NSMB's 30th anniversary

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Musings on art and science

In addition to the usual dose of compelling science, our March issue features thoughtful reflections on the last 30 years from readers, as well as past and present editors. Perhaps influenced by these pieces or by our stunning cover – or maybe it is just the changing seasons – we are in an introspective mood this month.

Our March 2024 cover features an original oil painting by the artist Leidy Churchman, entitled *Single-Nucleoid Architecture Reveals Heterogeneous Packaging of Mitochondrial DNA*. This painting illustrates the study by Isaac et al., where the authors use long-read single-molecule accessibility mapping to measure individual mitochondrial genomes packaging at near single-nucleotide resolution, observing heterogenous, all-or-none compaction, with a majority of nucleoids in an inaccessible state. This heterogeneity had been obscured by the bulk averaging inherent to the previously used methods.

Science, like art, shines a light, with beauty often in the details. This aphorism led us to the textbook quote from Werner Heisenberg, who wrote in *Physics and Beyond*[1]: "Science is made by men, a self-evident fact that is far too often forgotten. If it is recalled here, it is in the hope of reducing the gap between the two cultures, between art and science." While art arises from the struggle between expressive content and the limitations of the expressive medium, the possible colors and dimensions on a canvas, the tonal frequencies of a musical instrument, the malleable properties of a material and our ability to work it, in science, the expressive media are the conceptual systems we use to express the ideas that arise from experiments. Such as in art, progress in science is often limited by physical boundaries. We embrace the incomplete nature of the scientific process and the need to keep going back to the drawing board: the picture is never finished, always a work in progress.

Artificial intelligence (AI) now shows promise to empower productivity in both realms; however, it also threatens to corrupt the creative process by shifting the focus away from this expressive struggle that is so fundamental to one of the most human activities – making sense of the world. Instead, it shifts the focus to the final product, which is usually not the point of either endeavor. AI-generated illustrations lack life, intention, authenticity and, in the case of science, scientific rigor. Artistic representations of scientific knowledge are not perfect, often incomplete and simplistic, being only a proposed representation. But they are drawn with purpose and intentionality, and while their beauty is meant to captivate the audience, scientific accuracy is the guiding principle and omnipresent constant. It is also important to understand that science is not always a pretty picture; just because a model is elegant does not mean it is correct. Returning to our cover work, we note that Leidy Churchman painted it to illustrate the work of their sibling, Stirling Churchman, a tribute to how these two human passions are deeply intertwined.

Oil painting of a mitochondrion.

As a scientific journal, the brightest highlights of our March issue shine on the new science it features. In addition to the above-mentioned work on mitochondrial genome organization, we feature other exciting studies in the fields of genome architecture and regulation of gene expression. In Bignaud, Cockram et al., the authors use sub-kb Hi-C and chromosome engineering to visualize bacterial transcriptional units, showing that they form transcription-induced domains that restrain nearby sequences and affect their (re) localization. On the other hand, a study by Chervova, Molliex et al. reveals simultaneous mitotic binding of two nuclear receptors, which promote the reactivation of the pluripotency network in embryonic stem cells. This work implicates nuclear receptors as functional, yet redundant, mitotic bookmarking factors. Furthermore, Saredi et al. show that the histone chaperone SPT2 can bind H3–H4 and that this chromatin interaction is required to maintain chromatin structure and function in worms and human cells. In an insightful Review, Monteagudo-Sánchez et al. present an overview of the current understanding of the relationship between DNA methylation and chromatin architecture, discussing the extent to which DNA methylation affects the folding of the genome.

Focusing on the regulation of gene expression, Kokic et al. provide pertinent missing information in transcription-coupled repair, by showing how ELOF1 repositions repair factors on the surface of DNA damage-stalled RNA polymerase II to facilitate its ubiquitylation by the CRL4CSA E3 ligase and inactivation by UVSSA. Notably, Gibson et al. illustrates the nuances of pioneering activity of key transcription factors in *Drosophila* by showing that such pioneering activity is not an intrinsic, binary property. Instead, it is heavily influenced by the level of chromatin occupancy of the pioneer factors, which is controlled by multiple protein domains and protein extrinsic features. We are also excited to feature some innovative and creative approaches to study gene regulation. In a study from the de Boer lab, the authors investigated the regulatory activity of evolutionarily naive DNA introduced as yeast artificial chromosomes, providing evidence that activity does not imply function. In a companion study published in *Nature*, Camellato et al.[2] use large-scale genome synthesis methods to construct synthetic DNA with the reversed (not complemented) sequence of the human *HPRT1* gene locus, introducing it in yeast and mouse embryonic stem cells. In this study too, signatures

of active chromatin are observed in yeast. In an accompanying news & views, Sean Eddy[3] reflects on these 'Random Genome Project' approaches to test the baseline activity of genomic DNA in the absence of any evolutionary selection for biological functions and what they teach us about gene regulation. Manipulating gene regulation remains of wide interest as a potential therapeutic avenue. In work that may contain important insight for the treatment of patients with estrogen receptor-positive (ER+) breast cancer, Achinger-Kawecka, Stirzaker et al. investigate how decitabine-induced DNA hypomethylation can potentially overcome endocrine resistance in such cancer cells, by targeting the three-dimensional epigenome to reverse gene deregulation and suppress tumor growth.

We continue to celebrate the 30th anniversary of *Nature Structural & Molecular Biology* with a Feature where past and present editors look back at some of their more memorable experiences of working at the journal. Patrick Cramer looks back at all the amazing developments and advances in the field of structural biology and presents his hopes for future technical breakthroughs and 'serendipitous findings' that will break new molecular and cellular ground. Writing on structure-guided drug discovery, Cheryl Arrowsmith reflects on how these structural and mechanistic breakthroughs can be leveraged towards designing and perfecting new drugs. This is truly an exciting moment in structural biology, with its many achievements being celebrated. Just a couple years ago, we celebrated the Protein Data Bank's 50th anniversary. Our colleagues at Cell Press have recently celebrated the 30 years of the launch of *Structure*[4] and have featured a focus on structural biology as part of the celebration of *Cell*'s 50th anniversary. We extend our congratulations to all our colleagues at Cell Press for these achievements, with sincere wishes that the field continues to produce exciting developments and discoveries in the decades to come.

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References

1. Heisenberg, W. *Physics and Beyond: Encounters and Conversations* 1st edn (Harper & Row, 1971).
2. Camellato, B. R., Brosh, R., Ashe, H. J., Maurano, M. T. & Boeke, J. D. *Nature* https://doi.org/10.1038/s41586-024-07128-2 (2024).
3. Eddy, S. R. *Nature* https://doi.org/10.1038/d41586-024-00575-x (2024).
4. Kühnel, K. *Structure* **31**, 1283 (2023).