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Dear Origins Project Postdoctoral Prize Lectureship Selection Committee Members,

After a 12-month visit during my PhD to the world's leading group in the artificial pancreas research area (University of Cambridge), I came back to Canada and initiated a new research program that applies feedback control theory and Bayesian modeling techniques to solve diabetes physiological and clinical problems, using a highly interdisciplinary bench-to-bedside approach. I work closely with clinicians and the medical device industry, and my research program has received more than $1.2M in research funds over the last 4 years. Although registered as a postdoctoral trainee under the supervision of a clinician, I have been working as an independent engineering researcher in collaboration with clinicians, and have initiated and established a solid, well-funded (> $1.5M), research program.

I currently work in three research areas. First, I am developing an external artificial pancreas that automatically regulates glucose levels in patients with type 1 diabetes. Type 1 diabetes is a chronic disease resulting in an autoimmune destruction of pancreatic beta cells and requires life-long insulin replacement therapy. It is one of the most common chronic diseases in young people, affects 5-15% of the 285 million diabetics worldwide, and its incidence is increasing by 2 to 5% (current global incidence rate is around 80,000 children per year). Despite advances in treatment options, most patients (> 75%) still do not achieve glucose targets, which increase the incidence of long-term devastating complications such as blindness, kidney failure, heart disease and lower extremity amputations. Hypoglycemia (dangerously low glucose levels) is also a fact of life for patients with type 1 diabetes; it causes significant physical and psychosocial morbidity and is estimated to be the direct cause of 10% of patient deaths. Life expectancy of patients with type 1 diabetes is currently around 15 years less than the general population.

The artificial pancreas is the "Holy Grail" for millions of patients with type 1 diabetes and will likely revolutionize diabetes care and significantly improve quality of life, and its development falls within the interest of the Origin Project whose ultimate goals include: "*helping solve pressing global problems, improving quality of life, and informing the development of sound public policy*"[1]. In the artificial pancreas, a portable pump infuses insulin (a hormone that reduces glucose levels) and glucagon (a hormone that raises glucose levels) subcutaneously based on a control-dosing algorithm that is driven by continuous glucose sensor readings (Figure 1). The novelty of this approach resides in the real-time feedback between glucose levels and hormonal delivery. This feedback control problem is challenged by the large intra- and inter-patient variability, sensor inaccuracies, meals, exercise, and the time-lag in insulin absorption. In 2012, I compared my first prototype of the system, based on adaptive model predictive control, in a randomized human trial against conventional pump therapy for 15 hours in 15 patients. The results were significant; the artificial pancreas reduced the time for which glucose levels were in

[1] https://origins.asu.edu/about

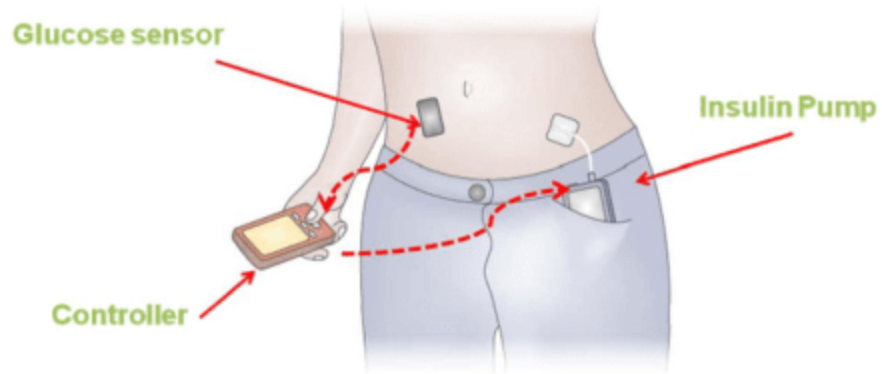

Figure 1. Artificial Pancreas System. A sensor measures glucose levels and transmits them to a mobile-phone-sized controller, which runs a control algorithm. An infusion pump delivers insulin and glucagon subcutaneously. Reprinted from Nature Reviews Endocrinology.

hypoglycemia 8-fold. This work was published in *Canadian Medical Association Journal*, which is a general medical journal that is ranked ninth among the 151 journals in the general and internal medicine category, and is read by physicians with various medical backgrounds. My paper was accompanied with an editorial by the leading figure in diabetes research, David Nathan, where he labelled artificial pancreas system as "the most promising therapy for type 1 diabetes". The media coverage report provided by the journal indicated that my paper was covered by more than 90 media items in more than seven languages. We consequently developed different aspects of the system (night, meal, and exercise control) and conducted 6 more clinical trials, and 3 additional trials are ongoing. My latest paper that tested two versions of the artificial pancreas in 30 patients was recently published by *The Lancet Diabetes & Endocrinology*, and was highlighted by an editorial and a Research Highlight from *Nature Reviews Endocrinology*.

During my research, I have consistently conducted knowledge dissemination activities to increase public awareness of our research. I have been interviewed four times on TV and five times in magazines/newspapers, contributed to three press releases, contributed to two YouTube videos about my research[2], and presented in one Café Scientifique (with over 80 attendees). This falls within the interests of the Origin Project in increasing public awareness and understanding on science issues and to create enthusiasm for science among public.

My second research area is to develop mathematical models of virtual patients with individualized parameters to test artificial pancreas systems in computer-simulation environments. Clinical trials are an integral part of the development process but are time-consuming, resource-intensive, and costly. Pre-clinical testing in computer-simulation environments accelerates development and facilitates the optimization of control algorithms. However, mathematical models of virtual patients need to be driven by real data and need to capture realistic higher order and time-varying dynamics, as well as intra- and inter-patient variability. To this end, I developed models within the Bayesian framework (utilising Markov chain Monte Carlo methods) of the gluco-regulatory system, insulin and glucagon absorption kinetics, and sensor dynamics. I currently supervise students to model hepatic glucagon sensitivity, post-meal glucose excursions, and human errors in carbohydrate counting.

My third research area is to use mathematical modelling to answer physiological questions. I developed a computational method based on Bayesian inference to estimate glucose fluxes

[2] See for example https://www.youtube.com/watch?v=Xgy6MXt60u0

during the meal tolerance test that employs glucose isotope tracers (input estimation problem that is ill-conditioned). The method was then used to validate the double- and triple-tracer methods, widely-used in physiology studies measuring meal glucose fluxes. I have thus far applied my method to six academic and two industrial physiology studies. For example, I applied it to assess 1) absorption patterns of meal-related glucose appearance in adolescents after slowly and fastly absorbed meals; 2) glucose metabolism in pregnant women during different trimesters; 3) the efficacy of under-development inhaled insulin; and 4) glucagon pharmacodynamics in type 1 diabetes. All academic studies were published in high-profile journals.

My research is highly interdisciplinary combining automatic control, diabetes, clinical research, and mathematical modelling. I have published as a first author in journals in a variety of fields including Automatica, American Journal of Physiology, Lancet Diabetes and Endocrinology, Canadian Medical Association Journal, IEEE Transactions on Biomedical Engineering, and Diabetes Care, among others. I have supervised students from different backgrounds as well, including engineering, nutrition, endocrinology, mathematics, and pharmacy. I have also given talks to audiences from medical, nutrition, engineering, and physiology backgrounds. This interdisciplinary approach to research and teaching is one that is highly connected with the interests of the Origins project.

In addition, I created a YouTube channel to help other graduate students. My videos discussed topics like: "How to write a response to Reviewers", "Should you do a PhD?", and "How to write a scholarship application". I am also currently preparing a series of Arabic educational physics and biology videos based on the Cassiopeia Project (http://www.cassiopeiaproject.com/). My videos have been, admittedly, of an ordinary quality due to my lack of resources and experience but are currently improving and the new series of videos will be of better quality.

I also have an enormous interest in science education policy. I read in detail the NSF Science and Engineering Indicators 2014 report, the Sigma XI Postdoc Survey report, the 2012 Doctorate Recipients from US Universities report, the 2008 Characteristics of Doctoral Scientists and Engineers in the United States report, among others. This led me to write a letter to the tri-council Canadian funding agencies suggesting modifications to their PhD and postdoctoral award programs. When I obtain a faculty position, I hope to conduct a longitudinal observational study to identify factors at the time of graduate school application which predict eventual graduate education success. This could help us improve our graduate admission system and even conduct interventional randomized trials to test new admission strategies. Currently, approximately 30% of PhD students do not complete their doctoral education, and we have no data that identify factors for such a high drop-out rate.

I believe that my short academic career (finished PhD < 20 months ago) overlaps with the goals of the Origins Project in several significant ways. I work on an area of global interest tackling a global problem, use a highly interdisciplinary approach, frequently inform the public of my research results, and I have an interest in higher education policies and graduate education.

I appreciate your attention to my application.

Yours sincerely,

Ahmad Haidar