Curriculum Vitae
Part I: General Information

Name: FIRAS H. EL-KHATIB, Ph.D.

Office Address: 44 Cummington Street (BME), Boston, MA 02215
E-mail: fhkhatib@bu.edu **Fax:** (617) 358–2835

Education:

09/2001 – 12/2005	Ph.D.	University of Illinois at Urbana-Champaign (UIUC)
01/2000 – 08/2001	M.S.	University of Illinois at Urbana-Champaign (UIUC)
10/1993 – 07/1998	B.Eng.	American University of Beirut (AUB), Lebanon

08/2001 – 12/2005 ***University of Illinois @ Urbana-Champaign***
- Doctor of Philosophy (**Ph.D.**) in Mechanical Engineering
  Department of Mechanical & Industrial Engineering
  Focus: Biomedical Engineering & Control System Design. **GPA**: 4.0/4.0.
  Ph.D. DISSERTATION– *EL-KHATIB, F. H.* (2005) System identification and adaptive closed-loop glucose control in a type 1 diabetic swine model

01/2000 – 08/2001 ***University of Illinois @ Urbana-Champaign***
- Master of Science (**M.S.**) in Mechanical Engineering
  Department of Mechanical & Industrial Engineering
  Focus: Bio-fluidics. **GPA**: 3.975/4.0
  M.S. THESIS– *EL-KHATIB, F. H.* (2001) A non-Newtonian model of pulsatile blood flow in a cylindrical tube

1993 – 1998 ***American University of Beirut***
- Bachelors of Engineering (**B.Eng.**),
  Department of Mechanical Engineering
  Ranked first throughout program years. **GPA**: 4.0/4.0
  High distinction, Dean's **Honor List** 1993, 94, 95, 96, 97 & 98. Granted university scholarship 1997–98. Awarded Procter & Gamble scholarship 1998

1981 – 1993 ***Al-Choueifat International School, Abu-Dhabi, UAE***

CONCENTRATION*: Undertook courses in the following fields:*

- Control Systems: Theory and Design
- Digital Control of Dynamic Systems
- State-Space Design Methods in Control
- Mathematical Methods for Engineers
- System Identification
- Adaptive (online) Control
- Nonlinear Systems
- Programming

Languages:

English	Language of instruction throughout academic education
Arabic	Native language

Postdoctoral Training:

01/2006 – Present	Senior Research Associate, Biomedical Engineering,	BU
03/2008 – Present	Research Fellow, Diabetes Research Center,	MGH

Academic Appointments:

01/2006 – Present	Senior Research Associate in Biomedical Engineering,	BU
01/2000 – 12/2005	Research Assistant in Mechanical Engineering,	UIUC

Awards and Honors:

02/2006 – 07/2007	JDRF Post-doctoral Research Fellowship

Part II: Research, Teaching, and Clinical Contributions:

Narrative Research Report

The overarching objective of my research is to develop an engineering device that will provide automated regulation of blood-glucose in people with diabetes, particularly those with type 1 diabetes. This device is described in the literature as an "artificial (endocrine) pancreas" or a "closed-loop glucose-control system" and is intended to automate the management of insulin-dependent diabetes by automating the delivery of insulin (and a counter-regulatory drug). In essence, this technology will enhance the standard of care and provide consistent, tight, and safe regulation of blood glucose. Diabetes afflicts about 20 million individuals in the USA, and about 200 million worldwide, with about 10% having type 1 diabetes. It is well established that tight blood-glucose control is essential to eradicate the deleterious, acute and long-term, chronic complications associated with diabetes. Acute complications of poor diabetes management include convulsions, seizures, coma, and paralysis, whereas long-term chronic complications include cardiovascular disease, vision disorders, kidney malfunction, nerve degeneration, neurocognitive deficits, and skin disorders, all of which may cause serious, debilitating, consequences and some may lead to death. On the other hand, it is also a compelling fact that consistent, tight, and safe blood-glucose regulation using conventional open-loop insulin therapy is a challenging and often elusive target for many people with diabetes. My envisioned control device will normalize the blood-glucose regulation process and will convert it, from the daunting task it is, to an automated reality. In terms of a patient's perspective, this will profoundly reduce the painstaking and stressful tasks of frequent pricking, carbohydrate counting, and insulin-dose decision making, which demand relentless diligence and vigilance, and could become overwhelming or are beyond grasp for non-cognizant individuals.

My control system employs subcutaneous administration of insulin or of both insulin and glucagon. When properly orchestrated, delivery of these exogenous (dual counter-) regulatory hormones serves to limit hyperglycemia and preemptively stave off or reverse hypoglycemia. The control system is designed to solely respond to glucose measurements obtained from blood or alternatively sensed and estimated from a bodily fluid space such as the interstitial fluid. Continuous monitors that sense interstitial-fluid glucose have recently been FDA approved. The thrust of my contribution in developing this system pertains to the development of the underlying control logic that would respond to the glucose readings reported by the continuous glucose monitor on one end and orchestrate the real-time operation of a drug infusion system on the other end. The control logic is being developed to interface with various end technologies, i.e. different glucose monitors and infusion pumps is possible. Based on extensive research of the existing literature, and knowledge of the leading studies that were recently presented in conference meetings, it is my conviction that my control algorithm possesses facets that render it novel, thus unique, in its design. Unlike the other, countable, control systems being developed, my system has been thoroughly tested and practically validated in both a diabetic pig model as well as in an inpatient pilot clinical trial. Subsequent inpatient pilot clinical trials are planned to commence soon in order to systematically develop the control system and take it to outpatient and pivotal studies in timely fashion. Upon obtaining FDA approval and being marketed, my control system will provide robust regulation in a truly automatic fashion, with no (feed-forward) contribution being required from the patient during operation. The control system will furnish a genuine prospect for eradicating the deleterious complications of diabetes. It will simply and utterly set a normalized standard of care that is not predominantly proportional in efficacy to the patient's skill or level of cognizance or diligence.

I am also currently adapting my control system and testing it in a pig model to ultimately serve in an intensive care setting in people under critical conditions, e.g. post-accidents, war wounds, severe illness, etc, since it is common for critically ill patients to exhibit profoundly poor blood-glucose regulation, even in the absence of diabetes. Regulating blood glucose under such stressful conditions poses a problem of different underlying pathology and is well regarded as a challenge, especially since only crude and discrete measures are currently employed in hospitals. It is argued that tight glycemic control in critically ill patients improves clinical outcome by in terms of survival rates and reduced morbidity.

Part III: Bibliography:

Original Articles:

- EL-KHATIB*, F. H., RUSSELL*, S. J., NATHAN, D. M., SUTHERLIN, R. G. & DAMIANO, E. R. (2010) Bi-hormonal Closed-loop Blood Glucose Control for Type 1 Diabetes. *Science Trans. Med.* **2** (in press).
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R. (2010) Practical Implementation of a prosthetic endocrine pancreas in diabetic swine. (in preparation).
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R. (2009) Closed-loop blood-glucose control using dual subcutaneous infusion of insulin and glucagon in ambulatory diabetic swine. *Diabetes Sci. Technol.* **3**, 789–803.
- EL-KHATIB, F. H., JIANG, J., GERRITY, R. G. & DAMIANO, E. R. (2007) Pharmacodynamics and stability of subcutaneously infused glucagon in a type 1 diabetic swine model *in vivo*. *Diabetes Technol. Ther.* **9**(2), 135–144.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R. (2007) Adaptive closed-loop control provides blood-glucose regulation using dual subcutaneous insulin and glucagon infusion in diabetic swine. *Diabetes Sci. Technol.* **2**(1), 181–192.
- DAMIANO, E. R., LONG, D. S., EL-KHATIB, F. H. & STACE, T. M. (2004) On the motion of a sphere in a Stokes flow parallel to a Brinkman half space. *J. Fluid Mech.* **500**, 75–101.
- EL-KHATIB, F. H. & DAMIANO, E. R. (2003) Linear and nonlinear analyses of pulsatile blood flow in a cylindrical tube. *Biorheology* **40**, 503—522.

Reviews, Chapters, and Editorials:

- IEEE Transactions of Biomedical Engineering
- Journal of Diabetes Technology & Therapeutics
- Journal of Diabetes Science & Technology
- Annals of Biomedical Engineering
- Journal of Biomedical Engineering

Theses:

- Ph.D. DISSERTATION (University of Illinois at Urbana-Champaign) –
  EL-KHATIB, F. H. (2005) System identification and adaptive closed-loop glucose control in a type 1 diabetic swine model.
- M.S. THESIS (University of Illinois at Urbana-Champaign) –
  EL-KHATIB, F. H. (2001) A non-Newtonian model of pulsatile blood flow in a cylindrical tube.

Patents, Intellectual Property, and Provisional Disclosures:

- EL-KHATIB, F. H. & DAMIANO, E. R. (2005) A fully automated control system for type 1 diabetes. (*Pending US and International Application. Priority date* May 15, 2005).
- RUSSELL, S. J, NATHAN, D. M., EL-KHATIB, F. H. & DAMIANO, E. R. (2009) Formulations for blood glucose management and methods of use thereof (*Provisional US patent application. Priority date* Nov. 13, 2008).
- EL-KHATIB, F. H. & DAMIANO, E. R. (2009) Tuning of closed-loop glucose control algorithm by adjustment of parameters that model the pharamcokinetics of insulin. (*Provisional US patent application. Priority date* June 4, 2009).
- RUSSELL, S. J, EL-KHATIB, F. H. & DAMIANO, E. R. (2009) Multiplex pharmacokinetic profiling to select rapid-acting insulin analogs for treatment of diabetes mellitus. (*Provisional US patent application. In preparation*).

Abstracts and Conference Proceedings:

- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2009) Automated blood-glucose regulation in diabetic swine using bi-hormonal and insulin-only closed-loop control systems. *69th Scientific Session of the American Diabetes Association*, New Orleans, LA, June 5–9, 2009.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2008) Bi-hormonal closed-loop control of blood glucose using dual subcutaneous infusion of insulin and glucagon in type 1

diabetes. *Eighth Annual Diabetes Technology Meeting*, Bethesda, MD, November 13–15, 2008.

- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2008) Closed-loop blood-glucose control using dual subcutaneous infusion of insulin and glucagon in ambulatory diabetic pigs. *68th Scientific Session of the American Diabetes Association*, San Francisco, CA, June 6–10, 2008.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2007) Closed-loop blood-glucose control using dual subcutaneous infusion of insulin and glucagon in ambulatory diabetic pigs. *Seventh Annual Diabetes Technology Meeting*, San Francisco, CA, October 25–27, 2007.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2007) Adaptive closed-loop control provides robust blood-glucose regulation using dual subcutaneous infusion of insulin and glucagon in ambulatory diabetic swine. *67th Scientific Session of the American Diabetes Association*, Chicago, IL, June 22–26, 2007.
- EL-KHATIB, F. H., JIANG, J., GERRITY, R. G. & DAMIANO, E. R. (2006) Pharmacodynamics and stability of subcutaneously infused glucagon in a type 1 diabetic swine model *in vivo*. *Sixth Annual Diabetes Technol. Meeting*, Atlanta, GA, November 2–4, 2006.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2006) Closed-loop blood-glucose control using dual subcutaneous infusion of insulin and glucagon. *Sixth Annual Diabetes Technology Meeting*, Atlanta, GA, November 2–4, 2006.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2006) Closed-loop blood-glucose control using dual subcutaneous infusion of insulin and glucagon. *BMES Fall Annual Society Meeting*, Chicago, IL, October 11–14, 2006.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2006) Optimized self-learning in vivo blood-glucose control using dual subcutaneous infusion in a diabetic swine model. *66th Scientific Session of the American Diabetes Association*, Washington, DC, June 9–13, 2006.
- EL-KHATIB, F. H., JIANG, J. & DAMIANO, E. R (2006) Closed-loop blood-glucose control using dual subcutaneous infusion in vivo. *Massachusetts Biotechnology Council Diabetes Summit Conference*, Boston, MA, May 31, 2006.
- EL-KHATIB, F. H. & DAMIANO, E. R. (2001) A numerical study of a non-Newtonian model for blood under pulsatile flow in cylindrical tube. *Ann. Biomed. Eng.* **29**, Supp. 1, S-78 (Abstr).

Current Research Activities

To design a closed-loop control system for regulating blood-glucose in type 1 diabetes

The aim of this project is to develop an integrated control system for regulating blood glucose in type 1 diabetes using subcutaneous infusion of insulin and glucagon. The system has been developed and assessed in pre-clinical studies in a swine model for type 1 diabetes. The system has been tested in a first-phase clinical trial using venous blood-glucose sampling in adults (18 years and older) with type 1 diabetes and will be tested further in the same population as well as in children (12–18 years old) with type 1 diabetes using interstitial-fluid glucose sampling from a continuous glucose monitor.
Role: Co-investigator Research Effort: 75%

To design a closed-loop control system for regulating blood-glucose in the ICU

The aim of this project is to develop a novel automated closed-loop control device intended to provide effective and safe blood-glucose regulation in ICU patients, using intravenous infusion of insulin and dextrose.
Role: Co-investigator Research Effort: 25%

Teaching

Local Contributions:
2008 Poster presentation at the Engineering Dean's Board Meeting in BU
2007 Senior design project report grading

2006 Poster presentation at the Diabetes Summit in Joslin Diabetes Center
2001–2004 Fluid Mechanics course exam grading

Regional, national, or international contribution:
2009 Poster presentation at the American Diabetes Association, New Orleans, LA
2008 Poster presentation at the Diabetes Technology Society, Bethesda, MD
2008 Poster presentation at the American Diabetes Association, New Orleans, LA
2007 Poster presentation at the Diabetes Technology Society, San Francisco, CA
2007 Poster presentation at the American Diabetes Association, Chicago, IL
2006 Poster presentation at the Diabetes Technology Society, Atlanta, GA
2006 Poster presentation at the Biomedical Engineering Society, Chicago, IL
2006 Poster presentation at the American Diabetes Association, Washington, DC

Part IV: Funding Information:

ACTIVE
12/01/2009–11/30/2012
1R01 DK 085633 $695,080 + $678,450 + $672,695
NIH/NIDDK (primary) and NICHD
Clinical trials of a closed-loop control system for type 1 diabetes management
Role: Co-investigator

The aim of this project is to test our closed-loop, bihormonal and insulin-only, glucose-control system in adults (18 years and older) with type 1 diabetes. The inpatient trial will be performed in the Clinical Research Center at Massachusetts General Hospital. The control system will administer subcutaneous doses of insulin and/or glucagon based on interstitial-fluid glucose measurements from a continuous glucose monitor. The trial will include periods of exercise.

09/01/2009–09/30/2010
Clinical Research Grant $961,635
Leona M. and Harry B. Helmsley Charitable Trust
In-patient trials of automated glucose control in children with type 1 diabetes
Role: Co-investigator

The aim of this project is to test our closed-loop, bihormonal and insulin-only, glucose-control system in children (12–18 years old) with type 1 diabetes. The inpatient trial will be performed in the Clinical Research Center at Massachusetts General Hospital. The control system will administer subcutaneous doses of insulin and/or glucagon based on interstitial-fluid glucose measurements from a continuous glucose monitor. The trial will include periods of exercise.

08/01/2009–07/31/2010
Clinical Investigations Research Grant $511,866
Juvenile Diabetes Research Foundation
Closed-loop glucose control for automated management of type 1 diabetes.
Role: Co-investigator

The aim of this project is to test our closed-loop glucose-control system in adults (18 years and older) with type 1 diabetes. The inpatient trial will be performed in the Clinical Research Center at Massachusetts General Hospital. The control system will administer subcutaneous doses of insulin and/or glucagon based on interstitial-fluid glucose measurements from a continuous glucose monitor.

04/01/2009–03/31/2010
Translational Partners Grant $100,000
Wallace H. Coulter Foundation
Development and preclinical testing of a closed-loop control system for blood-glucose regulation in the ICU

Role: Co-investigator

The aim of this project is to develop an automated closed-loop control device intended to provide tight and safe blood-glucose regulation in ICU patients. This phase is intended for preclinical testing in a stress-hyperglycemic swine model under anesthesia, in order to transition to a pilot clinical trial. The envisioned end product is an integrated control system for blood-glucose regulation in the ICU, where a commercial bedside glucose monitor is linked, via our control algorithm, to a medical-grade infusion system delivering intravenous insulin and dextrose.

COMPLETED
09/01/2007–07/31/2009
Clinical Investigations Research Grant
Juvenile Diabetes Research Foundation
Closed-loop glucose control for automated management of type 1 diabetes.
Role: Co-investigator

The aim of this project was to test of our closed-loop glucose-control system in adults (18 years and older) with type 1 diabetes. The inpatient trial was performed in the Clinical Research Center at Massachusetts General Hospital. The control system administered subcutaneous doses of insulin and/or glucagons based on venous blood glucose regularly sampled from an intravenous catheter.

04/01/2007–09/30/2007
Translational Partners Grant
Wallace H. Coulter Foundation
Closed-Loop Blood-Glucose Regulation in Type 1 Diabetes: A Clinical Trial
Role: Co-investigator

The aim of this project was to develop an integrated closed-loop control system for regulating blood-glucose in type 1 diabetes, and to clinically test the system in clinical trials on healthy volunteers with type 1 diabetes.

04/01/2006–03/31/2007
Translational Partners Grant
Wallace H. Coulter Foundation
Closed-Loop Blood-Glucose Regulation in Type 1 Diabetes: A Clinical Trial
Role: Co-investigator

The aim of this project was to build a robust automated blood-glucose control unit consisting of our closed-loop control algorithm, state-of-the-art FDA-approved drug-infusion pumps, and an FDA-approved interstitial-fluid continuous glucose monitor.

02/01/2006–07/31/2007
Post-doctoral Fellowship Grant
Juvenile Diabetes Research Foundation
The design of a closed-loop controller for blood glucose in type 1 diabetes
Role: Principal Investigator

The aim of this project was to develop an adaptive control algorithm that utilizes model predictive control strategy for closed-loop glucose control in type 1 diabetes, and to preclinically test the system in a type 1 diabetic swine model.