Experimental physics

# Accelerator-based light sources get a boost

Alexander Brynes

The structure of matter can be explored using the light emitted by particle accelerators. An experiment demonstrates how the properties of two such light sources – synchrotrons and free-electron lasers – can be combined. See p.576

For decades, particle accelerators have been used across a wide range of fields, enabling the study of matter in ever-increasing detail. Charged particles emit light when they are accelerated, and accelerators that exploit this phenomenon are among the brightest artificial sources of light available, allowing scientists to probe the properties of matter over unprecedentedly short scales of length and time. On page 576, Deng *et al.*[1] report a proof-of-principle experiment on an accelerator that could extend the capabilities of these machines even further, potentially yielding applications in a next-generation chip-etching technology called extreme-ultraviolet lithography[2] and an advanced imaging method known as angle-resolved photoemission spectroscopy[3].

The two main types of accelerator-based light source are synchrotrons (circular machines) and free-electron lasers (linear machines). Synchrotrons have a high average power (number of photons produced per unit time) and can generate pulses of light that have tunable wavelengths and a wide bandwidth (range of wavelengths). The high power is possible because 'bunches' of particles cycle around the machine many times, producing light at every turn as they travel through a series of magnets of alternating polarity, known as an undulator or a wiggler.

Free-electron lasers have a lower average power than do synchrotrons, because they use a bunch of electrons only once. However, they can generate pulses of light that have a smaller bandwidth and a much higher brightness (up to 10 billion times brighter[4]) than those produced by synchrotrons. In a free-electron laser, the radiation emitted by the electrons acts back on these particles, causing them to bunch together into regions about the size of the radiation wavelength. The light waves generated by these 'microbunched' electrons are coherent (in sync), and reinforce each other to achieve the remarkable brightness mentioned above.

Deng and colleagues' results are based on a concept called steady-state microbunching[5], which aims to bridge the gap between high-power synchrotrons and small-bandwidth, high-brightness free-electron lasers. In steady-state microbunching, an electron bunch in a synchrotron is forced to become microbunched before it emits radiation (Fig. 1). This effect is achieved by firing a (conventional) laser pulse at the electrons while they travel through an undulator. The undulator makes the electrons oscillate transversely, and the laser pulse causes different particles to have different energies.

As this modified bunch travels around the machine, higher-energy electrons are deflected less by the magnetic fields used to steer the particles (and therefore take a longer path) than are lower-energy electrons, making them slip backwards. By the time the electrons have completed a turn through the accelerator, this longitudinal slippage has caused the particles to become microbunched, giving them properties resembling those of the electrons used to drive a free-electron laser. The distance between these microbunches is approximately the wavelength of the incident laser pulse.

As mentioned previously, coherent emission by a microbunched electron beam produces pulses of light that have a much higher power than those generated through incoherent emission. Deng *et al.* detected the radiation produced by a typical electron bunch at the Metrology Light Source, a synchrotron in Berlin. They then compared this radiation with that of a beam that had been microbunched using their new process.

After using a device called a band-pass filter to remove residual incoherent radiation, Deng and colleagues detected a clear signal from the microbunched beam, indicating that coherent emission was taking place. They corroborated this finding by investigating the dependence of the radiation power on the charge of the electron bunch. The radiation power of a bunch that emits coherently is proportional to the square of the bunch charge, and the authors observed this quadratic dependence by varying the bunch charge and analysing the radiation produced.

Although this paper represents a crucial step towards generating high-power,

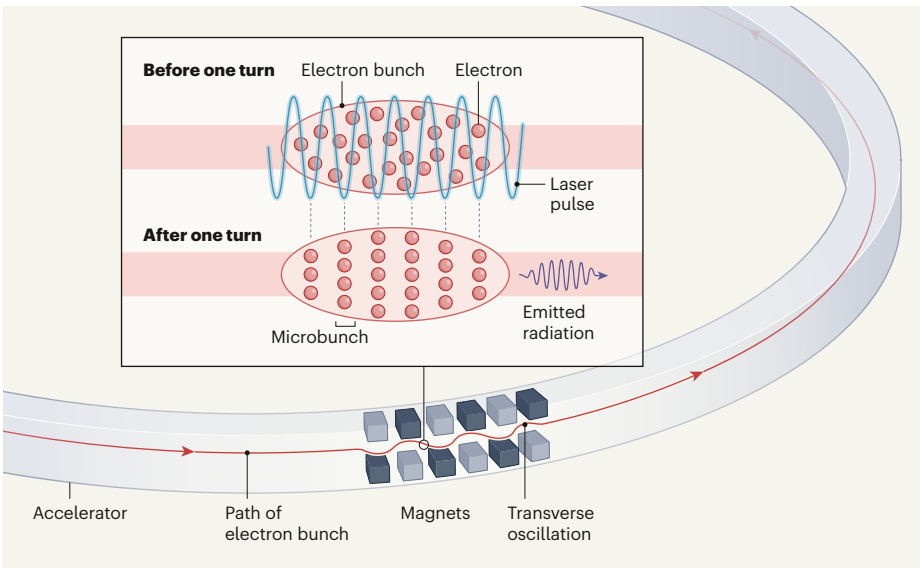


**Figure 1 | Radiation emission from microbunched electrons.** Deng *et al.*[1] carried out a proof-of-principle experiment in which a 'bunch' of electrons travelled around a circular particle accelerator called a synchrotron. The electron bunch oscillated transversely as it passed through a series of magnets of alternating polarity (indicated by the two different colours). During this stage, the authors fired a laser pulse at the electron bunch, causing different electrons to have different energies. The electron bunch then completed one full turn through the accelerator. After this turn, the electrons were grouped into 'microbunches' that were separated by a distance roughly equal to the wavelength of the laser pulse (as shown by the dashed lines). Finally, Deng and colleagues detected the radiation emitted by these microbunches. (Adapted from Fig. 1 of ref. 1.)

small-bandwidth light pulses in a particle accelerator, steady-state microbunching has not yet been demonstrated. Deng *et al.* have shown that, after one turn in the synchrotron, the microbunched beam can produce coherent radiation. The next challenge is to prove that this scheme can achieve such a feat over many turns. This will be difficult to accomplish experimentally for at least three reasons.

First, longitudinal slippage would degrade the microbunching over many turns. Second, for high-power (kilowatt-level) steady-state emission of radiation to occur, incident laser pulses must be synchronized to the arrival of the electron bunch at every turn and confined to an arrangement of mirrors known as a laser cavity. And third, collective interactions between the electrons in the beam, if not controlled using feedback loops, would eventually reduce the power and brightness of the radiation.

A few schemes[5–7] that are variants of the original concept could improve the properties of the radiation produced and go beyond Deng and colleagues' results. Demonstrating such schemes represents a considerable technical challenge, but the authors' proof-of-principle experiment shows a path towards achieving high-power, high-brightness, small-bandwidth light sources that could outperform current synchrotrons. Moreover, other types of light source, such as storage-ring free-electron lasers[8] and energy-recovery linear accelerators[9], are under development, and could lead to the next generation of these machines. Although substantial hurdles need to be overcome before such schemes are reliably demonstrated, the authors' findings provide a glimpse into the future of high-power, accelerator-based light sources.

**Alexander Brynes** is at the Accelerator Science and Technology Centre, Science and Technology Facilities Council Daresbury Laboratory, Warrington WA4 4AD, UK.
e-mail: alexander.brynes@stfc.ac.uk

1. Deng, X. *et al. Nature* **590**, 576–579 (2021).
2. Bakshi, V. *EUV Lithography* (SPIE Press, 2018).
3. Damascelli, A., Hussain, Z. & Shen, Z.-X. *Rev. Mod. Phys.* **75**, 473–541 (2003).
4. *Nature Struct. Biol.* **5**, 657–658 (1998).
5. Ratner, D. F. & Chao, A. W. *Phys. Rev. Lett.* **105**, 154801 (2010).
6. Ratner, D. & Chao, A. *33rd Int. Free Electron Laser Conference (FEL 2011)* 57–60 (2011).
7. Jiao, Y., Ratner, D. F. & Chao, A. W. *Phys. Rev. Spec. Top. Accel. Beams* **14**, 110702 (2011).
8. Lee, J. *et al. J. Synchr. Radiat.* **27**, 864–869 (2020).
9. Nakamura, N. *et al. J. Phys. Conf. Ser.* **874**, 012013 (2017).

Pancreatic tumours

# Mutation alters injury response to drive cancer

**Dane Vassiliadis & Mark A. Dawson**

Cancer-associated mutations promote the formation of pancreatic tumours after tissue injury, but how this occurs is unclear. Changes to chromatin in injured cells with such mutations explain this predisposition to malignancy. **See p.642**

It is increasingly clear that, as humans age, many, if not most, of our tissues become composed of populations of cells, termed clones, that often harbour genetic mutations found in the malignant tumours that arise from the same type of tissue. Although these clonal populations seem to be normal cellular lineages apart from the cancer-associated mutations, little is known about how these cells respond to damage caused by exposure to ultraviolet light or toxic chemicals, for example. A process called metaplasia — the replacement of one cell type with another after tissue damage — increases the risk of cancer formation[1]. Why abnormal repair during metaplasia predisposes cells to form cancer is mainly unknown. On page 642, Alonso-Curbelo *et al.*[2] report a study of pancreatic cancer in mice that reveals how a mutation biases the outcome of metaplasia towards the development of cancer.

Most human pancreatic cancers contain mutations in the *KRAS* gene, which encodes a type of enzyme, termed a GTPase, that has a key role in signalling. The KRAS enzyme contributes to the control of cell growth in healthy tissues, but cancer-promoting mutations cause enzyme hyperactivation that leads to continuous cellular growth. Epithelial cells in pancreatic ducts can, driven by cancer-promoting *KRAS* mutations, become a type of malignant tumour called pancreatic ductal adenocarcinoma (PDAC)[3,4].

Generally speaking, *KRAS* mutations alone are insufficient to drive tumour development[3,4]; however, they can act in concert with environmentally mediated tissue injury to accelerate malignant transformation. This occurs by the aberrant regulation of metaplasia (Fig. 1), in which one type of pancreatic epithelial cell (an acinar cell) is reprogrammed temporarily into another sort (a cell similar to a ductal cell). This transition is called acinar-to-ductal metaplasia (ADM), and such an epithelial-cell-state conversion occurs in response to environmental stress[1,5].

The authors sought to understand why mouse pancreatic cells with mutations in the *Kras* gene respond differently to environmental insult compared with cells lacking such mutations. Cells grown *in vitro* do not faithfully reproduce events inside living tissues, so Alonso-Curbelo *et al.* used sophisticated genetic engineering to develop mouse models. These animals enabled the authors to specifically track the fate of pancreatic acinar and ductal cells that had normal or mutant versions of *Kras*, and determine their response to tissue injury mediated by chemical treatment.

Consistent with previous work[3,4], the authors found that the regeneration of damaged pancreatic cells after tissue-injury-mediated ADM was impaired in mice with a *Kras* mutation. Unlike normal mice, those with mutant *Kras* rapidly developed a type of premalignant cellular growth — described as pancreatic intraepithelial neoplasia — that is a precursor to PDAC formation[3].

The rapid emergence of this neoplasia specifically in *Kras* mutant mice after tissue injury led the authors to speculate that aberrant regulation of chromatin (the complex of DNA and histone proteins in the nucleus) might explain how PDAC subsequently develops. To investigate this, Alonso-Curbelo and colleagues examined cells that had normal or mutant *Kras* to assess any genome-wide differences in chromatin accessibility. Accessibility here refers to genomic regions that are in an 'open' conformation that allows DNA-binding transcription-factor proteins to gain access to DNA and regulate the expression of nearby genes.

After injury, cells with *Kras* mutations gained a chromatin-accessibility profile that closely resembles that found in PDAC cells. By contrast, the newly accessible chromatin regions identified in cells with *Kras* mutations remained in a 'closed' conformation in normal pancreatic cells after injury. These data, consistent with findings[6] published this year, suggest that the combination of *Kras* mutation and tissue damage by environmentally