The Optimist

A journal to help you survive the valley of shit

MARCH 2019 EDITION

WELCOME TO THE OPTIMIST

Not long ago, we found ourselves at the pub The Optimist asking ourselves: why the hell did we ever decide to pursue a career in science?

A few drinks in, we realized that we would not be doing relevant science if it was easy. Moreover, in any other job we would probably be bored. To be able to survive our PhD – in a healthy mental condition – we realized we had to change our mindset. We need to learn how to deal with failure, how to be patient and how to create a healthy work-life balance.

In order to bring optimism back for ourselves and our fellow PhD students, we came up with the idea for this interactive journal *by* PhD students *for* PhD students. Our goal is to become healthy scientists that are hardworking but relaxed, ambitious but sharing, and confident but humble. We are convinced that the best way to achieve this is by sharing our struggles and by seeing the humor in it.

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But that is not enough. We believe the efficiency of science can be improved. The scientific method has proven very successful over the last decades. Nothing we write down here will change this.

However, we would like to step away from the idea that the current way of doing science is the only way and encourage constructive discussions. Therefore, in every edition we will focus on a topic that merits some thought.

The optimist team
Matthias, Donya and Joni

Publication

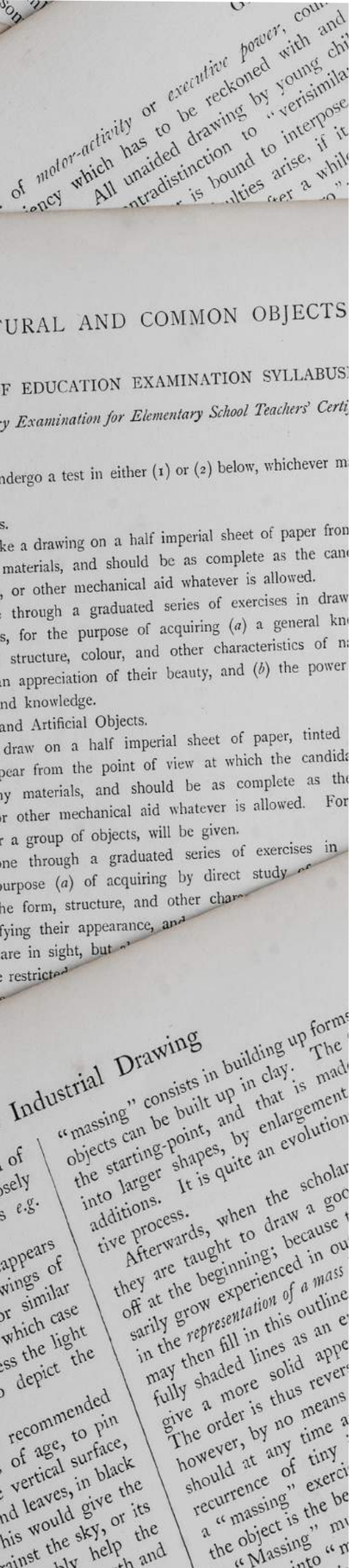
The drawbacks of the obsession

Articles allow us to share and gain knowledge. So why do most of us experience such a love-hate relationship with publishing? This is because the most valuable work doesn't always get the biggest reward, but the fastest, most sexy or most shiny work does. This is understandable. New and exceptional work in the past has made it possible for science to make big steps forward. However, this is only half the story. The current way of publishing is threatening the integrity and efficiency of science by discouraging important scientific work: replication studies, negative results and asking the big questions. Here is why.

As scientists we have responsibilities: we have a duty to contribute to the progress of science,[1] but we also have our duty to society.[2] Not only does science depend on public money, it also affects policy decisions and offers risks and benefits to society. Because of this duty towards the scientific community and towards humanity, our main motivation should not come from pursuing personal fame[1] but rather arise from curiosity to understand the world around us. However, the current mindset in biomedical sciences goes exactly against this responsibility expected from scientists.

Because of the attitude that new and positive work is more publication worthy we do not pursue the truth. Instead, we compete with each other to be the first ones finding new "truths".[3] Even though the strength of science lays in the importance of reproducibility and in the acknowledgment that claims should be exposed to critical scrutiny before being accepted[1], we believe that it is better not to waste our time reproducing—or failing to reproduce—the work of others. This approach creates a publication bias, making it harder to distinguish false from true facts.[4] In addition, because of this pressure, scientists will take shortcuts resulting in lower quality science being published.[5,6]

The self-correcting nature of science will eventually lead us to the right answers: labs will individually and quietly discover the irreproducibility of claims and clinical trials will fail. However, this can take



years and in the meantime millions in funding are lost and, in case of biomedical sciences, people are literally dying.

The high failure rates that pharmaceutical companies Amgen and Bayer encounter when trying to validate published research, show exactly how serious the problem is. These companies were able to reproduce only 11%[7] and less than 25%[8] of published studies, respectively. Because scientific claims are only valuable when reproduced, this data suggests that the majority of the claims out there are hollow.

> We can be humble in our claims, complete in our discussion and transparent in our methods

In order to support a true scientific mentality and make progress that is more efficient in biomedical sciences, we should publish a substantial fraction of negative results[4] and reward qualitative follow-up papers and replication studies.[7] We should shift away from rewarding flashy unexpected results to valuing reproducible and high-quality science.

Because of this rat race, we also do not dare to ask the big questions. These questions require time, which is not always available at institutions where the "publish or perish" rule is applied.[9] However, this mentality of trying to run when we cannot even walk, in most biomedical fields, will keep working against us.

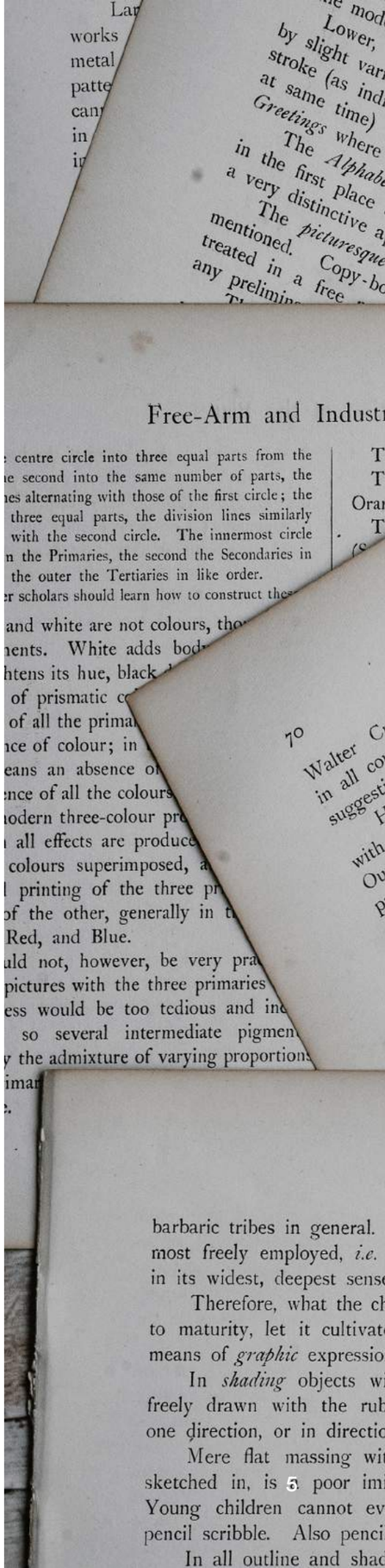
How can we fix this?

Should we get rid of the ordered listing of authors such as Gretchen L. Kiser suggests in Nature?[10] Could this improve collaborative science? But how do we differentiate between the real brains behind the science and the ones just riding along? Maybe it is a solution to combine this idea with an approach that makes a distinction between authors and collaborators? Are open accesses journals a solution? Or will this have a negative impact on overall quality because these journals will be forced to publish more to cover the lowered income?[11,12] Can we lower publication bias by allowing editors only to judge an article based on research question and methods? Are anonymous grant applications without a required CV a solution? Should labs be encouraged to do replication studies? Can this be achieved through separate research funding? Should funding agencies have their own journals and oblige all grant holders to publish in this journal regardless of the outcome? Should there be a link on PubMed connecting articles with alternative findings to the initial article? Are third parties, like the Reproducibility Initiative,[13] going to solve something?

Because science and economics are intertwined, the core of this problem goes beyond us PhD students. So what can we do? We can be humble in our claims, complete in our discussion and transparent in our methods. We can try to publish our negative results and we can have honest and open conversations about our data at conferences. These are small steps but with massive importance.
Do not forget that we will decide how science is done in the future. If we have the desire to change the current culture, it can be changed.

Written by Joni Vanneste

Edited by Donya Pakravan and Matthias Koch



DOING A PHD IN THE STONE AGE

Interview with a PI

Adrian Liston
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Adrian Liston heads the Laboratory of Translational Immunology at VIB. He obtained his PhD at the Australian National University in 2005 and moved to Seattle for a Postdoc at the University of Washington. He became head of the Translational Immunology Laboratory at VIB and KU Leuven in 2009. Adrian recently took a faculty position at the Babraham institute at Cambridge university, and will be travelling back and forth between the UK and Belgium for the coming months.
His main research interests comprise immune deficiencies, regulatory T cells and the local interaction between the immune system and tissues. He has been very involved in bringing new technologies to VIB, founding and directing the flow cytometry and CrispR (Mutamouse) cores. A drian Liston is also an avid science communicator, talking about topics such as animal rights and the use of animals in medical research on twitter and his online blogs.
We went ahead and asked him a few questions about his time as a PhD student.

Thinking back to your PhD, how would you describe this experience, what are you proud of and was there also something that did not go quite as planned?

I quite enjoyed my PhD. The key success in a PhD is to find a match between supervisor and student. I only spoke to my supervisor every 3 or 4 months, and it was always about concepts and strategy rather than trouble-shooting. For me, I loved the independence that this gave me, and the amazing post-docs in the lab gave me more than enough technical advice. However, some of the other students around me did not like this approach to mentoring, and would have preferred weekly meetings going into the detail of their experiments. This was pure luck on my behalf - I could easily have ended up in a lab that I found stifling, because I didn't ask the right questions going in. This independence let me mould my PhD to my strengths. I learned just a few basic techniques and then applied them to novel questions. It was an approach that let me generate data and papers quickly, and led to an "easy PhD".

To ask the famous question: is there anything you would like to change retrospectively regarding your PhD?

The flip side of having an "easy PhD" is that I never really had to leave my comfort zone. Since I didn't spend months (or years) painfully learning and optimizing new techniques, I never became as technically skilled as the other PhD students around me.

"I didn't have the versatility or skill of other postdocs around me, who were picking up and using the latest techniques with trained ease, earned by blood, sweat and tears earlier on"

Science is so fast moving, that the best strategy is to learn how to learn, which you only get the hard way. Instead, I had my couple of techniques and I had learned how to plan experiments and write papers. This made my postdoc really difficult. I didn't have the versatility or skill of other postdocs around me, who were picking up and using the latest techniques with trained ease, earned by blood, sweat and tears earlier on. Now as a PI, this deficit is not so important, since my job is all planning and writing, but even now I regret never learning to become a great experimentalist.

What advice would you give to PhDs like us?

1. Analyze experiments as you go. I started the habit very early on of always analyzing experiments once I finished them. By this I mean a full

analysis, including a publication level graph, a figure legend and a few lines of text describing the result. It takes a little time, but it means you get real-time feedback on the quality of your experiments. Did you have all the right controls? Were the numbers high enough to make conclusions? Are your conclusions solid enough to plan the next stage, etc. It also made writing papers and a thesis very simple: I just cut and paste my analyzed data in, and I was half-way there. Since editing is much less intimidating than writing, I never developed that writing paralysis that some students get.

2. Don't stress about careers! The infamous "bottleneck" in the academic career is mostly illusional. In Flanders, perhaps 15–20% of PhD students go on to a long-term academic career, but even in countries with lower rates (2–5% would be normal) this this not due to a bottleneck. A PhD in biomedical science is one of the most desirable training programs possible for a modern career. The vast majority of people who leave academia are not pushed out; instead, biomedical PhDs are leaving academia because of pull-factors. They find highly desirable jobs that they believe they will enjoy more. When I look around at the PhDs that I trained with or that I have trained, I can honestly say that not one has had a career failure. Yes, very few are now research professors, but that is because almost all of them found something else they liked more. Doctor, CEO, start-up company, scientific writer, senior public servant—all great jobs. Very, very few of the 100+ academic careers that I have followed have ended with someone getting pushed out of academia (i.e., timing out of the postdoc fellowship system), and those that did landed on their feet and found a great career that they now say is better suited to them.

"The vast majority of people who leave academia are not pushed out; instead, biomedical PhDs are leaving academia because of pull-factors"

So don't stress about your future career. Concentrate on doing well in your PhD, and start planning your career a year in advance of any decision, but don't make yourself unhappy about uncertainty in which successful career path you will end up taking.

PhD confessions

Because we've all been there...

SEMINOGRAM

Once upon a time, in my last year of bachelor, I followed the course Biology of Reproduction, which addressed basic mechanisms such as gametogenesis, fertilization and contraception. Practical sessions were mandatory and included a full week of lab work where we did all sorts of cool stuff. What we did not know back then is that in one of those sessions we had to perform a seminogram or semen analysis. The main issue was that the material needs to be fresh... And to make things worse, there was a much higher proportion of girls than boys (around 20 girls and 2 boys). So, when we all got there for that session, they handled some sample tubes to the two guys and encouraged us to provide samples for the whole class. I will never forget that walk of shame back and forth to the bathroom, nor the 3h scrutiny our little buddies went through...

Anonymous

FORGOTTON CULTURE

During the first year of my PhD, when working with mouse primary neuronal cultures to study the giant hippocampal mossy fiber synapses, I forgot about a dish in the cell culture incubator for about two weeks longer than necessary. These are normally very sensitive cultures that require maintenance every other day to survive and be healthy. Just before leaving for Christmas holidays I realized about this forgotten dish and instead of trashing it immediately, I had a quick look at the cell culture microscope: to my surprise the neurons were looking great! I decided to fix, stain and take them to have a look under the confocal microscope and I just could not believe how great they were. It turns out there were plenty of those large synapses! One of the pictures I took that day is now displayed just outside our lab in the corridor wall.

Nuno Apostolo

ELECTRIC CURRENTS

In my first year of PhD, I did not come in with a lot of wet bench experience. One day, I was running a protein SDS-PAGE gel for the first time and my PI asked me if I knew how to check if the electrodes were connected properly and the electric current was flowing. Upon telling him that I did not know how to do this, he told me that all I have to do is to put my pinkie finger in the running buffer and see if I get a little electric shock. I then proceeded to try to stick my finger in the gel box, at which point he rushed forward and stopped me. I realized then that he was just messing with me. The lesson I learnt that day is that there is almost never a reason to stick your fingers into any electric apparatus in the lab.

Anonymous

LOST RESULTS

Labs are a mess, and from time to time cleaning is necessary. Unfortunately for me, the cleaning day was on the same day that I would receive one of the most exciting results of my PhD. I started early with mice behaviour experiments, which took several hours to be completed, and annotated everything on a few papers. However, due to the cleaning rush I had to postpone transferring my data to my computer. After the cleaning session, my results were mysteriously gone. My supervisor thought they had ended up in a garbage bag. I was terrified. The data could not be recovered without those papers and losing them would have meant losing a big crucial experiment. I needed to find them back! I ran to the administrative office, where I was told that the trash bags had already been sent to those huge industrial paper shredders. We ran there, stopped the machine and jumped in it. Most bags had already been destroyed by the machine, but we found one intact bag. I emptied it and luckily, I found my papers inside undamaged. This was one of my happiest moments of my PhD, since without those papers I would still be waiting to get a date to defend.

Anonymous

You have a confession to make?
Mail us at Optimist.PhD@outlook.com

PHD SURVIVAL TIPS

HOW TO DEAL WITH AN "UNLUCKY" PROJECT?

What do you do if your project does not turn out as expected? We asked three talented scientists who finished or are about to finish their PhDs to give us some tips and share their experiences.

Caroline Eykens recently had an impressive PhD defense in which she received praises from jury members and colleagues despite presenting nothing but negative results. This is what she would like to share with younger PhD students in a similar situation

Having reached this point, you would probably prefer to quit, move to the other side of the world and do something completely different. From my own experience, there might be several reasons underlying the fact that a project still needs to be continued.

- Discuss your general concerns with your promotor to ensure that you remain on track to reach your PhD milestones.
- Make an outline of the experiments necessary to conclude the current project with minimal effort. This will allow you to focus on the start of a new project.
- Discuss your vibrant ideas with your supervisor, but make sure your research goals are realistic within the given amount of time.
- Connect with and reach out to as many people as possible you think might be able to help you out.
- Try to explore new avenues and keep up the good work. You will gain a lot of personal and professional growth by doing so, I can assure you.
- Most important: remember that you are not alone. You might not be able to see through this at the time when you are in the middle of the valley of shit (well known amongst PhD students), but persevere.

This is a golden tip from Rocco Stirparo, who did not have the most thrilling PhD project but managed to start an exciting side project about using DNA for data storage:

Think about a side project. It may turn out to be interesting and become your main project. You can start your own project or use your expertise to start collaborations. In addition, you can ask your colleagues and friends if they need extra help in their project.

Some advice from a great scientist and honest personality in the building Evgenia Salta:

I did my PhD in Greece. I know some of you may rush to conclusions, which is not a proper thing for a scientist to do. Actually, you are right. Because doing a PhD in Greece adds a whole new layer of 'tough' onto the baseline 'toughness' that doing a PhD generally involves. From developing your western blots by yourself locked up in a 2 m^2 dark room; and making your own polyclonal antibodies using otherwise very cute but also gigantic and lumbago-causing rabbits; to dissecting fish brains on a floating platform in the sea in the middle of nowhere for 5 hours; and pumping water out of the basement lab at 11:00pm during a massive flood; you name it, I had it all. Actually, for the first 2.5 years of my PhD, I think that the only positive thing I had was my Rhesus status. Do I regret it? Not at all. All this made me the person (and hopefully the scientist) that I am today.

- Sacrifice is a noble thing to do, as long as it does not turn into compromise.
- You are not obliged to always have positive data, make zero mistakes and only publish in high-impact prestigious journals.
- Doing a PhD is a unique opportunity that was offered to you for a good reason; that's why you ARE obliged to do your best and make it worth it. And remember: the PhD is like every Mission Impossible movie that ends with the same 'stupid' twist, where the mission turns out to be possible.

We also advise you to trust yourself. If your project is not working out and you have well designed data, have the courage to drop it on time.

There is no shame in concluding that your project is not worth pursuing any further. Moreover, have confidence in your data. If you did all necessary controls, trust your data even if it goes against previously published literature. A good example is the story of Alexis Carrel who won the Nobel Prize for

pioneering work on vascular suturing techniques, which opened the way to organ transplantation.[14] Unfortunately, he is also known for his famous chicken experiment.[15,16]

Carrel claimed he was able to culture heart cells from a chicken embryo for 34 years! This lead Alexis to conclude that immortality belonged potentially to all cells and that death is only the consequence of how cells are organized in the body. Despite the fact that many scientist failed to replicate Carrels experiments, most people did not dare to doubt him. He was a Nobel prize winner after all. The dogma of cell immortality was upheld for more than 50 years. It is only when Leonard Hayflick discovered that ordinary body cells have a finite life span that the scientific community reconsidered Carrels hypothesis.

In conclusion, dare to trust well-designed negative data and have confidence in the importance of this work for the scientific community.

HEY, IT'S OKAY TO...

Science is serious business, but we may share similar frustrations

... enjoy going to the toilet because it's the only time you have for yourself (some days are just too busy)

... work with a hangover

... start a rescue mission to save your cells after forgetting about them (maybe a little TLC will help!)

... swear at you laptop (who's listening anyway?)

... leave things on ice and find them in a lake the next day (actually this is not ok but we've all been there)

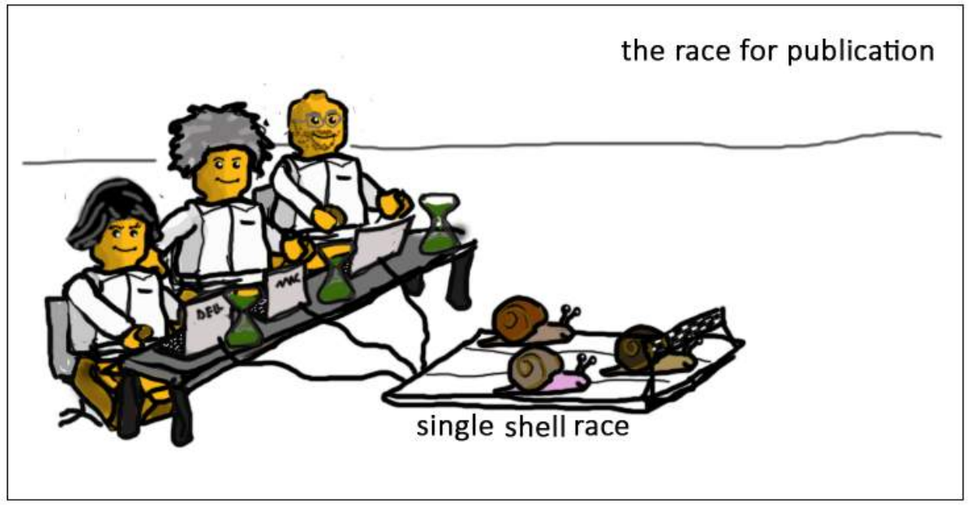
... have two lunches on Tuesdays (who can say no to that pizza?)

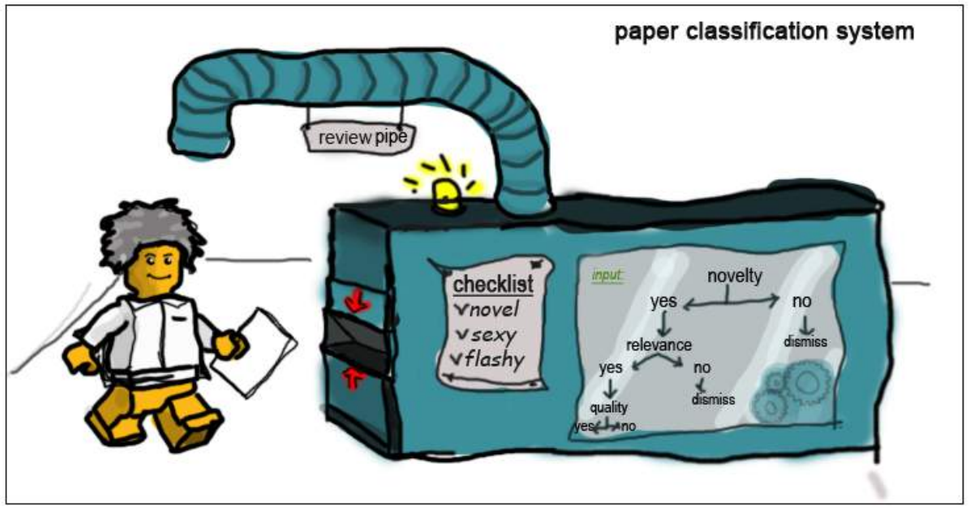
... feel stupid ALL THE TIME (remember imposter syndrome is eminent amongst your colleagues)

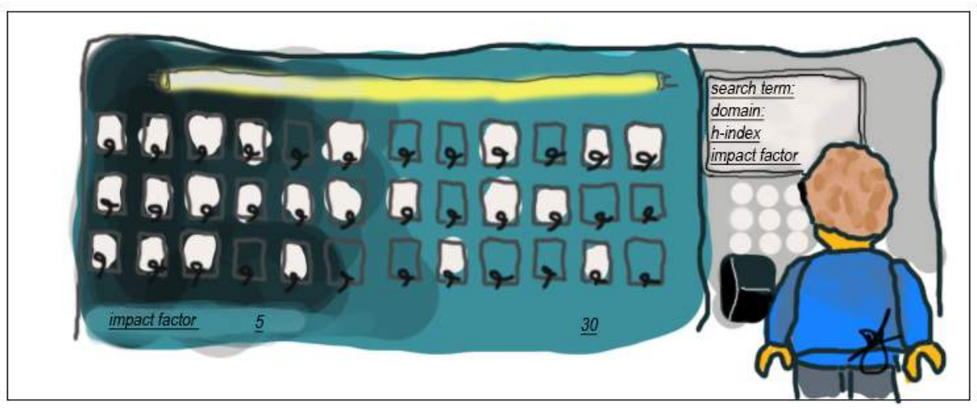
... spend six hours on the confocal before realizing you've been using the wrong settings

... hate your project sometimes (your project is like a baby, you can hate it and love it at the same time)

... email your input to Optimist.PhD@outlook.com







Dries T'Syen

With the help of

PhD survival tips and confessions
Caroline Eykens, Rocco Stirparo, Evgenia Salta, Nuno Apostolo, Anonymous 1, 2 and 3

PI interview
Adrian Liston

Supported by the VIB-KU Leuven Center for Brain & Disease Research
Editing and lay-out by Liesbeth Aerts
Comic by Dries T'Syen

The Optimist Team
Matthias Koch, Donya Pakravan & Joni Vanneste

@OptimistPhD

References

1 Merton RK. The Sociology of Science: Theoretical and Empirical Investigations. University of Chicago press; 1973
2 Pain E. The social responsibilities of scientists. Science. Published 2013 https://www.sciencemag.org/careers/2013/02/social-responsibilities-scientists?r3f_986=https://www.google.com/
3 Ioannidis JPA. Why most published research findings are false. PLoS One. 2005;2(8):e124
4 Nissen SB, Magidson T, Gross K, Bergstrom CT. Publication bias and the canonization of false facts. Elife. 2016; 5(DECEMBER2016):1-19.
5 Sarewitz D. The pressure to publish pushes down quality. Nature. 2016;533(7602):147-147
6 Binswanger M. Excellence by Nonsense: The competition for publications in moderns science. In: Bartling S, Friesike S, eds. Opening Science. Springer; 2014:49-72 https://link.springer.com/book/10.1007%2F978-3-319-00026-8
7 Begley G, Ellis LM. Raise standards for preclinical cancer reserach. Nature. 2012;483(997):10
8 Prinz F, Schlange T, Asadullah K. Believe it or not: how much can we rely on published data on potential drug targets? Nat Rev Drug Discov. 2011;10(9):712-712
9 Rawat S, Meena S. Publish or Perish: Where are we heading? J or Res Med Sci. 2010;19(2):87-89
10 Kiser GL. No more first authors, no more last authors. Nature. 2018;561(7724):435-435
11 Shaw C. Hundreds of open access journals accept fake science paper. Guard. 2013
12 Vrieze J de. Open-acces journal editors resign after alleged pressure to publish mediocre papers. Science.
13 Reproducibility initiative. http://validation.scienceexchange.com/#/
14 Nobel Media AB 2019. The Nobel Prize. https://www.nobelprize.org/prizes/medicine/1912/carrel/lecture/
15 Witkowski JA. Dr. Carrel's immortal cells. Med Hist. 1980;24(2):129-142
16 Rasko J, Power C. What pushes scientists to lie? The disturbing but familiar story of Haruko Obokata. The Guardian. https://www.theguardian.com/science/2015/feb/18/haruko-obokata-stap-cells-controversy-scientists-lie

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