# Challenges and Future Directions

A short while ago, the IEEE Control Systems Society (CSS) led by Tariq Samad and Anu Annaswamy, put together a large report "Impact of Control: Overview, Success Stories, and Research Challenges" (IOCT report, see http://www.ieeecss.org/main/about-the-society/ioct-report). Of course, this is not the first or the only effort in looking at future directions for control, but it does represent a substantial piece of work with input from many different people. These activities are important both for our own research community and for society more generally.

For our own research community, some have at times been willing to describe control as a "mature" field, or perhaps more provocatively state that control is dead. Of course I don't believe this latter statement, at least not in its raw form, and I would prefer to modify Mark Twain's famous statement to "rumors of the untimely death of control are greatly exaggerated." Our conferences are well attended, and our journals continue to show high citation counts, impact factors, and submission rates. These are all necessary indicators of health, but they are not sufficient to establish the vitality and relevance of the field. We need to ensure that we do not fall into the trap of studying "more and more about less and less until we know everything about nothing." It is essential that we connect our research to interesting new domains and applications.

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To explore this concept of connection a little further, note that IEEE's core purpose is "to foster technological innovation and excellence for the benefit of humanity." It seems clear that in a broad sense, humanity does not readily understand the value of control systems research. Therefore, it is incumbent on us to explain what we do and its value, and, conversely, to take time to study and understand some of the key problems facing humanity. In this way, we can both learn from and help society in general.

Thankfully, the IOCT report does a lot of this work. There are a large number of contributions covering broad fields including transportation, aerospace, process industries, energy systems, telecommunications, logistics, finance, and biological systems. There are no doubt other areas that we have missed, and in fact it could be argued that systems and control forms part of the fabric of almost all of modern society, albeit usually at a level that is hidden from the user.

The IOCT report also gives an excellent list of challenges for control systems research. These cover numerous specific examples, such as personalized medicine, synthetic biology, electric energy system dynamics, control system validation and certification, and high-speed nanopositioning. In all these cases new advances in control systems are essential and would give important practical benefits to society. One particular example that I am very interested in is systems biology.

## SYSTEMS BIOLOGY

Concepts such as adaptation, regulation, amplification, interaction, robustness, causality, and sensitivity are all crucial to a fundamental understanding of the behavior of biological

The CSS Executive Committee dinner in Barberstown Castle, Ireland (from left): Francesco Bullo, Mario Sznaier, Alessandro Astolfi, Masayuki Fujita, Sam Ge, Warren and Lisa Dixon, Roberto Tempo, Frank Doyle, Magnus Egerstedt, Christos Cassandras, and Panos Antsaklis.

A Segway ride in Dublin (from left): Christos Cassandras, Warren and Lisa Dixon, Francesco Bullo, Sam Ge, Magnus Egerstedt, Roberto Tempo (in front), and Frank Doyle.

systems. However, each of these concepts has been studied, sometimes extensively, in the case of artificial systems within the feedback control and dynamic systems communities. Although the applications and details of these concepts are not identical, I believe there is great potential for the control systems versions of these concepts to be adapted, extended, and applied to biological systems.

To make this bilateral connection between dynamic systems and biological research, there are several significant bridges to be made. Control systems research is largely based on mathematical analysis while biological research is heavily empirically driven. The academic communities therefore have very different languages, research, and publication styles and are not always able to interact productively. Other major challenges to achieving this nexus include the relative infancy, and therefore gaps, in foundational biological sciences when compared to electro, mechanical, or chemical systems and also significant limitations in the ability to accurately and rapidly sense the required variables in the real practical environment.

## THE EXAMPLE OF PARKINSON'S DISEASE

One example where systems biology may be very useful, which is a current research interest of mine, is mathematical modeling, energy metabolism, and calcium dynamics in relation to Parkinson's disease. I'm indebted to Peter Wellstead for introducing this area to me, and some of the details of this disease are explained in his February 2010 *IEEE Control Systems Magazine* article "Systems Biology and the Spirit of Tustin." Earlier this year, I attended the 10th International Conference on Alzheimer's and Parkinson's Disease in Barcelona, where I couldn't help noting several differences between it and our conference style. For example, the conference presentations are based on abstract-only submissions, and therefore there is no sense of peer review. This undoubtedly helps in allowing more current work to be presented, but in many talks, it was very hard to record all the information that might be relevant to investigate later. It also leads to some interesting discussions when a speaker challenges the conventional wisdom in a field. Furthermore, there are very few oral lectures, and these are reserved for a few high-profile papers. In these lectures, even semiplenaries are allocated a mere 20 minutes.

The conference also highlighted to me that there remains a very wide range of opinions about the key causes of Parkinson's disease. The broad pathology itself, that is, the "what" is reasonably well understood, namely, neurodegeneration, typically starting in a part of the brain called the substantia nigra, which slowly spreads to other areas of the brain. The pathogenesis, that is, the "why" of the disease, remains hotly debated, with many different factors suggested, such as dopamine toxicity, external toxins, inflammatory responses, alpha-synuclein excess, reactive oxygen species, iron load, nitric stress, excito-toxicity, energy deficit, genetic susceptibility, inadequate lysosomal activity, and mitochondrial dysfunction. As a consequence, proposed remedies for the disease are similarly very diverse, from adult stem cell derived microglia, to anti-inflammatories and antioxidants, through to exercise and mental/social stimulation. Unfortunately, despite decades of research in this area, as yet none of these proposals have resulted in a readily available treatment with clinically proven efficacy for halting, reversing, or even slowing disease progression.

I would join with those from a systems background, and also some from the biomedical community, who would argue that the disease is very likely a dynamic interaction of multiple factors involving many if not all of the elements noted above. As such, there is potentially a lot to be gained by the appropriate combination of mathematical modeling, analysis, and simulation based on experimental data (where available) for the relevant biochemical components in the neuronal system. While I am not naïve enough to suppose that systems biology will yield an immediate and simple answer to the problems of Parkinson's disease, I am optimistic enough to hope that in the long run it can and will provide valuable insights to this and a wide range of other diseases—if we are prepared to make the effort to study new areas, learn what the problems are, and develop the techniques needed to address them.

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