Left is right, right is wrong

The cover illustration of the August 2009 issue of *EMBO reports*, although aesthetically pleasing, is unfortunately erroneous and could come as a shock to researchers in the chromatin field. Canonical nucleosomes are indeed left-handed, such as the nucleosomes in the left 'column' of chromatin fibres on the cover. However, in the right 'column', the chirality of the nucleosomes has been inverted: they are drawn in a non-canonical, right-handed conformation.

This mistake is sadly quite common: many textbooks, publications and websites feature images of nucleosomes displaying the wrong chirality. Try a search for "nucleosome" in Google Images: there is a good chance that the first hit will display the right-handed nucleosome originally—and incorrectly—drawn for a popular textbook. To make things worse, this image has been frequently adapted in many other contexts. For instance, it acts as an illustration for the Wikipedia nucleosome entry in several languages, including French. If you would like more examples, I am happy to provide a full collection of 'wrong' nucleosomes on request.

Nucleosomes depicted with right-handed chirality are usually the result of inadvertent infographics errors, because many artists who draw chromatin fibres are perhaps not aware of chirality matters. They also arise if the image of a canonical nucleosome is accidentally mirrored upon publication (Fig 1A,B). This was the case in another popular textbook, in which the mirror image managed to survive several editions—and the scrutiny of thousands of teachers and students—before I finally mentioned it to the authors, who promptly fixed it in the following edition. Note also that if the DNA helix is resolved on these erroneous images, mirror inversion will also inverse its canonical right-handedness (Fig 1B). DNA is another victim of neglected chirality, which results in journal covers, advertisements and other pictures ending up full of left-handed DNA that is not intended to be Z-DNA.

Fig 1 | Nucleosome chirality. Front and side views of (A) a canonical nucleosome (L-octasome), (B) an artefactual right-handed nucleosome, which shows how a simple mirror inversion also changes DNA chirality, and (C) a true reversome (R-octasome). Original nucleosome and reversome drawings kindly provided by Hua Wong.

I would therefore encourage readers to play the 'chirality game': each time you see a nucleosome or a DNA molecule, check its handedness! Incidentally, while this text was being edited, another journal provided an appropriate entry for the chirality game: on the cover of *Nature Structural and Molecular Biology's* September issue, the first nucleosome is left-handed, whereas the second is right-handed. Who will be next?

Should we care so much about nucleosome chirality? The answer is yes, because nucleosome chirality must have evolved as a consequence of DNA chirality. Indeed, since a canonical nucleosome constrains one negative turn of DNA (Prunell, 1998), the removal of a nucleosome to gain access to a particular sequence, such as a promoter, simultaneously favours the melting of DNA, which is a necessary step for initiating transcription. In other words, a chromosome with right-handed nucleosomes would be condemned to silence: each time a nucleosome was removed, the DNA helix would tighten and thus restrict access to the message it carries.

Now, one might use the erroneous cover of *EMBO reports* to raise an important

question: are nucleosomes invariably left-handed? In other words, is the *EMBO reports* cover picture really wrong? Nucleosomes in their canonical form consist of about 146 base pairs of DNA that are wrapped twice, as a left-handed superhelix, around an octameric core of two copies each of histones H2A, H2B, H3 and H4 (Luger *et al*, 1997). However, several papers have challenged the idea of unalterable cylindrical nucleosomes and provide evidence of the existence of alternative histone/DNA assemblies, some of which are potentially topologically reversed (right-handed; Lavelle & Prunell, 2007; Zlatanova *et al*, 2009). For instance, Prunell and co-workers recently suggested that nucleosomes subjected to large positive torques—such as those produced by RNA polymerases—could absorb topological constraints by transiently shifting into a right-handed conformation to form metastable nucleosomes, which they call 'reversomes' (Bancaud *et al*, 2007; Fig 1C). Remarkably, recent results provide the first *in vivo* evidence of constitutively right-handed supercoiled chromatin in yeast centromeres (Furuyama & Henikoff, 2009).

Therefore, instead of taking this *EMBO reports* cover for yet another incorrect chromatin picture, one might actually take it as a courageous and pioneering illustration of what future advances could show: that chromatin is a dynamic and polymorphic histone/DNA complex, the function of which partly relies on its topological properties and, therefore, on the control of the chiralities of its constituents.

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Is the end in cite?

How Jacobs's light-hearted exploration of where the perverse incentives surrounding the quest for publication in high impact-factor journals might lead paints a gruesome picture. Of course, there is a serious message in his October editorial, and even now many would argue that our fixation with judging the scientific influence and importance of people, articles, labs and departments on the basis of a single statistic is deeply flawed and ultimately, detrimental to science (Anon, 2006; PLoS Medicine Editors, 2006; Lawrence, 2008; Adler *et al*, 2008; Simons, 2008). Even *Nature's* own editor-in-chief has bemoaned the deficiencies of the impact factor (Campbell, 2008), although his own journal still celebrates its metric

to three decimal places (www.nature.com/nature/about).

But what is to be done when the journal impact factor is so tightly woven into the fabric of research assessment? How could we escape Jacobs's nightmare scenario? At PLoS, we believe articles should be judged on their own merits, rather than on the basis of the journal in which they happen to be published. After all, most readers now use search engines such as Google and PubMed to find research that is relevant to them, rather than browsing a particular set of journals. We also think it is important to look beyond citation counts; although they do provide some indication about how the academic community values a piece of work, they are only one of many possible measures.

Over the past months, we have therefore taken what we hope are some useful steps towards improving research assessment. In March of this year, we launched an 'article-level metrics' programme, whereby every PLoS article includes information about the possible measures of its impact. In addition to citations, we add online usage data—page views and downloads—as well as the number of social bookmarks, comments, notes, blog posts and ratings that are made concerning the article (www.plos.org/cms/node/485). As far as we know, this is the most comprehensive and transparent set of article data that any publisher is providing.

Article-level data are not without their problems, and so it is important to interpret the data carefully. But, we believe that providing the data in the first place will inspire new ideas about how to assess research. Rather than limiting attention to the journal impact factor, it will be possible to ask sophisticated questions about the impact and influence of published research, and to obtain meaningful answers. For example, for a piece of research that is aimed at practitioners, we might want to know the extent to which it has actually changed practice—citation metrics probably would not be of much help in that case. And it should be possible to find work that only emerges with the passage of time as crucial for the development of a particular field.

Another potential consequence of focusing attention at the article level is that it might matter less where a piece of work is published, so long as it is openly available. In turn, this might reduce the tremendous amount of energy and pain that is associated

with trying to publish work in the highest possible impact journals (Raff *et al*, 2008). It would also reduce the risk of another element in Jacobs's nightmare vision—that the journals with the highest impact factors can charge ever-escalating fees for publication, and that only the richest labs would be able to afford to publish in those journals.

As alternatives begin to emerge, the primacy of the impact factor will be challenged. But this will only happen if other stakeholders also take a stand. The Wellcome Trust has made its position clear in its policy on open access by affirming “the principle that it is the intrinsic merit of the work, and not the title of the journal in which an author's work is published, that should be considered in making funding decisions” (Wellcome Trust, 2008). And it was encouraging to see the recent statement that journal impact factors “should not be used as a basis for evaluating the significance of an individual scientist's past performance or scientific potential,” which was unanimously adopted at the International Respiratory Journals Editors Roundtable (Adler, 2009). In addition to focusing on article-level metrics, at PLoS we have also decided to no longer promote impact factors anywhere on our sites—we would love to see other publishers do the same.

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