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Commentary

Physiology has found its voice

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More than a decade into the twenty-first century, and more than a decade following the first complete sequencing of a human genome, physiology has found its voice. The physiological sciences are now where much of the important action is in biological and medical science. This was very evident at the Birmingham World Congress of IUPS in July of 2013.

> "Whether wandering around the posters to find nuggets of pure gold in unexpected new results, or debating the progress towards gender equality in special lunchtime sessions, or joining a large contingent from African countries working overtime one evening with IUPS to discuss their future organisation, or listening to top-rate plenary lectures, or attending symposia to delve in further depth, the feeling was of excitement that our science is not just alive and well. It is also a great time to be in it. You could sense this also at the social events, as people exchanged their enthusiasms and – dare one say it? – feelings of pride to take part in such a celebration." (Noble, 2014).

I refer to Africa deliberately in the above paragraph, which is taken from an Editorial appearing in *Physiology*, the joint journal of IUPS and the American Physiological Society. The reason is that this message is particularly relevant to your continent. Yours is the continent of the young. The great majority (85%) of your population is less than 45 years of age. By contrast, in Europe the figure is just 56%. The difference is even more striking for those less than 15 years: 40% for Africa, 16% for Europe.[1] Many people in your continent will still be alive to see the 22nd century. They will see, and hopefully take part in, the transformation of the biological sciences that is now well under way, and which may well take the rest of this century to deliver its most spectacular results.

What is that transformation and why is it happening? This was the subject of the Opening Plenary Lecture that I gave at the Birmingham Congress. The title was deliberately provocative: "Physiology moves back onto centre stage: a new synthesis with evolutionary biology"[2] and it was based on an article with the even more provocative title "Physiology is rocking the foundations of evolutionary biology" (Noble, 2013b). I will write more about the science of that article for a future issue of your journal. The science has rapidly developed ever since the article was published. In this perspective article I wish to signpost the implications for the future of physiology.

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[1] http://www.geohive.com/earth/population_age_1.aspx
[2] http://www.voicesfromoxford.org/video/evolution-and-physiology-a-new-synthesis/355

The sequencing of the complete genome of a human being was a fabulous and impressive achievement. The comparisons between different species have already revealed many new insights into evolutionary history. The consequences for legal processes have also been remarkable, with DNA evidence now being used routinely in courts of law. But the main public reason given for the project when it was launched was that there would be great benefits for healthcare, with the suggestion that these benefits would be evident within ten years. Quite simply, 14 years later, we are still waiting for even a very small fraction of that promise to be fulfilled. An editorial in *Nature* expressed this disappointment very clearly:

> "The activity of genes is affected by many things not explicitly encoded in the genome, such as how the chromosomal material is packaged up and how it is labeled with chemical markers. Even for diseases like diabetes, which have a clear inherited component, the known genes involved seem to account for only a small proportion of the inheritance… the failure to anticipate such complexity in the genome must be blamed partly on the cosy fallacies of genetic research. After Francis Crick and James Watson cracked the riddle of DNA's molecular structure in 1953, geneticists could not resist assuming it was all over bar the shouting. They began to see DNA as the "book of life," which could be read like an instruction manual. It now seems that the genome might be less like a list of parts and more like the weather system, full of complicated feedbacks and interdependencies." (Editorial, 2010).

Ever since the work of Claude Bernard in the nineteenth century (Bernard, 1865, 1984; Noble, 2013a) physiology has been concerned precisely with "complicated feedbacks and interdependencies." He introduced the concept of the control of the "internal environment" as a key feature of organisms and can therefore be regarded as one of the first systems biologists (Noble, 2008). In the twentieth century, it was the Nobel laureate Barbara McClintock who clearly stated that "the genome is an organ of the cell" (McClintock, 1984). She discovered mobile genetic elements ('jumping genes'), which have now been found to be a ubiquitous feature of all kinds of organisms (Shapiro, 2011), not just the plants on which McClintock worked. The genome is therefore itself subject to physiological control. Physiologists have understood this for many years. After all, the same genome is used to make the 200 or so different types of cells in our bodies. The genome must therefore be controlled in different ways during the process of development that takes us from the single fertilised egg cell to the adult organism. As Beurton et al say "it seems that a cell's enzymes are capable of actively manipulating DNA to do this or that. A genome consists largely of semi-stable genetic elements that may be rearranged or even moved around in the genome thus modifying the information content of DNA." (Beurton *et al.*, 2008).

The full significance of these discoveries for the discipline of physiology is still being assessed. The reason for the dramatic titles of my Birmingham IUPS lecture and the article on which it was based is that recent work has shown that this manipulation of the genome extends to trans-generational effects and can therefore be of great significance for the theory of evolution. We are rapidly moving away from the narrow view of evolution represented by the Modern Synthesis (Huxley, 1942), often also called neo-Darwinism, towards a more inclusive theory which has been signposted by a number of recent books (Noble, 2006; Beurton *et al.*, 2008; Pigliucci & Müller, 2010; Gissis & Jablonka, 2011; Noble, 2011).

These are the reasons why one of the most successful symposia at the IUPS Congress was devoted to Physiology and Evolution. It involved some of the key players in the field and attracted a large audience. In an article for a future volume of this journal I will explain more fully the reasons why this area of biology is developing so rapidly and why the implications for physiology are so profound.

It will take at least the rest of this century to work those implications out in terms of physiological mechanisms. That, in a nutshell, is the reason why the physiological sciences are now

where the action is and why physiology has found its voice.

IUPS, its regional members, and national members and adhering bodies, therefore carry a major responsibility. This is to explain to our young students and researchers the opportunities that are opening up for physiology. IUPS is keen to interact with and help the development of our science in your continent.

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