PSSA Newsletter

Physiology Society of Southern Africa

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Issue 9

Editorial message

Physiology in SA — Crisis or New Beginning?

Two recent papers caught my eye and made me think about the positioning role of physiological sciences, globally, and of course in South Africa.

In the one physiology journal, Denis Noble writes: "Almost everywhere I have encountered anxiety about the role of physiology and how it is under-value in modern biological and medical courses in universities. Many departments of physiology have disappeared or been assimilated." (D Noble, Physiology, Vol 26, 2011). And in a recent Nature article, Sidney Brenner says: "Biological research is in crisis. Technology gives us the tools to analyze organisms at all scales, but we are drowning in a sea of data and thirsting for some theoretical framework with which to understand it" (S Brenner, Nature, Vol 482, 2012).

We seem to face a very similar scenario, of merging or disappearing departments on the one hand, and the hunt for more data, more "-omics", with little time to interpret and link data to function, to connect the dots. So, do we have reason to worry? In my opinion, the opposite is the case: If we consider the definition of physiology, it appears that our discipline is, compared to the rest of the natural science disciplines, tailor-made, to deal with the apparent crisis. Who, if not us (physiologists) should be able to "zoom in" but also to "zoom out", from molecular to cell, to tissue, to organ, to organ system.

A dictionary definition of physiology goes like this:

"The study of the functioning of living organisms or their constituent tissues or cells. Physiology was usually considered separately from anatomy until the development of high-powered microscopes made it clear that structure and function were inseparable at the cellular and molecular levels. An understanding of biochemistry is fundamental to physiology. Physiological processes are dynamic; cells change their function in response to changes in the composition of their local environment, and the organism responds to alterations in both its internal and its external environment. Many physiological reactions are aimed at preserving a constant physical and chemical internal environment (homeostasis)"

This already indicates the unique position physiology takes up, to utilize tools from various disciplines (anatomy, biochemistry, genetics) in order to make sense of the data, to link data to function, to connect the dots. What it requires is the oversight, to combine a reductionist research approach with a downward causation approach, and the skill to swap between them depending on the research question. But it is exactly that skill, that should set us apart from the rest of the biological science community. So, let us use our skills as physiologists, and assist in making sense of the huge pool of data. In doing so, the unique and crucial role of physiology will become apparent again.

Ben Loos, Physiological Sciences, Stellenbosch University

This debate urged me to ask some of our HOD's of Physiology in South Africa for their opinion and those that managed to respond had this to say :

Inside this issue:

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Prof Stefan Du Plessis—Stellenbosch University Medical Physiology

Question I:

Do you think that the discipline of physiological sciences is indeed at risk, globally and in SA?

This truly depends on how Physiology as a discipline is defined and perceived. Traditionally the principal level of focus of physiology was merely at the level of organs and systems, but it has evolved and entails much more than that. The discipline of Physiology includes the science of the mechanical, physical, and biochemical functions of the body, their organs, and the cells of which they are composed. According to this definition Physiology is still alive and kicking. However, many new fields of research such as molecular biology, bioinformatics and genetics have evolved from Physiology. Sadly these scientists regard physiology as quaint and anachronistic and branched off to create their own identities. This has led to the disappearance of many Physiology departments as they were absorbed into a cluster of Medical Biosciences. Despite all of this Physiology is still practiced, taught and remains one of the most essential pillars of medicine and human biology and would therefore never disappear. I think we as Physiologists have come at a crossroad where we should figure out how to hold on to the best of the past and traditions of the discipline's extraordinary history while at the same time making the scientific community at large aware of its tremendous breadth and promise for the future. We as Physiologists are probably best equipped to make sense of the explosion in molecular and cellular information and relate it back to organs and systems.

Question II:

What role should physiology play in SA?

Physiology must maintain its integral role as the basis of training students in life and medical sciences. Physiologist must continue to bring science, industry and education together in order to inform, educate and discover while applying findings and putting it into practice. We should remind the scientific community of the important role that physiology fulfill.

Question III:

In order to compete globally, is there anything that we could do more of or less of?

Find a niche area and focus on that. Furthermore make use of uniquely South African models to differentiate your research from the rest. We should not try to do everything as it takes a lot of resources and funding to become globally competitive. Rather think strategically

Prof DH VAN PAPENDORP—Pretoria University

Rather think strategically and forge strong national and international collaboration networks to strengthen your research capabilities.

Prof DH VAN PAPENDORP—Pretoria University

Question I:

Do you think that the discipline of physiological sciences is indeed at risk, globally and in SA?

Physiology sometimes looks like a sinking ship, with the Physiologist battling against the breaking waves of molecular biology that has expanded into the era of 'omics' (e.g. interactomics, metabolomics, transcriptomics). People sometimes define Physiology as the physics and chemistry of life. How can the existence of Physiology then be at stake? I don't believe that Physiology is at risk at all. Molecular and cellular research i.e be it RNA interference assays, live-cell imaging, or any genome annotation - there is always a lack of something crucial to the understanding of living systems or the control of the "internal milieu"- i.e. the determination of the modus operandi of living systems. Lets take the manipulation of the amino acid sequence of membrane channel proteins. Somehow and somewhere the physiologists must explain and unravel these phenomenon and this makes that Physiology will independently exist as a subject and not be at risk.

The significance of molecular biological features must be seen in the context of higher order systems, whole cells, whole organs, whole organisms, species, their environment and mankind. In short Physiology is the science of functional adaption in biology. The combined Physiology / Anatomy departments is a threat to independently existing Physiology departments. The incorporation with clinical departments (as happened at UCT) will be the final dead end for Physiology.

Training students who envisage careers in medicine, dentistry, pharmacy, physiotherapy, occupational therapy, communication therapy, radiography, nursing sciences will always need to know how the normal body functions and this core knowledge is inevitable. Pathophysiology should be taught as it makes Physiology more interesting and applicable.

Prof DH VAN PAPENDORP—Pretoria University cont.

Question II:
What role should physiology play in SA?

The role that we as Physiologist in SA should play is that of good quality pre- and post graduate training, partnerships, inter departmental and inter institutional and inter disciplinary research exposure of post graduate students to other disciplines. Collaboration with departments and faculties contribute to their field of study and learning to communicate science.

Question III:
In order to compete globally, is there anything that we could do more of or less of?

Whether one works as a practitioner or as a scientist, both must contribute towards the health challenges in SA and globally. Unfortunately it has become extremely difficult for us in SA to compete globally. We should however strive "to evolve up to the angels rather than the apes"

Prof Baghyamala Umapathy - Walter Sisulu University

Question I:
Do you think that the discipline of physiological sciences is indeed at risk, globally and in SA?
No. I don't think so. Although systems physiology may be on the decline, cellular and molecular physiology research is on the rise. Basic physiological principles can be better understood using applied physiology concepts.

Question II:
What role should physiology play in SA?
In SA, human physiology should be emphasised more at school level and foundations of basic physiology principles must be highlighted at this level.

Question III:
In order to compete globally, is there anything that we could do more of or less of?
A point was made in the last Asian physiological society conference in Taiwan that Physiology as a subject should be taught at school level and its role as a basis of medical practice must be emphasized in the curriculum, I would even advocate that concepts of human physiology mechanisms should be emphasized not just for medical students but also for those who are doing basic research at cellular or molecular level.

Marking funny:

What is metaplasia? Give an example:

Afwyking by kliere.

Te veel sekresie

Metaplasia is the differentiation of cells.

It's a disease. It occurs due to lack of keratin.

Metaplasia is a disorder due to the lack of nutrition and bone begins to degrade

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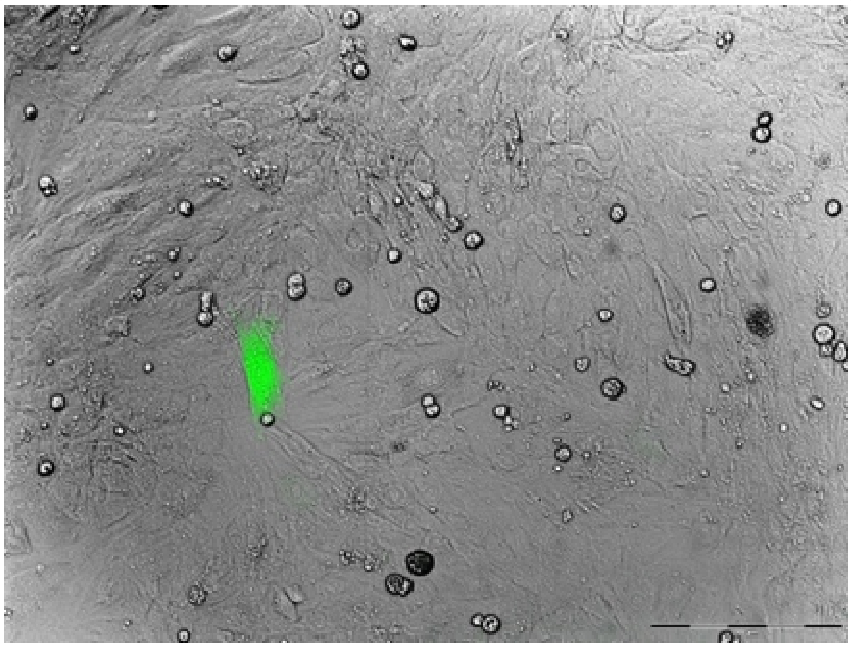
Microscopy in Cellular Physiology—a start up touch down

Zooming in-some key questions to be answered by Fluorescence Microscopy.

DEPARTMENT OF PHYSIOLOGICAL SCIENCES
UNIVERSITEIT STELLENBOSCH UNIVERSITY

The planned arrival of the super-resolution confocal microscope platform in the middle of this year prompted me to summarize, what type of questions **can potentially** be answered by utilizing fluorescence microscopy. It is hoped that some of the research areas in our physiology community, especially new postgraduate students, could benefit from this short summary. The extensive work with our wide field instrument in the past 6 years has taught me:

With the help of fluorescence, we can visualize structures, which we usually can't resolve. Our favourite protein of interest (POI) can be visualized in 3 ways: 1. we can label it with a primary antibody, followed by a fluorescently linked secondary antibody. 2. we can utilize a plasmid containing the sequence of our POI together with a sequence encoding a fluorescent protein (eg GFP) or 3. we may be able to utilize fluorescent probes which possess an inherent binding capacity.
Once we have decided for one of these methods, we need to cross check, that the fluorescent label with its spectral properties matches the excitation and emission settings of your fluorescent microscope. It may have laser lines or emission filters, that do not match the excitation or emission spectrum of the fluorochrome, so, one needs to choose and buy the fluorchromes AFTER checking the instrument specs. This is also most important, if a multi-colour experiment is planned (eg 2 POI's and a counterstain for the nucleus). In that case one needs to be certain, that the fluorochromes chosen occupy their own spectral space, without emitting signal into another fluorchrome's emission range (so called bleedthrough and we would like to avoid it at all costs). One example which is a bad match of fluorochromes is GFP and YFP, they are spectrally very close. One also needs to cross-check, that the primary antibodies are raised in different species, eg mouse and rabbit, otherwise we have off course some nice cross reactivity.



"Is it there or is it not there, and if it's there, where is it?". In many cases, a research questions is answered only by showing whether a POI is present or not and what the nature of the signal pattern is (dot-like, homogeneous, nuclear, network-like). That gives us immediately clues about the potential functional role of the POI.

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Marking funny:

Did you know that aging leads to:

"loss of muscle mass and strength which will later lead to loss of will power, due to less neuromuscular junctions"

"Some sarcopenia patients become so weak that they become morbid and can't do anything for themselves"

What is wharton's jelly? Where do you find it?

It's a solution found in gelatineous glands

It is found in the umbilical cord. It serves as fuel for the cells.

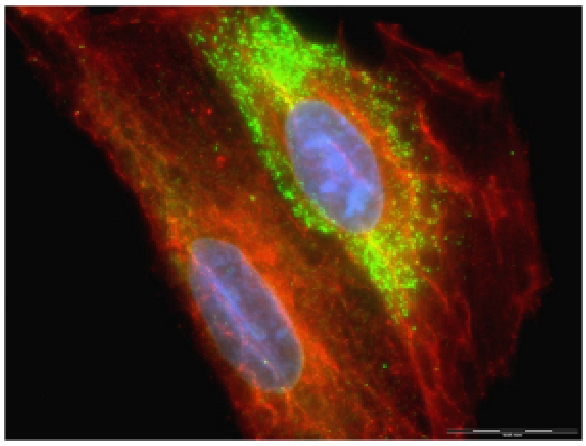
Its an amorphous substance found in a plasma blood cell.

Its an anagous ground substance

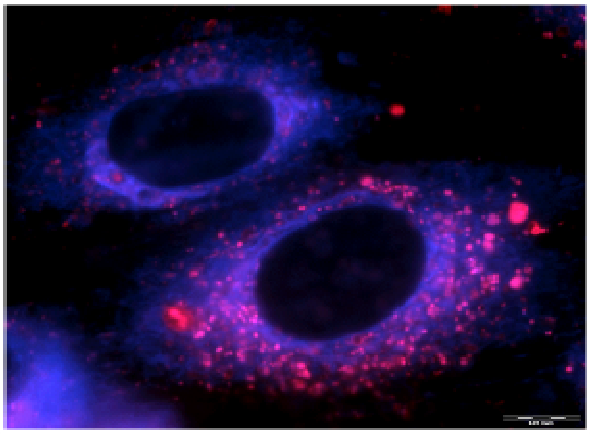
Protection layer around kidneys

It is a watery substance between cells. Found in the collagen fibers.

...and more **Microscopy in Cellular Physiology—a start up touch down**



By utilizing an antibody-based immunofluorescence approach, we can visualize our POI. In this case cytochrome c (green), beclin-1 (red), counterstained with Hoechst 33432 (blue).



By using appropriate trackers, we can exploit the fluorochromes inherent binding capacity and visualize organelles of interest. In this case the ER (blue) and lysosomes (red).

Once that is done, one may want to ask, which is the **primary research question** one hopes to answer by utilizing fluorescence imaging? 2 main information units can always be gained with fluorescence microscopy (there are more but they require more complex acquisition and analysis techniques). These are: the **localization** of the signal/POI as well as the abundance of the POI. In other words "*where*" is my POI and "*how much*" of it is present. The "how much" is based on mean intensity analysis, and requires a large number of cells and regions to be analysed. The "where" does not require that many images, as it is not so much about data points. It however requires a GOOD image, meaning, the best achievable signal/noise ratio. In many cases, the "where" is more important.

If the image is about data ("how much"), then the next question which may be useful to ask is: Am I interested in a single data point (***static*** data) or data points over time (***dynamic*** data)? Both are useful, but they allow different types of analysis (see graphs below). Dynamic data are off course highly interesting in Physiology, as they allow us to describe the magnitude of a change over time. Static data are only a representation of that single time point, which may or may not be enough for the specific research area. It certainly will not allow us to make conclusions of how rapidly it got to the observed change, and whether it is remaining in that state.

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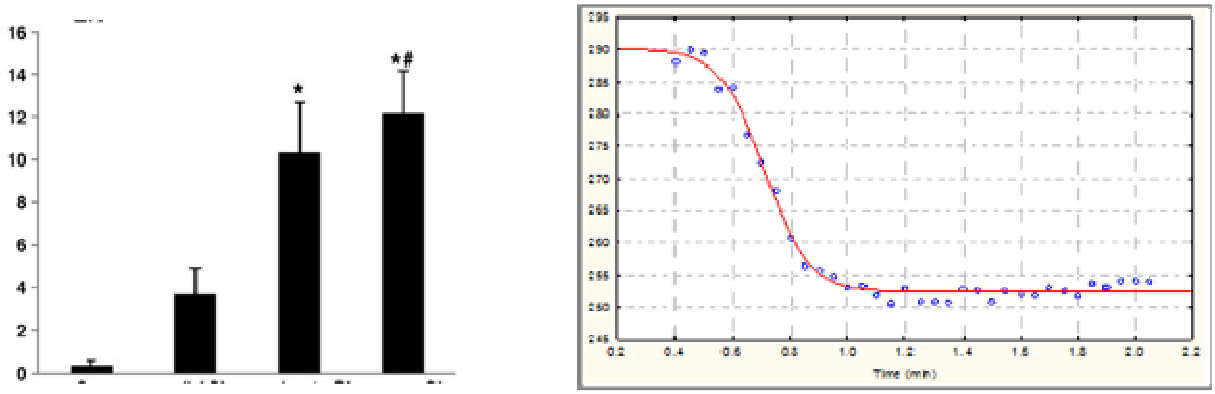
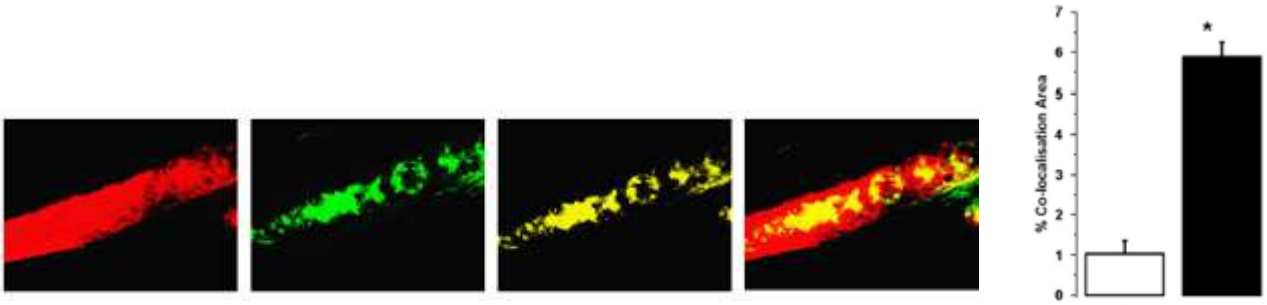
… and more **Microscopy in Cellular Physiology—a start up touch down**



Static data (left) or dynamic data (right) allow us to answer very different questions and require the appropriate imaging/ staining conditions.

Very often we see a signal or a certain pattern from our POI, and we may have the suspicion that it is expressed in- or on a certain organelle, eg the endoplasmic reticulum. How can we verify that? We can utilize the ***co-localization*** technique and provide evidence, whether we are correct or not. There are a large number of fluorescent probes for organelles, such as mitochondria, the ER, lysosomes, Golgi etc, which have inherent binding capacity. Keeping the spectral space in mind, we can then perform a double-stain, and co-localize the signal. This allows us to answer 2 questions: 1. Is there co-localization? 2. ***How much*** of co-localization is present? The area of co-localization can be quantified and expressed in "***area of co-localization in %".*** This approach is also most useful when studying the interaction of 2 POI's, eg a receptor and a ligand or 2 POI within a certain signalling pathway.

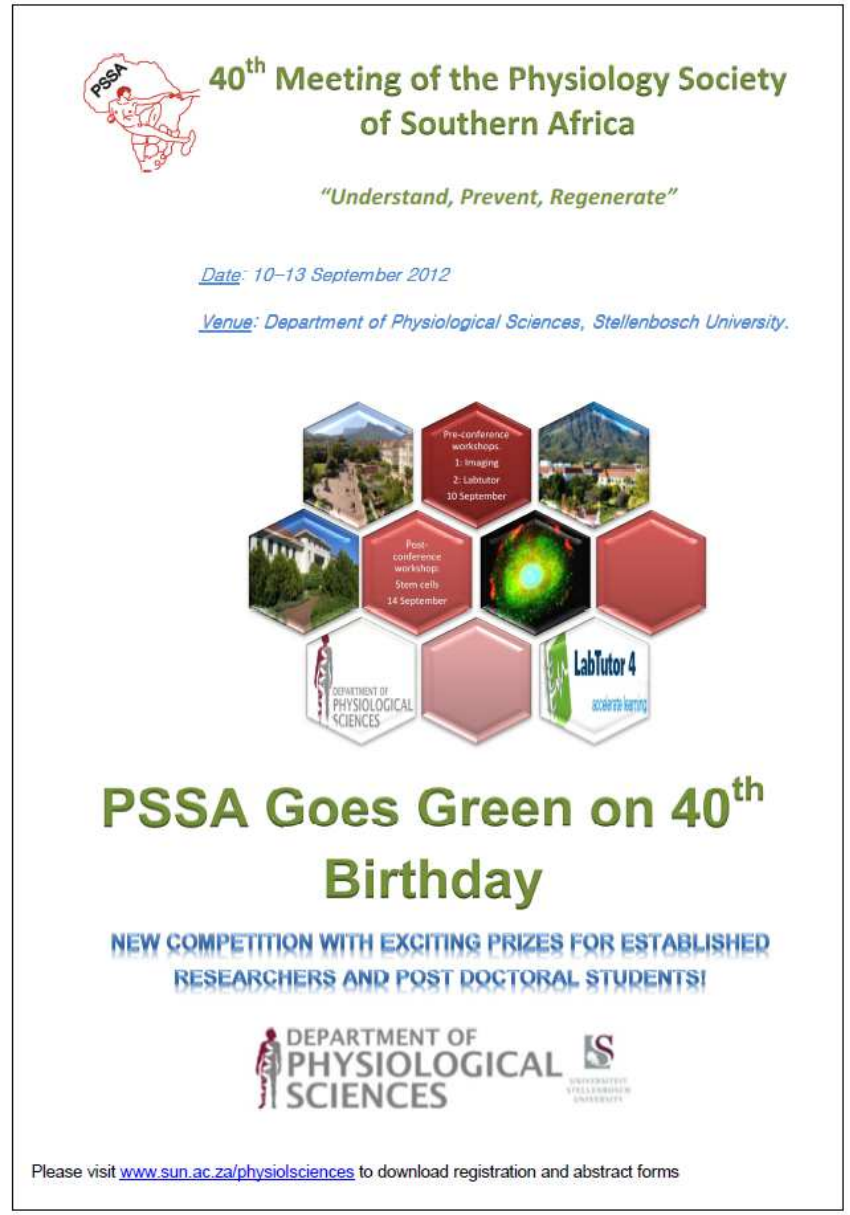


Co-localization analysis gives us an idea about potential interaction between two POI's. The extend of co-localization between groups can also be expressed in %.

So, in summary-although there are many more techniques not addressed here-to get started analysing your POI under the fluorescent microscope, you only need to ask yourself: ***"where", "how much", "static or dynamic", "co-localization"***? Happy imaging and best wishes. Ben

Ben Loos, Dept Physiological Sciences, Stellenbosch University

Don't miss out-be there… PSSA conference



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We would like to hear from you

If you would like to contribute to the newsletter, be it with news from your department, news regarding your research, issues centred around physiology and teaching, or anything you feel should be shared with the PSSA community, please contact the editorial team (bloos@sun.ac.za).