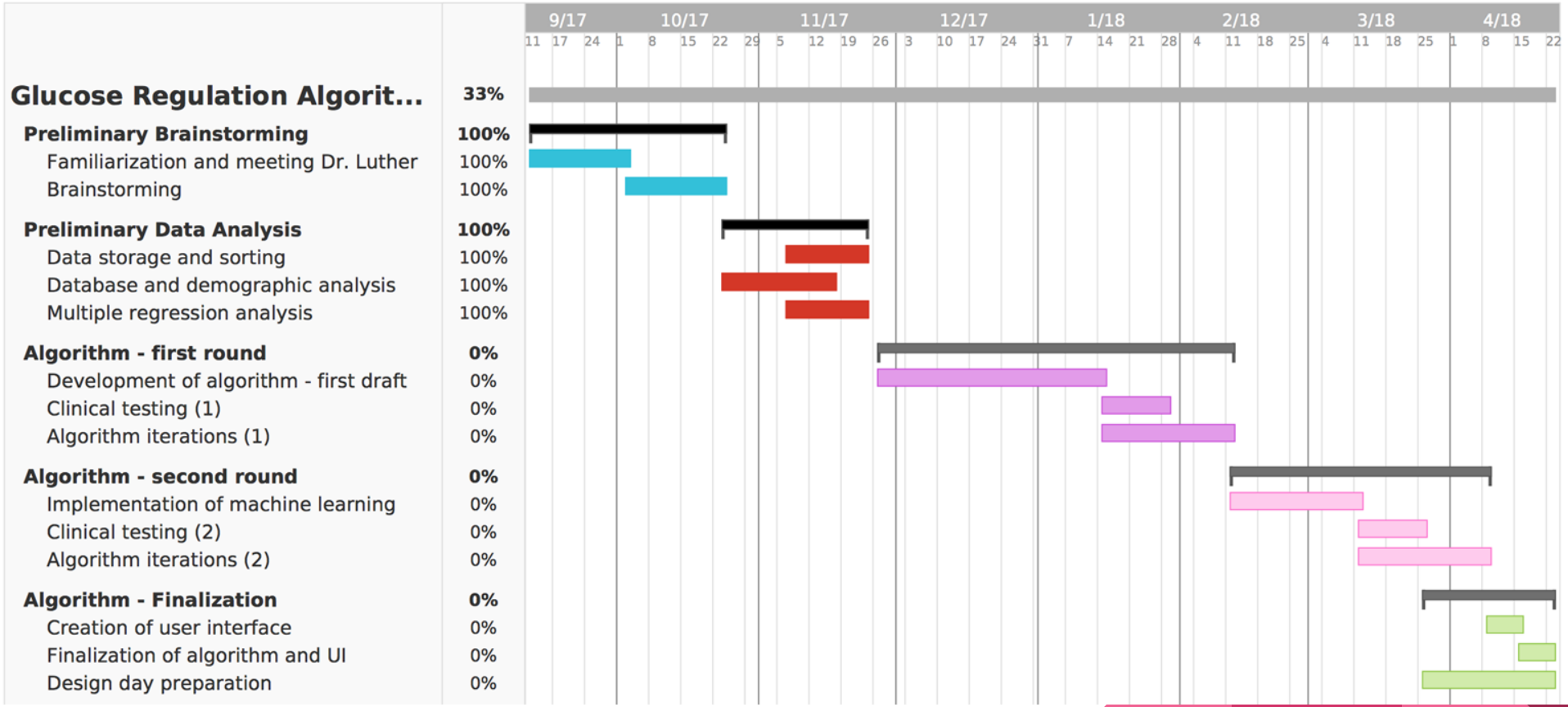
1. Ensure that glucose levels do not exceed or drop below safe levels, as determined by the physician
2. Measurements need to be taken every 5 minutes to ensure glucose levels are where they should be. If not, the program should alert the physician (future iteration)
3. Must run smoothly so that no bugs interrupt the program

Needs Assessment: System

Applicability and cost

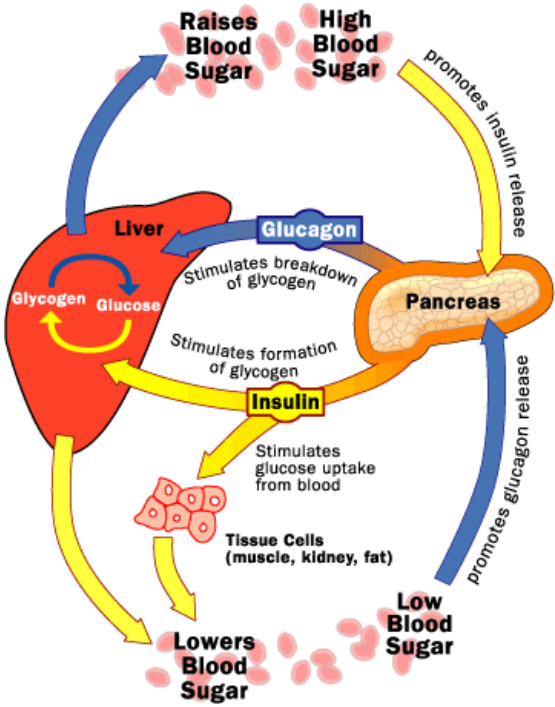
1. Should be applicable to different physicians and different hospitals performing the same studies
2. Should be open source
3. Results from these studies should lower healthcare costs in future

Gantt Chart


9/17
10/17
11/17
12/17
1/18
2/18
3/18
4/18
11 17 24 1 8 15 22 29 5 12 19 26 3 10 17 24 31 7 14 21 28 4 11 18 25 4 11 18 25 1 8 15 22
Glucose Regulation Algorit... 33%
Preliminary Brainstorming 100%
Familiarization and meeting Dr. Luther 100%
Brainstorming 100%
Preliminary Data Analysis 100%
Data storage and sorting 100%
Database and demographic analysis 100%
Multiple regression analysis 100%
Algorithm - first round 0%
Development of algorithm - first draft 0%
Clinical testing (1) 0%
Algorithm iterations (1) 0%
Algorithm - second round 0%
Implementation of machine learning 0%
Clinical testing (2) 0%
Algorithm iterations (2) 0%
Algorithm - Finalization 0%
Creation of user interface 0%
Finalization of algorithm and UI 0%
Design day preparation 0%

Progress

- Familiarization of study aims and insulin/glucose physiology



Glucose clamp technique: a method for quantifying insulin secretion and resistance

RALPH A. DEFRONZO, JORDAN D. TOBIN, AND REUBIN ANDRES
Department of Medicine, Yale Un. ersity School of Medicine, New Haven, Connecticut 06510; and Clinical Physiology Branch, Gerontology Research Center, National Institute of Aging, Baltimore City Hospitals, Baltimore, Maryland 20014

Defronzo et al., 1979

Progress

- Clamp data

	A	B	C	D	E	F	G	H	I	J	K	L
1		study_id	redcap_even	time	gir	glucose	insulin (***can mostly ignore because this data is recorded after the fact)					
2	1	7832001	period_1_arı	-120	0	99	NA					
3	2	7832001	period_1_arı	-115	0	101	NA					
4	3	7832001	period_1_arı	-110	0	96	NA					
5	4	7832001	period_1_arı	-105	0	96	NA					
6	5	7832001	period_1_arı	-20	0	93	NA					
7	6	7832001	period_1_arı	-10	0	93	24.43804					
8	7	7832001	period_1_arı	-1	0	92	30.07894					
9	8	7832001	period_1_arı	0	0	93	NA					
10	9	7832001	period_1_arı	5	0.17	93	43.4504					
11	10	7832001	period_1_arı	10	0.17	93	41.34766					

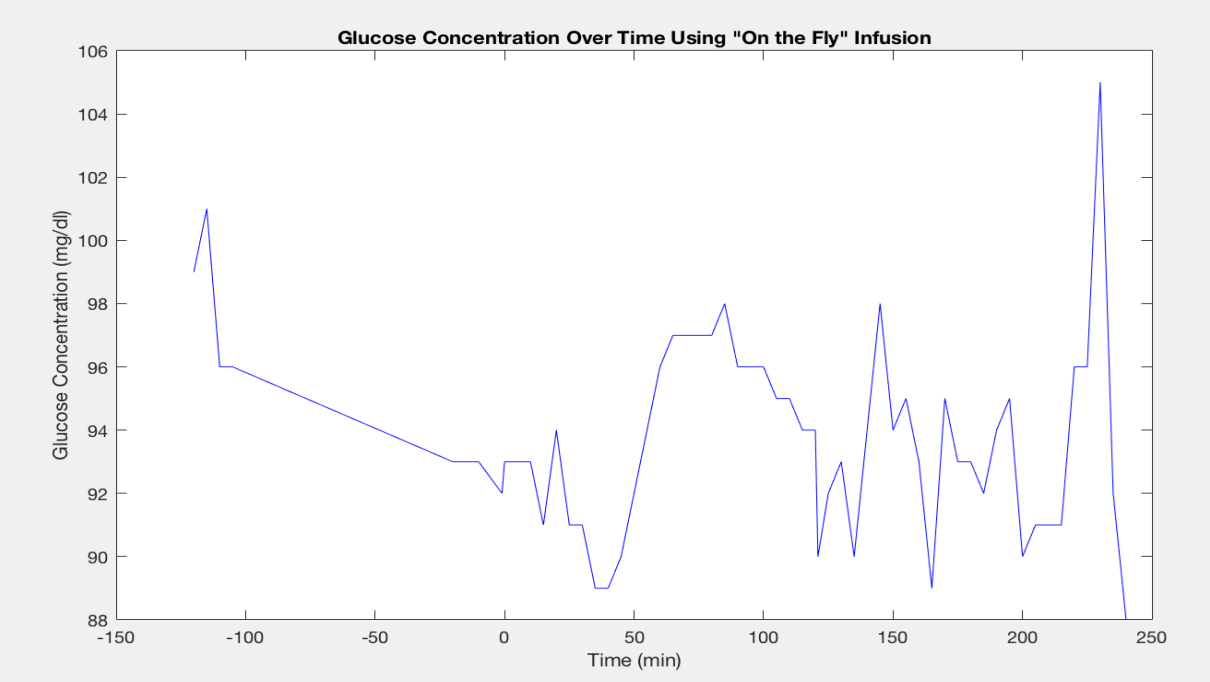
Progress

- Demographic data

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1		study_id	aim	redcap_even	redcap_even	height_m_hi	weight_kg_h	bsa_m2_hie	insulin_inf_r	insulin_inf_r	age	gender	gender.facto	race	race.factor
2	1	7832001	Aim1	period_1_ar	Period 1	1.63	89.7	2.01529568	20	80	62.7	2	female	5	White
3	2	7832001	Aim1	period_2_ar	Period 2	1.63	90.8	2.02761491	20	80	62.7	2	female	5	White
4	3	7832001	Aim2	period_3_ar	Period 3	1.62	95	2.06760731	20	120	65.9	2	female	5	White
5	4	7832001	Aim2	period_4_ar	Period 4	1.62	94.4	2.06106768	20	120	65.9	2	female	5	White
6	5	7832002	Aim1	period_1_ar	Period 1	1.7	111.8	2.29770417	20	120	60.6	2	female	5	White
7	6	7832002	Aim1	period_2_ar	Period 2	1.7	112.2	2.30181088	20	120	60.6	2	female	5	White
8	7	7832002	Aim2	period_3_ar	Period 3	1.7	113.8	2.31816498	20	120	60.8	2	female	5	White
9	8	7832002	Aim2	period_4_ar	Period 4	1.68	113.5	2.30144882	20	120	60.8	2	female	5	White
10	9	7832004	Aim1	period_1_ar	Period 1	NA	89	NA	20	120	40.8	2	female	5	White
11	10	7832005	Aim1	period_1_ar	Period 1	1.62	81.2	1.91154388	20	120	59.2	2	female	5	White

Progress

- Sorted and visualized data from Dr. Luther's previous studies



Progress: Multiple Regression Analysis

Linear regression model:
GIR ~ 1 + Height + Weight + BSA + Age + Gender + Race

Estimated Coefficients:

	Estimate	SE	tStat	pValue
(Intercept)	3.2236	2.011	1.603	0.11325
Height	15.35	5.7597	2.6651	0.0094679
Weight	0.19485	0.083456	2.3348	0.022309
BSA	-20.895	8.0997	-2.5797	0.0119
Age	-0.014226	0.0054871	-2.5927	0.011498
Gender	0.14254	0.16286	0.87521	0.38433
Race	-0.32696	0.22619	-1.4455	0.15261

Next Steps

- Multiple Regression analysis on Insulin Sensitivity
- Familiarization with machine learning
    - Resources online such as the Stanford Machine Learning Course
- Develop first iteration of algorithm
- Continuous glucose monitor for more time samples and more accurate infusion rate adjustment

Potential barriers

- Dr. Luther only runs a study once every 1-2 weeks
- Existing data set is limited
- Programming language differences

Market Potential

- Market potential may be large
  - 5-10 researchers at VUMC alone perform similar studies and have expressed interest in an algorithm
- Open access
- Pharmacological impact
  - Dr. Luther has demonstrated that aldosterone impairs insulin secretion
  - May be interested in drugs to mediate this response
- Could ultimately benefit a patient field consisting of diabetics, obese persons, and those with endocrine imbalances

Questions?