Syllabus (subject to update before the start)

Course #/name: PH797, Special Topics: mathematical models of glucose tolerance

credit hour: 2-4
Course Description: This course will go through several major mathematical models relevant to the study of human glucose tolerance, the insulin action component, the insulin secretion component, and the two major signaling pathways (triggering and amplifying pathways) that regulate insulin secretion rate in response to glucose changes. We will start from Richard Bergman's minimal model MINMOD, we will review a set of mathematical models on whole body glucose and insulin dynamics, discuss the success stories in insulin action evaluation, and limitations in describing the insulin secretion regulation. We will also review models of the triggering and amplifying pathways and the role of beta cell mass. More specifically, the oscillatory insulin exocytosis of beta cells; and the insulin granule dynamics within beta cells, which is believed to lead to the biphasic insulin secretion pattern after glucose stimulus.

In each class, we will go through 1-3 representative paper of the topic. Reading of these articles before the class is required. There will also be opportunity to run simulations using some of the models.

Learning Objectives:

1. basic modeling issues in glucose tolerance
2. major existing models
3. assumptions of the underlying regulating mechanisms
4. application in clinical studies
5. limitations and potential future research directions

Textbook: no

a set of key articles will be provided.

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Course duration: 06/01/10-7/30/09 (9 week)
Course meet at: W 9:30-11 am, in SH1207
Office hour: MW, 2:30-3:30, Shelby 1203

Grading Scheme:
Course grades in terms of letter grade, or "P" or "F", will be determined based on attendance (>70%) and one presentation. each student is expected to present minimally one time, of one paper,

assigned or self-selected. presentation can be 15-30 min. If the paper is lengthy, it can be shared between two students. Reading of the assigned articles before the class is required.

Course schedule (to be update)

week	date	Topics	Required reading
1	06/02	Introduction. MIMMOD original article [1, 2] computer simulation program: [3]	[1-3]
2	06/09	MINMOD, Recent update [4], success stories Criticism: too minimal:? [5] Problems in clinical study [6, 7] Problem in the mathematical model itself [8, 9]	[4-8]
3	06/16	Protocol modification [10]. Extensions of the mathematical models Two-compartment models [11, 12]	[10-12]
4	06/23	Overview of the structure of most models [13] What need to be done [14]	[13, 14]
5	06/30	Glucose-stimulated insulin secretion regulation, First model of Biphasic insulin secretion [15] Two pathways (Triggering and amplifying pathways) stimulated by glucose [16, 17]	[15] [16, 17]
6	07/07	Rate limiting steps in biphasic insulin secretion Insulin granule dynamics[18] Mathematical model [19]	[18, 19]
7	07/14	Oscillatory insulin secretion Biological review [20] Mathematical model [21]	[20, 21]
8	07/21	Oscillatory insulin secretion	To be assigned
9	07/28	The role of beta cell mass. Student presentation	To be assigned

PDF of assigned reading available at http://zen.dom.uab.edu/ph797/home.php

General reading material

1. Whole body models of glucose tolerance

1.1 MINMOD

- original article [1, 2]
- computer simulation program: [3, 22, 23]
- ADA consensus on insulin sensitivity measure [24]
- Disposition index DI was found predictive of T2D incidence [25]
- Its QTL being mapped to chromosome 11 [26, 27].
- Recent update [4, 22], also see Berman's ADA Banting medal speech.

1.2. Criticism [5-8, 28-32]

- too minimal
- insulin sensitivity
- glucose effectiveness
- under-modeled insulin secretion
- application to T1D
- mathematical problems

1.3. Modifications

- modification of the laboratory protocol (insulin-, tolbutamide- modified): [10, 33]
- modifications of the simulation protocol

2. Other whole body models of glucose tolerance

[13, 34-50]. A review of current status: [14].

3. Insulin secretion, the triggering and amplifying pathways

overview [16-18]

3.1. Oscillatory insulin release models (the triggering pathway)

[20, 21, 51-62].

3.2. Insulin granule trafficking and biphasic insulin secretion, both triggering and amplifying pathways

[18, 19, 63-65].

4. The issue of beta cell mass in glucose tolerance

[14, 66, 67].

Reference

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