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Holger Schútz á- Peter Wiedemann are in the Programme Group MUT at Research Centre Jiilich, Germany E-mail: h.schuetz@fz-juelich.de E-muil: p.wiedemann@fz-jueHch.de Martin Clauberg is in the Department of Civil & EnvironmentalEngineering and the Institute forEnvironmentalModelling, University ofTennessee, OakRidge, Tennessee, USA E-mail: dauberg@utk.edu

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Proper science in moist biology

Last year, Ceoffrey Chang and co-workers retracted tive papers that contained a faulty protein structure prediction—the result of an error in their software (Chang eí a/, 2006). Although the ensuing debates and arguments about this 'great pentaretraction' nave slowly dissipated, it is useful to shed some light on the context in which such mistakes occur. We believe that there are fundamental differences in the scientific philosophy and methodology underlying the discussion that cannot and should not be explained by current definitions of good or bad science. This is not exclusive to protein crystallography; it is alsotypical of other large-scale, high-tech research fields including nanotechnology, systems biology and imagingtechnologies.

In general, structural biology is a 'hot' research field, involving the constant development of analytical approaches and technologies—combinations of tvvo specific styles of science (Hacking, 1992): classical 'wet' bench work, and 'dry' computational and mathematical work.

Each style of science—wet and dry—represents a tramework for getting at the truth, and comes with its own scientific method, distinct protocols, technologies, theories, language and more general 'ways of doing'. Consequently, it is possible to make claims within one style that make no sense from the viewpoint of the other. For example, the claim that "MsbA is a member of the MDR-ABC transporter group by sequence homology" (Chang & Roth, 2001) is the result of an *in silico* comparison of sequences that can neither be performed at the bench, nor understood or proven by wet work alone.

This implies that wet and dry science differ in terms of what their proponents regard as 'proper science'. In an article in 5c/ence, Chris Miller, from the Howard Hughes Medicai Institute (Waltham, MA, USA), wrote that structures are "just models, not data" and argued that the danger lies in "ignoring biochemical results, conventional but logically solid" (Miller, 2007). He was clearly commenting on the penta-retraction from a wet point of view. From a dry perspective, comments about the error were generally less harsh. It is a wice . accepted practice—necessary for doing dry science—to trust a model or an algorithm and believe the outcome. Consequently, dry scientists have generally attributed the error resulting in the Chang retractions to bad luck, an honest mistake, or 'much ado about nothing'. Conversely, the wet community hás tended to use more harsh terms including: debacle, fiasco, monumental blunder, sloppy science and inexcusable.

In scientific fields such as structural biology, wet and dry styles are becoming increasingly interdependent. As the complexity of their data far exceeds the computing ability of the human mind, scientists have no choice but to trust computer models. This interaction hás become commonplace to a levei at which claims, technologies and tools are no longer either wet or dry. They can only be understood and used within a new framework or style that we call 'moist' science—an integration of dry and wet styles. Accordingly, moist science creates a new way of doing 'proper science'. Critiques directed at Chang and co-workers exclusively from a dry or a wet point of view therefore cannot fui lyevaluate the 'properness' of their research, or fully assess the magnitude of any mistakes.

As moist science is a science in the making, some of its technologies are still experimental and protocols have not yet been unanimously accepted. The specific criteria for what it deems to be 'proper science', or what exactly counts as a mistake, have not yet been set. For example, should the code of an algorithm—which in this case created the error—be included in the methods section of a publication, or made available as supplementary material online? This and other questions must be settled in order to reach a new consensus on what constitutes 'proper science'. Therefore, the lesson is not whether to blame, but how to learn from and improveon this new moist scientific style.

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Bart Penders, Klasien Horstman & Rein Vos are at the Department of Health, Ethics ú- Sociely, Maastricht University, Maastricht, the Xetherlands.
E-mail: b.penders@zw.unimaas.nl

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Philanthropy in Portugal

At the European Councíl meeting in Lisbon in 2000, the European Union (EU) established the strategic goal of becoming "the most dynamic and competitive knowledge-based economy in the world" by 2010 (Fontaine, 2000). To achieve this, eac[u] F.U member state would be required to increase its investment in research and development (R&D) to 3% of its Gross DomestiC Product (CDP), which would necessitate an increase in both public and private investments.

An important component of private investment is philanthropy. A group of experts recently proposed several policy recommendations to strengthen the role of philanthropy in financing R&D in Furope i.EC, 2005). Their report concluded that the EU must further exploit the potential of philanthropy to achieve the strategic investment goals established in the Lisbon Agenda i EC, 2006a).

However, many European societies do not have a well-established philanthropic framework. This is in contrast to the USA and Canada, which have strong philanthropic

traditions including specialized institutions to promote fundraising. For example, from 2003 to 2004 the Faculty of Medicine at the Memorial University of Newfoundland in Canada raised 12% of its research funding exclusively from private donations (Memorial University of Newfoundland, 2005).

In Europe, the UK hás the strongest tradition of philanthropy in science, with many organizations devoted to attracting non-governmental funding. University College London (UK), for example, hás raised more than GBPfSO million in private donations over the past two years for research and other strategically important áreas. Even more well known is the charity Câncer Research U K (London)—the world's leading independent organization dedicated to câncer research. It hás an annual scientific budgetof CBP£2S7 million donated almost entirely by the public, This is possible owing to a well-established framework for philanthropy that encourages Britons to give money to specific causes. In recent years, small European countries such as Ireland, have also successfully boosted philanthropic donations for science, following the trend observed for many years in the U K. By comparison, scientific philanthropy in Portugal remains undeveloped.

The difference between Ireland and Portugal might be explaíned from a historical perspective. Despite both being small, predominantly Catholic countries at the geographical fringe of the EU, their approaches to philanthropy for science have been fairly different. Similarly to the UK, Ireland hás had a long tradition of philanthropy in many áreas of society. For example, The Ireland Funds (Dublin) hás raised money for a wide range of causes in Ireland for 31 years with branches in 11 different countries. The Children's Medicai & Research Foundation (Crumlin, Ireland) supports Our Lady's Children's Hospital and the Children's Research Centre, both in Crumlin, and illustrates how Irish research institutes are able to secure philanthropic money.

!n the 1990s, Ireland experienced strong economíc growth—the 'Celtic Tiger' period—that generated a significant increase in wealth. The combination of a strong economy and a philanthropy-friendly society boosted R&D fundraising significantly. According to Kingsley Aikins, CEO of The Ireland Funds, this might be "the opportunity for the Celtic Tiger to become a Philanthropic Tiger" (Aik'ns, 2006). His statement is backed up by the fact that, since its creation, The Ireland Funds hás raised US$300 million—US$210 million of which was raised in the past 10 years alone. Although exact figures for philanthropic funding are difficult to determine, the overall private investment in R&D in 2005 in Ireland was just over €387 million, compared with a total of just over €17 million in Portugal. Furthermore, 12 Irish companies are among the world's 1,000 best investors in R&D, whereas only two Portuguese companies appear on the list(EC, 2006b).

In Portugal, the Catholic Church hás always driven charitable fundraising. However, despite this religious influence—which is also present in Ireland—philanthropy for science hás never truly developed. The single exception to this is the legacy of the businessman Calouste Sarkis Culbenkian: the Fundação Calouste Culbenkian. This foundation hás sha^ed the artistic, educational and scientific scene in Portugal during the past 50 years. Apart from this contribution, Portuguese society hás few examples of charitable institutions dedicated to fundraising for science.

Additionally, the Portuguese economy hás not undergone a growth period similar to the'Celtic Tiger'period in Ireland. Before joining the EU in 1986, the Portuguese economy was predominantly based on agriculture, fishing and trade. Despite new investment and developments since joining the EU, the Portuguese economy is still outperformed by most other EU countries—a potential factor contributing to the small philanthropic effort seen in Portugal.

Despite this, there are some recent examples of philanthropy in Portugal that suggest that the private sector and the general population are becoming more aware of the benefits of giving for science.

The most striking example is the recent creation of the Fundação Sommer-Champalimaud by a Portuguese entrepreneur. This fund aims to invest a total of around €400 million in biomedical research, making it the second largest foundation in Portugal. More good examples are Fundação Bial, which hás funded researchers and research projects in biomedicine and the neurosciences since 1994, and the campaign, 'Friends of IPATIMUP', launched for the first time in 2004 to raise funds for the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP; Portugal), which is dedicated to câncer research.

More recently, ot~er institutions have emerged to support research into specific diseases in Portugal. One example is the Associação Portuguesa Contra a Leucemia, which was started in 2002 by leukaemia patients and regularly organizes fundraising events. The most famous of these is a biennial concert, which attracts significant public attention and money. The success of this association suggests that the Portuguese are ready to contribute to specific causes, as long as an organized infrastructure raises awareness and channels people's generosity.

The non-profit organization Associação Viver a Ciência was cresred in 2004 by a group of young scientists concerned with the future of philanthropy in Portugal. The Associação Viver a Ciência believes that if citizens become engaged with science, they will appreciate its benefits and contribute to it. The association hás organized several science-promoting events including publications, exhibitions and workshops, and hás iuccessfully attracted private investment for research by creating twosponsored annuai prizes for Portuguese life scientists. The Crioestaminal Award is awarded for an outstanding biomedical research project, whereas the Citomed Award is given for a peer-reviewed scientific paper in immunology. In addition, Viver a Ciência collaborated with the media, several companies and other organizations throughout 2005 and 2006 to promote the Law of Scientific Sponsorship (Lei do Mecenato Científico). This law provides tax benefits for science-related donations.

These and other examples indicate that the time is right to create a framework for philanthropic donation to science in Portugal, similar to those in Ireland and the UK. Despite a ciimate of economic crisis—and perhaps even as a consequence of it—people realize that they can directly influence the future through charitable donations. Importantly, the Portuguese people are starting to acknowledge the need for accountability and transparency—they want to make sure that their money is used efficiently, fairly and ethicaliy.

However, much work remains to be done to create such a framework for philanthropy—and it hás to involve ali of Portuguese society. Well-established systems similar to those in Ireland and the UK should be used as models for Portugal, and International recommendations, similar to those made in the report, *Civing more for*

research in Europe (FC, 2005), should be embraced by ali parties involved. It is clear that science and the scientists in Portugal—and in the rest of Europe—would appreciate and benefit from such a collective effort. Therefore, it is vital to achieving the goals set by the Lisbon Agenda.

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Sofia Rodrigues, Maria Mota, Leonor Saúde, Sheila Vidal ó-Margarida Trindade are at the Associação Viver a Ciência in Lisbon, Portugal. E-mail: mtrindade@viveraciencia.org

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