

12. Tsiairis, C. D. & Aulehla, A. *Cell* **164**, 656–667 (2016).  
13. Niwa, Y. *et al.* *Genes Dev.* **25**, 1115–1120 (2011).  
14. Sonnen, K. F. *et al.* *Cell* **172**, 1079–1090 (2018).  
15. Matsuura, M., Tomita, T., Yoshioka-Kobayashi, K., Isomura, A. & Kageyama, R. *Development* **145**, dev156836 (2018).  
16. Matsuda, M. *et al.* *Science* **369**, 1450–1455 (2020).  
17. Sparrow, D. B. *et al.* *Cell* **149**, 295–306 (2012).

18. Lewis, J. *Curr. Biol.* **13**, 1398–1408 (2003).  
19. Sueda, R. & Kageyama, R. *Dev. Growth Differ.* **62**, 59–66 (2020).  
20. Goh, G. H., Maloney, S. K., Mark, P. J. & Blache, D. *Biology* **8**, 15 (2019).

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## Astronomy

# Shock waves spark blazing light from black holes

Lea Marcotulli

Radiation from a jet of ultrafast particles powered by a supermassive black hole suggests that the particles are accelerated by shock waves propagating along the jet, making them shine with the brightness of 100 billion Suns. **See p.677**

Most of the 200 billion galaxies in the Universe are centred around enormous black holes that can weigh as much as one billion Suns. Many of these black holes are dormant, but some are still growing, devouring gas from their surroundings and releasing vast amounts of radiation. Even fewer of these active supermassive black holes are capable of launching powerful jets from their cores – ultrafast streams of particles that shine brightly, and can travel distances of up to 100 times the size of their own galaxy. But what provides the initial kick that enables these particles to release so much energy? On page 677, Lioudakis *et al.*<sup>1</sup> report that the push comes from shock waves that are generated naturally when the rapid particle outflow encounters slower material moving along the jet.

In the early 1960s, a new class of astronomical object known as the quasi-stellar radio source, or quasar, was revealed. As the name suggests, early observations noted that these objects looked like stars. However, something was not quite right: they radiated very brightly at radio frequencies, and their optical spectra contained strange emission lines<sup>2</sup> that are not associated with ‘normal’ stars. It was soon realized that these sources were not stars at all: they were gigantic black holes in the middle of galaxies that were millions, or even billions, of parsecs away from Earth<sup>3</sup>.

The revelation that these black holes could launch such energetic jets from their cores came in the decades that followed, as radio astronomy advanced and the first satellites dedicated to observing emissions in X-ray and  $\gamma$ -ray frequencies were launched. These jets can be thought of as cones, in which charged particles are accelerated close to the speed of light, and release huge amounts of energy in the form of radiation. If a jet is oriented towards Earth, the generating quasar is known as a blazar, and

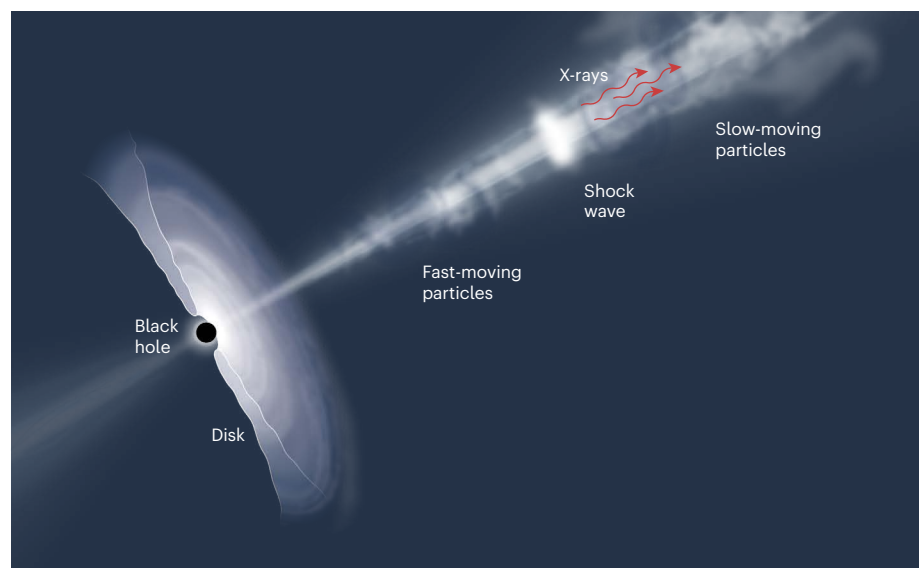
light emanating from the jet can be seen at all possible wavelengths – from radio waves all the way up to  $\gamma$ -rays.

Since the discovery of these jets, much effort has been devoted to understanding how they form. One commonly used technique, known as polarimetry, is based on the wave-like nature of light. In simple terms, polarimetry measures the extent to which the light waves emanating from a source oscillate in the same direction. If the waves all oscillate in random directions – as with light from an electric bulb – the light is not polarized. If, instead, the waves all oscillate

in a specific direction, then the level of polarization is high. For example, the light from a computer screen is strongly polarized in a horizontal direction, and this is why it can't be seen through some polarized sunglasses, which are designed to filter out horizontal oscillations.

The physical process that makes an astrophysical source shine can be determined by looking at the polarization of the light it emits, because different processes result in different levels of polarization. Polarimetry measurements<sup>4,5</sup> have led to an understanding that the light radiating from the jets emitted by active supermassive black holes – from radio frequencies all the way up to X-ray frequencies – is produced by electrons through emission known as synchrotron radiation. This radiation is generated when the path of charged particles travelling close to the speed of light is bent by a magnetic field. As the particles change direction, they lose energy in the form of light, and the light is polarized.

This much has been known for several decades, but our understanding of what makes these particles start radiating away once they have been funnelled into jets has been incomplete. What was needed was an instrument capable of measuring polarization at X-ray frequencies. The Imaging X-ray Polarimetry Explorer, launched in December 2021, has provided just such an instrument<sup>6</sup>. One of the mission's first targets was a very bright blazar known as Markarian 501, which lies a mere 140 megaparsecs away from Earth. This is the first blazar ever observed through the lens of an X-ray polarimeter, and the results reported by Lioudakis *et al.* are dazzling.



**Figure 1 | Particle acceleration in the jet emitted by a supermassive black hole.** Large black holes consuming material from a surrounding accretion disk can launch jets of ultrafast particles that shine brightly enough to be visible from Earth. Lioudakis *et al.*<sup>1</sup> used measurements of the polarization of X-rays coming from one of these jets to determine that the particles were initially accelerated by a shock wave moving out along the jet. Particles lose energy when they move through a shock wave, resulting in the generation of highly polarized X-rays, which were measured by the authors. After moving past the shock, the radiation emitted by the particles becomes progressively less polarized.

The authors took two X-ray polarimetry measurements and, by comparing them with radio and optical polarimetric data, were able to deduce that the initial kick was given to the particles by a shock wave that propagated out along the jet (Fig. 1). Such shock waves occur naturally when particles travelling close to the speed of light encounter slower-moving material along their path<sup>7,8</sup>. Particles travelling through this shock wave lose radiation rapidly and efficiently – and, in doing so, they produce polarized X-rays. As the particles move away from the shock, the light they emit radiates with progressively lower frequencies, and becomes less polarized.

Blazar jets are some of the most powerful particle accelerators in the Universe. Their conditions could never be reproduced on Earth, so they provide excellent ‘laboratories’ in which to study particle physics. Thousands of blazars have now been detected, and at every accessible wavelength, but the mechanisms by which the particles are emitted and accelerated remain elusive. Lioudakis and colleagues’ multi-wavelength polarimetric data provide clear evidence of the particle-acceleration mechanism in Markarian 501, making the authors’ results a turning point in our understanding of blazars.

This huge leap forward brings us yet another step closer to understanding these extreme particle accelerators, the nature of which has been the focus of much research since their discovery. X-ray polarimetry will now enable us to study several of these jets to understand whether these shocks are common to all sources. The next big unknown is whether electrons alone produce all the light that we see coming from blazars – up to the highest  $\gamma$ -ray frequencies – or whether other charged particles (such as protons) also make them shine<sup>9</sup>. Solving this puzzle will be a milestone for the field, and X-ray polarimetry will no doubt have a crucial part to play in finding the answer.

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1. Lioudakis, I. *et al.* *Nature* **611**, 677–681 (2022).
2. Hazard, C., Mackey, M. B. & Shimmins, A. J. *Nature* **197**, 1037–1039 (1963).
3. Schmidt, M. in *Quasi-Stellar Sources and Gravitational Collapse* (eds Robinson, I., Schild, A. & Schucking, E. L.) 455 (Univ. Chicago Press, 1965).
4. Jorstad, S. G. *et al.* *Astron. J.* **130**, 1418–1465 (2005).
5. Marin, F. *Mon. Not. R. Astron. Soc.* **479**, 3142–3154 (2018).
6. Weisskopf, M. C. *et al.* *J. Astron. Telesc. Instrum. Syst.* **8**, 026002 (2022).
7. Marscher, A. P. & Gear, W. K. *Astrophys. J.* **298**, 114–127 (1985).
8. Tavecchio, F., Landoni, M., Sironi, L. & Coppi, P. *Mon. Not. R. Astron. Soc.* **480**, 2872–2880 (2018).
9. Böttcher, M., Reimer, A., Sweeney, K. & Prakash, A. *Astrophys. J.* **768**, 54 (2013).

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Cancer

# A spatial perspective on bacteria in tumours

Ilana Livyatan & Ravid Straussman

Bacteria are frequently present in human cancers. The use of state-of-the-art methods for tumour analysis that capture spatial information and single-cell molecular profiles paves the way to clarifying the roles of these microorganisms. **See p.810**

By gathering highly detailed ‘portraits’ of tumours, on page 810, Galeano Niño *et al.*<sup>1</sup> identify the locations of tumour-associated bacteria. The findings reveal how these bacteria interact with various cell types in the tumours.

A cancer and the associated components that surround it, termed the tumour micro-environment (TME), form a tissue ecosystem consisting of a variety of cells, including immune cells, along with structures such as blood vessels and the extracellular matrix<sup>2</sup>. Many of these constituents affect tumour growth and the tumour’s response to treatment, and are thus the focus of a rapidly growing field of study<sup>3,4</sup>. However, these studies have typically been host-centric, even though

**“The presence or absence of bacteria correlated with certain characteristics of cancer cells and immune cells.”**

organisms such as bacteria, viruses and fungi (the microorganisms that constitute the human microbiome) have been detected in the TME of a wide variety of tumours<sup>5–9</sup>. These previous studies<sup>5–9</sup> of the intratumoral microbiome have characterized its microbial profiles, uncovered their tissue-specific nature and indicated that microbes are located mostly intracellularly<sup>5</sup> in both cancer cells and immune cells.

Over the past decade, discoveries about how the human microbiome affects tumour biology<sup>10,11</sup> have resulted in the presence of intratumoral bacteria being designated a hallmark of cancer<sup>12</sup>. Yet our understanding of these bacteria is still rudimentary. This is partly because of a lack of tumour-microbiome studies that pinpoint precise bacterial locations in the tissue and reveal cellular contexts. Galeano Niño and colleagues used cutting-edge spatial and single-cell research methods to advance such investigations.

The authors focused on two types of tumour – oral squamous cell carcinoma and colorectal cancer – for which some cancer-promoting mechanisms mediated by microbes have been described<sup>13</sup>. Galeano Niño and colleagues split each of 11 human colorectal tumour samples into 4 pieces of tissue, and then subjected the tissues to an approach called 16S ribosomal DNA (rDNA) analysis. This revealed that, for seven of the tumours, the microbiome was heterogeneous across the four different pieces. The authors used various methods to explore this bacterial variation and to examine how it correlated with factors in the host.

Applying a technique called RNAscope, which allows visualization of RNA molecules in individual cells, the authors assessed the distribution of specific bacteria, such as *Fusobacterium* (a microbe thought to have a tumour-promoting role), and of bacteria in general, in tumour slices. This information guided the selection of areas of tissue that contained or lacked bacteria, and the selected areas were the focus of subsequent analysis. These regions were further subdivided using microscopy analysis into compartments that consisted of mostly tumour cells or mostly immune cells. The selected regions were also analysed using a technique called GeoMX digital spatial profiling. In this approach, 77 antibodies were used to detect immune-cell-related proteins, proteins characteristic of particular cell types and proteins involved in major cancer-associated signalling pathways. To capture a genome-wide picture of the tissue gene-expression repertoire, the authors used 10X Visium spatial transcriptomic technology, which profiles RNA transcripts while retaining information about their spatial location.

Although both GeoMX and 10X Visium technologies can characterize minute sections of tissue (microniches), they cannot achieve resolution at the single-cell level. As a step in this direction, the authors developed an RNA-sequencing method that they called INVADeseq, which enables human transcripts to be sequenced alongside bacterial rDNA