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Biochemistry on Stage

Systematic Absences

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In October 2019, deep underground in the bowels of the University of Melbourne's Bio21 Institute, a dozen VIPs are clustered around a scientific instrument resembling a large squat refrigerator. These aren't overseas scientists, entrepreneurs or politicians. They are actors. This is the cast of the Melbourne Theatre Company's production of Anna Ziegler's play, *Photograph 51*.

Nadine Garner as Rosalind Franklin and Gig Clarke as Ray Gosling. Photo: Pia Johnson.

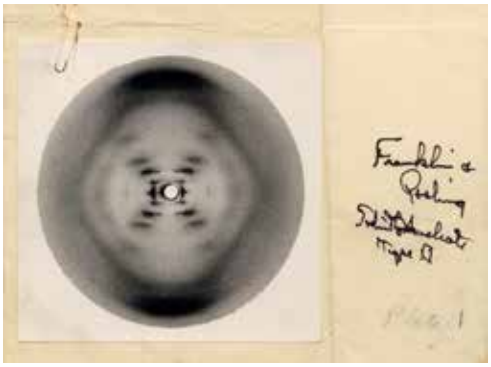
Since 2010, *Photograph 51* has been performed to packed houses from New York to Stockholm. In 2015, it played in London's West End with Nicole Kidman in the leading role. Pamela Rabe is to direct its run at the Fairfax Theatre in the Melbourne Arts Centre (1 November–14 December 2019). The cast, including Nadine Garner (*The Doctor Blake Mysteries*), are here to school themselves in the dark arts of X-ray diffraction and to hear the perspectives of real scientists on the motivations, rivalries and sexual politics at the heart of the story they will portray.

The group listen intently, as crystallographer Megan Maher explains the operation of the X-ray diffractometer. The bottom half, containing the X-ray generator, is completely enclosed by metal shielding, but a window in the top half reveals an assembly of gleaming metal devices. Several probe-like appendages converge to a single point. Here, a narrow powerful beam of X-rays is focussed onto a tiny crystal of biological material. The X-rays impinge on the crystal and are then scattered in all directions by the ordered crystalline lattice of molecules. The emergent waves of energy interfere with each other constructively and destructively. In some directions, they add together to become more intense but in other directions they annihilate each other and vanish. When the diffracted beams hit the detector, the result is complex and beautiful. Geometric patterns form composed of lines of spots of varying intensity with occasional gaps – so called 'systematic absences'. In days gone by, these images were captured on photographic film. Photograph 51 was the understated name given in 1952 by the trailblazing female scientist Rosalind Franklin, to the most famous X-ray diffraction image ever captured.

In a dank basement at King's College in post-second world war London, Rosalind Franklin used a much more rudimentary diffractometer to record photograph 51. Time and time again, she and PhD student Raymond Gosling painstakingly aligned semicrystalline fibres of DNA in the X-ray beam and recorded photographs. By controlling the humidity inside the diffractometer, Franklin was able to tease apart the contributions from the A and B forms of DNA. Photograph 51 was recorded under higher humidity, which favours the more hydrated and elongated B form that more closely resembles the state of DNA in living cells.

Photograph 51 subsequently fell into the hands of a brash young American working at Cambridge University, James D Watson. It contained the key information that allowed Watson and his older English colleague Francis Crick to propose their famous double helix structure of DNA. Their model for DNA was elegant in its simplicity and earth shattering in its significance. This great leap forward paved the way for the genomics revolution that we are immersed in today. In recognition of this discovery, Watson, Crick and Franklin's male colleague, Maurice Wilkins, received the 1962 Nobel Prize for Medicine. But not Rosalind Franklin. She died of ovarian cancer in 1958. Ironically, Franklin's premature death averted a controversy that was brewing. Watson and Crick's place in history was assured, but either Franklin or Wilkins would have had to miss out. Nobel Prizes can be shared by no more than three individuals.

The intellectual and emotional conflict of the fraught relationships still fascinates us, more than 70 years



Photograph 51.

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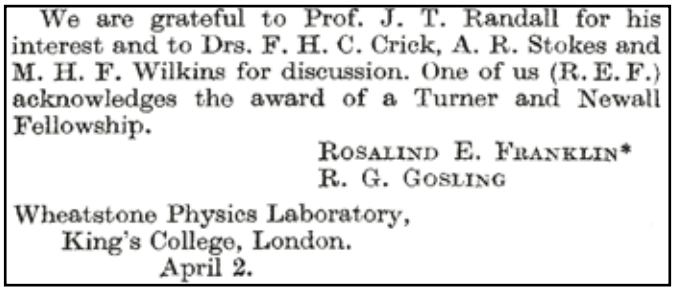
Rosalind Franklin on vacation in Tuscany, spring 1950. Photo: US National Library of Medicine.

on. The way Watson and Crick learned the details of Franklin's experiments and how Watson obtained her diffraction pattern speak volumes about the attitudes towards women in science and society of the time.

Back upstairs in the Bio21 boardroom, we show the cast 3D animations of DNA molecules and talk about the meaning of different geometric features of photograph 51. We explain how the X shape indicates helical structure and that the layer lines define repeating distances. The systematic absence of the fourth layer line indicates that the two twisted DNA strands are offset by 3/8 of a turn. This asymmetry gives rise to the major groove and minor groove in the structure where (as we now know) protein machines can nuzzle into the structure and read its blueprint.

We are bombarded with questions, both technical and about what it is like being a scientist. The most telling was, 'Do you think what Watson and Crick did was right?' The four scientists in the room, geneticist Karen Day, molecular biologist Heather Verkade and structural biologists Megan Maher and I momentarily pause and then, unanimously agree: 'No'. What they did was wrong. And it is not a matter of different standards for different times. It was wrong then and it is still wrong now. In Cambridge, Max Perutz improperly gave a report on Franklin's work to Lawrence Bragg, which then found its way into the hands of Watson and Crick. Although argument has ensued for decades, it is doubtful that Watson and Crick should ever have been allowed to see it. At King's College, Wilkins then overstepped his authority by handing Watson photograph 51 without consulting Franklin. Imagine how you would feel if your grant application containing unpublish data was 'shared' with your competitors; and then to top it off, a senior colleague gifts them your raw data behind your back?

Nobel Prize winners at the ceremony in Stockholm, Sweden, 1962. From left: biophysicist Francis Crick, biophysicist Maurice Wilkins, writer John Steinbeck, geneticist James Watson, biochemist Max Perutz and biochemist John Kendrew. Photo: Granger.



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ROSALIND E. FRANKLIN*
R. G. GOSLING

Wheatstone Physics Laboratory,
King's College, London.
April 2.

Acknowledgements section from Rosalind Franklin's April 1953 Nature *paper (3).*

The acknowledgements section of a thesis or paper can be fascinating and revealing. Like diffraction patterns, there is information in what is both present and missing. Three papers, authored by *Photograph 51's* key protagonists, appeared back-to-back in the April 1953 issue of *Nature*. Watson and Crick acknowledge having been 'stimulated by a knowledge of the general nature of the unpublished experimental results and ideas' of Wilkins and Franklin (1). In his paper, Wilkins thanks Watson and Crick for 'stimulation' and Franklin for 'discussion' (2). Tellingly, Rosalind Franklin is 'grateful' to just Wilkins and Crick (3). James D. Watson's name is a systematic absence.

References

1. Watson JD, Crick FH (1953) *Nature* 171:737–738.
2. Wilkins MHF, Stokes AR, Wilson HR (1953) *Nature* 171:738–740.
3. Franklin RE, Gosling RG (1953) *Nature* 171:740–741.

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