MICROBIOLOGY TODAY

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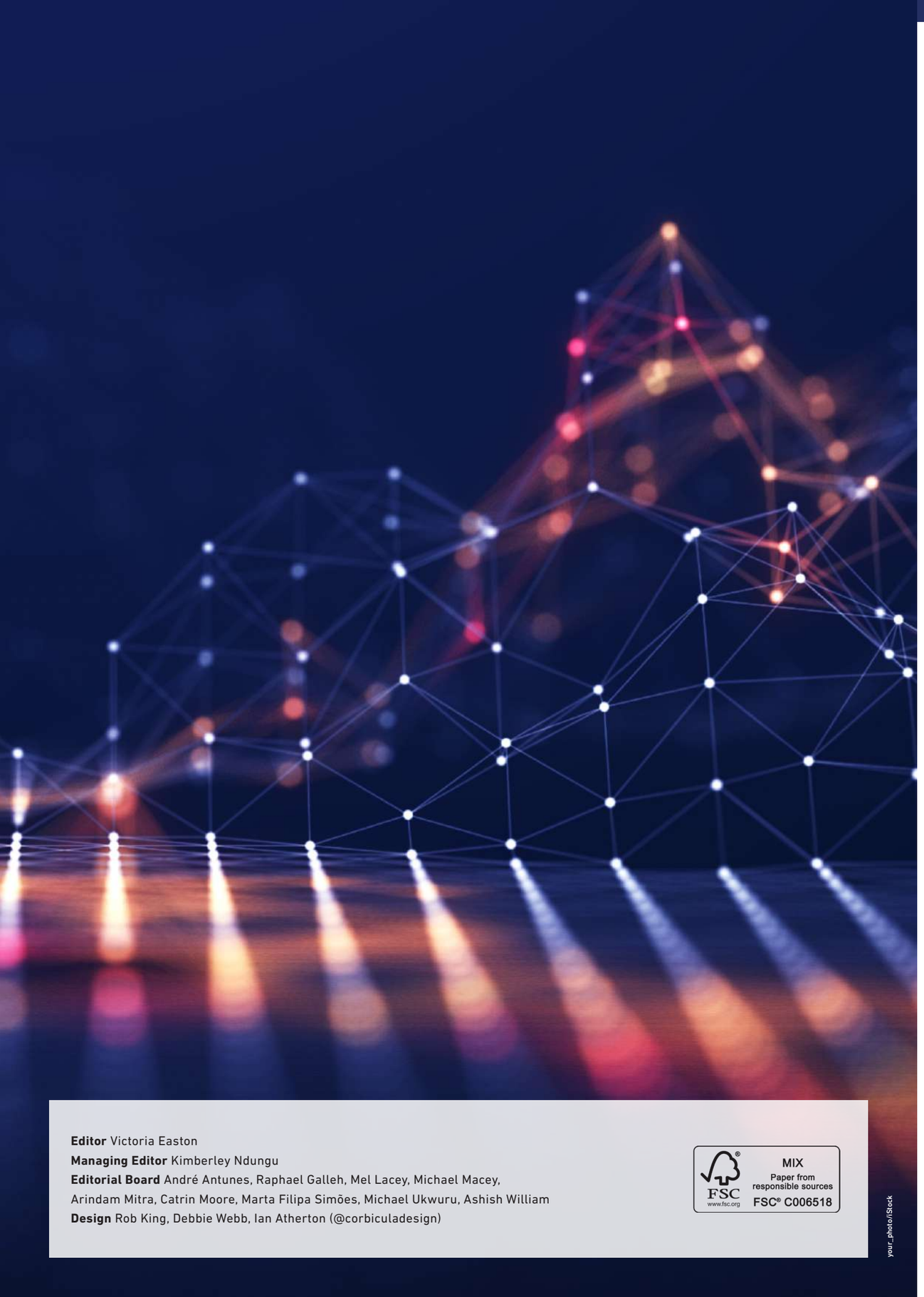
Emerging Threats

From climate change to artificial intelligence, in this issue explore a wide range of threats being faced by microbiologists and the wider community.

MICROBIOLOGY SOCIETY



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From the Editor

"In our first issue of 2024, we have a focus on 'Emerging Threats'."

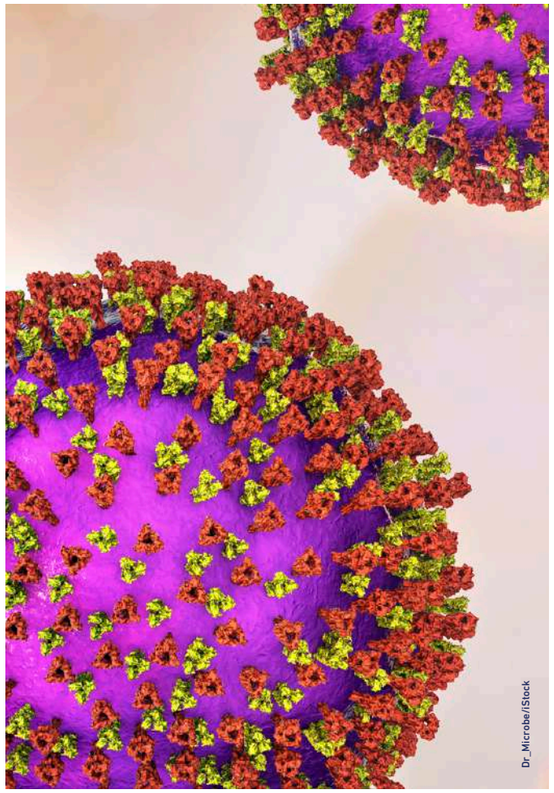
Writing my first editorial is a little daunting. The process to bring you all this issue has been a steep learning curve, but I have been supported the entire way by a fantastic team at the Microbiology Society and I am truly impressed at the generosity of a very diverse range of authors. It really has been a real pleasure to work so closely with you all. A special mention must go to Chris Randall. He did a stellar job as Editor of this magazine and gave a platform to so many fascinating voices – I only hope that I can continue this in my term as Editor.

I see 2024 as a year of change for *Microbiology Today*; with a new Editor, new online format, and the news that we will be evolving as of 2025. The move away from two dedicated issues a year, towards more flexible monthly magazine-style content that will be published on the Society's journal website is something that I feel, and the Editorial Board agree, is more responsive and meets the needs of our community better. As our readers know, the Society is a not-for-profit publisher which reinvests into the community, for the benefit of all. As well as increasing the reach and impact of our members, research, this new route to publish will help the Society demonstrate how it offers a variety and diversity of article types – away from the traditional research paper – which are open to microbiologists at all career stages, wherever they are in the world, and add to their publication record.

You can learn more about the benefits of this transition online (**microb.io/3VqSt0z**).

In our first issue of 2024, we have a focus on 'Emerging Threats'. The past few years have taught us all the power of preparedness, and that starts with looking towards the horizon. The first featured article in this issue is from Lucy Nixon from Cyber Security Partners. Lucy leads us through the threat posed by artificial intelligence, specifically generative AI. The possibilities posed by AI are huge, Lucy shows us the specific threats posed to science and poses the question many of us are thinking – "should we be worried?"

Our second featured article continues horizon-scanning for potential threats with Jessica Swanson from the University of Leeds outlining the growing dangers of measles. With cases growing due to falling vaccination rates globally, Jess explains how one of the most infectious viruses currently known is growing into an emerging threat despite an effective vaccine.



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Our final featured article comes from Leen Delang, Grace Roberts, Judith White and Stephen Polyak. This global team, which represents four different institutions (KU Leuven, University of Leeds, University of Virginia and the University of Washington), give us a whistlestop tour of the risks of mosquito-borne alphaviruses. With epidemics being driven by the growing reach of these mosquitos, the risks of alphavirus infection also grow. To combat these infections, this team propose leading with a combination drug strategy involving re-purposed drugs. An approach which could maximise positive synergistic effects and reduce the potential for antimicrobial resistance developing.

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From the President

"Welcome to the May 2024 edition of *Microbiology Today*."

It was fantastic to see so many of you at Annual Conference in Edinburgh this year. The breadth of microbiology was outstanding, and I know from the feedback you gave me how much you enjoyed the experience.

In this edition, our members highlight some of the very real challenges faced by microbiologists and wider society. Every day, you, the Microbiology Society community, go to your place of work and try to find solutions to these very real threats. Here we hear from just some of these voices.

One challenge the Society has been actively working on is the topic of its project 'Knocking Out Antimicrobial Resistance'. Launched last year with a special issue of *Microbiology Today*, it has progressed significantly, with a series of workshops in January involving over 100 participants from truly cross-disciplinary backgrounds and which were dedicated to the project's priority solution areas: diagnostics, surveillance, therapeutics and vaccines. More than 600 people have now signed up to get involved, and you can find out more at our Knocking Out AMR hub online.

The Society is doing what it can to reduce the impact of other challenges. In 2024, it has adopted a digital first policy: those of you who have attended a Society conference will know that programmes are now only available online and, as announced last year, both issues of *Microbiology Today* in 2024 will be published digitally, allowing readers everywhere to enjoy the content. As the first that ends up in inboxes rather than on doorsteps, I hope that there will be a wider variety of readers of this edition of *Microbiology Today* than ever before.

You may also have seen our news story that October's *Microbiology Today* will be the last in a traditional magazine format as we aim to expand the reach, influence of and engagement with our members' research work, at a time of rapid change across the scientific publishing landscape. From 2025, there will be a new home for magazine-style, member-authored content on our journals website. This serves several important purposes which our new Editor, Victoria Easton, has written about in her editorial; if you would like to know more, you are very welcome to get in touch with the Society team.

I believe this is an incredibly exciting opportunity to recognise the work of members of all career stages on an international platform, increasing the reach and impact of that content and, ultimately pushing forward the Microbiology Society's vision of advancing the understanding and impact of microbiology by connecting and empowering communities worldwide.

If you are new to the Society, welcome. If you are a well-seasoned member with years of *Microbiology Today* copies on your shelves, welcome back. I hope that you enjoy hearing from your community.

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From the Chief Executive

As Vikki says in her editorial on page 1, this issue's theme of 'emerging threats' encompasses a range of different scenarios – new infectious diseases, a resurgence of old ones, or the risks associated with wholly new technologies like some forms of artificial intelligence (AI).

It might be said that the biggest emerging threat to the Microbiology Society as an organisation in its current form is the global change in the business model of scientific publishing, which means that our income is falling.

But although the commercial changes to the way scientific research is published are certainly a massive challenge, it would be wrong to see them merely as an emerging threat for two reasons.

First, the evolution of publishing is no longer 'emerging' – it has well and truly emerged, and we are living in a changed world where most of our content is already published in a fully Open Access way and two further journals will make the shift on 1 January next year. That's the deadline when most European funders will refuse to allow researchers to use their money to publish in titles that do not meet Open Access criteria.

The other reason why it is wrong to define these important changes as a threat is because that is only half the story – they also open up all sorts of opportunities. It is undeniably true that as the Microbiology Society's income falls, the coming period will be financially very challenging. It is entirely possible that we may not be able to do everything we want for the next few years. But faced with a situation like this, we can respond in one of two ways – we can decide to accept decline, or we can come out fighting and carve out a new successful business model that allows the Society to carry on supporting our community, as we have been doing for nearly eight decades. I'm delighted that the trustees have opted for the second approach: to be on the front foot.

Increasingly, members of our community understand that publishing your research with the Microbiology Society does not just mean getting your science into a journal with internationally robust and respected peer review as a mark of quality, it also means contributing directly to the support that we give via conferences, grants, professional development events, prizes and all of the resources we make available to the community. Publishing in *Microbiology*, *Journal of General Virology*, *Journal of Medical Microbiology*, *Microbial Genomics*, *Access Microbiology* or the *International Journal of Systematic and Evolutionary Microbiology* is a way for you to support your community and ensure that despite the financial threats we face as the publishing landscape changes, we can continue to take advantage of all the opportunities that come when the Microbiology Society brings the community together.

Meeting these threats and seizing these opportunities means that you are starting to see several changes to our activities, ranging from the delivery of our communications to the way we administer grants and how we organise events. The President wrote to you all in April to describe how the Society's governing Council is getting to grips with the situation by ensuring the organisation's governance is fit for the future. What you will not see among these changes is any alteration in the Society's values. When our visionary founders first met to discuss forming a new Society, they felt very strongly that it should be welcoming to all scientists who were interested in microbes. The brilliant Muriel Robertson put it succinctly when she said nobody should feel they 'are only allowed in at the back door'.

As we adjust to the new funding model of scientific publishing – looking to ensure that all over the world people have access to our journals, and seeking out new and innovative ways of generating the income to support your efforts in advancing microbiology – that founding principle runs through everything we are doing.

So the massive upheaval in our finances could certainly be described as an 'emerging threat', but we prefer to see it as an opportunity to deliver what the first President said at our first ever meeting in 1945, when he announced that the Microbiology Society would be 'a great society'.

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The Natural Selection of Corals in the Face of Climate Change

Robert A. Quinn

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In this piece, Robert A Quinn, delves into the complex dynamics of coral bleaching, symbiotic preferences and the uncertain future of these invaluable ecosystems.

Scleractinians, which comprise the tropical reef-building corals, have been found in the fossil record for at least 240 million years [1, 2]. Surely then, these complex symbiotic organisms have encountered rising and falling ocean temperatures throughout their evolution. Perhaps never before, however, have they experienced warming oceans at such a rapid rate, due to anthropogenic-driven climate warming, which is threatening the future of coral reefs.

Corals are true symbionts, a eukaryotic Cnidarian organism hosting a dinoflagellate alga within its cells. The coral receives nutrients and fuel (believed to be primarily sugars) from algal photosynthesis, while the algae receive much-needed safe harbor and a place to thrive in the nutrient-deplete tropical seas. When water temperatures on tropical reefs begin to rise, it puts stress on this intricate symbiotic relationship, which can lead to a phenomenon called 'coral bleaching'. Bleaching occurs where the algae are expelled, leaving behind their Cnidarian host as a white-coloured shell of itself. Corals can survive and recover from bleaching, but the more severe and prolonged events can cause significant mortality, which has occurred worldwide in recent decades [3].

An interesting aspect of the coral–dinoflagellate symbiosis is the preference for coral hosts to choose particular algal symbionts over others [4, 5]. Even within the same coral species on the same reef, different coral colonies host different symbionts [6]. This has significant consequences for the outcomes of bleaching because it has long been known that some algal lineages are thermally tolerant, where others are more susceptible to thermal stress [4, 5, 7]. This is exemplified in the dominant coral species on the island of Oahu in Hawai'i, *Montipora capitata*. Colonies of *M. capitata*, even those physically adjacent, can host dinoflagellates from the genera *Cladocopium*, *Durusdinium*, or a mix of the two [6, 8]. Interestingly, those corals hosting *Cladocopium* symbionts readily bleach when water temperatures rise above their bleaching threshold (approximately 30°C depending on water and light conditions). *Durusdinium*-hosting *M. capitata* are more robust and can resist bleaching events even in the most extreme cases, such as the worldwide coral bleaching event observed in 2015 and 2016, driven at least in part by a strong *El Niño* southern oscillation compounding the effects of anthropogenic climate warming [9, 10]. Why then would a coral choose the *Cladocopium* symbionts at all? Is the future of *M. capitata*, and perhaps other corals in Hawai'i and across the Pacific Ocean, one dominated by a *Durusdinium* symbiosis? Perhaps most concerningly, some coral species on the Hawai'ian Islands and other reefs worldwide do not associate with thermally tolerant dinoflagellates, bringing into question their sustainability in a future of even warmer tropical seas.

The bleaching responses of Cnidarian–dinoflagellate symbioses observed in real time by scientists worldwide, especially in the past year during another strong *El Niño* event, are foreshadowing the perilous future of coral reefs. There is hope, however, as corals show the ability to select a symbiont of choice (or perhaps the algae chooses its host vice versa), and evolutionary selection mechanisms may drive a more robust symbiosis in warmer seas. But whether this process of 'natural selection', and the forces of Darwinian natural selection that act upon it, will occur fast enough is still in question. The future of one of nature's most magnificent and valued environments may depend on it.

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Emerging issues in biodefence

Tim Inglis

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Evolving threats

The white powder incidents of 2001 were a watershed moment in biodefence. In the years that followed, we woke up to the need for skills that were shelved at the end of the Cold War. Chemical, biological, radiological and nuclear (CBRN) weapon countermeasures were back in fashion, but the adversary was different. No longer was this the preserve of superpowers and their allies. It had become a more complex conflict with non-state actors, terrorist organisations and extremist groups. In the following two decades, many countries strengthened their civil and military biodefence, adding biosecurity, biopreparedness and surveillance functions to the public health remit [1]. The capability developed by public microbiology services in the USA in 2001 was driven by the need for rapid *Bacillus anthracis* rule-out tests, with chain-of-evidence protection for subsequent forensic analysis. The pathogen repertoire increased slowly to include other familiar threat agents from the Cold War biological weapons list. Greater emphasis was placed on early detection by first responders and hazard management agencies to ensure prompt response, and recruitment of specialist capability as required. Though chemical in nature, the Novichok incident in Salisbury, UK, was an example of how such a tiered hazard response works [2].

Rising complexity

The list of potential bioweapon agents continued to grow until 2020, when all eyes diverted to the emerging COVID pandemic. During the pandemic, the United States recognised the need for a review of biodefence measures in response to increasingly complex major biothreats. Their major conclusions are in the public domain and provide a short list of near-term priorities [3]. A key to the new biodefence risk environment is that the former preoccupation with a short list of dangerous pathogens, subject matter experts and approved response agencies working in isolation doesn't address the changing threat. The plan argues the need for better inter-agency cooperation, information sharing and collaborative work to deal with complex threats that may be hybrid in nature, involve genetic manipulation and possible backup by applied artificial intelligence. The ability to quickly and easily edit microbial genomes using CRISPR-Cas and other emerging technologies puts bioweapon construction within reach of an expanded range of persons with intent to harm others, highlighting a need for better regulation [4].

The COVID-19 effect

Despite this gloomy biodefence forecast, human-initiated biothreats are a lower priority than the predictably unpredictable emerging infections nature throws at us. A recurrent theme in the post-pandemic literature is the lesson learned from more than three years of pandemic countermeasures [5]. The scale of the SARS-CoV-2 threat put microbiology in the news and gave us a seat at the top table for a while. In the immediate aftermath, the extended professional network allows us to speak science to those in power. That window of opportunity will not last indefinitely and should be used strategically to advocate for public health microbiology as a key component of the response to emerging infection threats, whether deliberate acts or naturally occurring. In Western Australia, we prepared for the imminent arrival of COVID, securing research funding to develop adaptive diagnostics for emerging pathogenic threats (Project ADEPT). That work ranged from point-of-care COVID test development [6], to speeding up detection of antimicrobial-resistant bloodstream infections [7].

Watching the watcher

An emerging issue in biodefence is that of ethics and governance. One of the enduring concerns is that a disgruntled biodefence scientist may choose to unleash a dangerous pathogen on an unsuspecting public, or disclose gain-of-function experimental results to an extremist group [8]. As bad people will continue to do bad things, even if the science is good, the era of self-policed laboratory science has come to an end. The lone ranger researcher is fading from view. Transparency, disclosure, compliance audit, credentialling and external governance all have a place in the biodefence toolkit.

Trusting the data

A final emerging issue is the application of data science to biodefence. The COVID pandemic showed us how disease data could be used and, for that matter, abused. Indeed, it is likely public health disinformation was used to disrupt the MMR vaccination programme in Ukraine in 2015, resulting in a massive measles epidemic [9]. Data visualisation techniques can be used to good effect by presenting real-time disease risk in an accessible non-expert format to improve inter-agency communications [10]. It is becoming clear in the post-pandemic lull that a key obstacle to using artificial intelligence is trust. If we can develop trustworthy automated algorithms to do the baseline infection surveillance tasks, then we will be better placed to concentrate human effort on the unprecedented existential threat.

Competing interests. The author declares no competing interests

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Biography

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AI and Microbiology: Pioneering Responsible Discovery in the Modern Age

Nicole Wheeler

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Nicole Wheeler, a Research Fellow at the University of Birmingham, UK, explores the transformative potential of AI in unraveling the mysteries of microbial life.

Unlocking the microscopic world with AI

In an era where artificial intelligence (AI) is reshaping landscapes from finance to healthcare, its impact on microbiology is poised to create a revolution of its own. By augmenting human capabilities and pioneering new knowledge frontiers, AI is not just an enabler of research; it is also becoming a partner in the quest to understand the underpinnings of microbial life.

Microbes, despite their critical roles in ecosystems, human health and the economy, remain a vast and mostly uncharted territory. Their complex nature and diversity have long challenged scientists, but AI's prowess in managing and interpreting massive datasets could light the way forward. From decoding genetics to mapping behaviours and interactions, AI is accelerating our journey into the microbial world.

From sequences to solutions: AI's transformative impact

AI's potential to predict functions from genetic sequences could unlock the secrets of microbial life, offering glimpses into the unknown functions of countless genes. This insight is vital for understanding the dynamics of microbial communities, their interactions with hosts and their environmental impacts. Moreover, it is paving the way for breakthroughs in healthcare, from proactive vaccine development to the discovery of novel antimicrobials and the enhancement of our microbiomes for disease prevention.

However, the integration of AI into microbiology is not without its challenges. The technology's knack for identifying patterns can sometimes obscure the causal relationships vital for scientific discovery. Yet, advancements in AI, like those improving our grasp of protein structures and automating genetic studies, are bridging these gaps, linking genomic sequences to microbial functions with unprecedented precision.

Navigating ethical terrain

The rise of AI in microbiology brings to the fore significant ethical considerations. The manipulation of microbial life via AI could lead to unintended consequences, posing risks to public health, biosecurity and ecosystems. The potential for misuse by malicious entities adds a layer of urgency to the discussion on the ethical use of AI in biological research.

In this light, the scientific community and AI developers are called to a higher standard of responsibility. Maintaining public trust, as was crucial during the advent of genetic engineering, is paramount. This requires transparent communication about AI's role in microbiology, highlighting both its benefits and the measures in place to mitigate risks. Engaging with a broad spectrum of stakeholders – scientists, ethicists, policymakers, and the public – is essential to navigate these ethical landscapes thoughtfully.

Vision for the future: ethical, informed and united

The fusion of AI and microbiology holds the promise of unprecedented scientific discoveries, offering solutions to some of humanity's most pressing challenges. Yet, realising this potential demands vigilance, ethical commitment and a proactive stance on safeguarding against risks.

As we stand on the brink of this new era, the journey ahead is as much about navigating ethical terrain as it is about scientific exploration. The collaboration between the scientific community and AI developers will be pivotal in steering this course, ensuring that the integration of technology and biology leads to a future where both can thrive.

By fostering an environment of responsible innovation, we can unlock the full potential of AI in microbiology, paving the way for discoveries that respect our ethical boundaries while expanding our knowledge of the microbial world. The future beckons with the promise of solving mysteries that have long eluded us, guided by the principles of responsibility, ethics and collaboration.

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Microbiology Society Microbiome Safety Workshop

In January the Microbiology Society ran a two-day workshop on microbiome safety and how to ensure that microbiome-modulating products are safe and effective in the future. This was an excellent couple of days featuring lots of discussions from academics, investors, industry and regulators.

Microbiomes have been modulated for a long time, such as by changing diet and affecting the gut microbiome [1, 2] or by the application of cosmetics on the skin microbiome [3]; however, there remains a lack of knowledge on the long-term effects of modulating microbiomes and therefore a gap around how to ensure safety. With increased research and public interest in the microbiome, more products are being created for 'targeting the microbiome', and it is important for consumers and manufacturers that these are both safe and can fulfil the claims.

One of the main challenges around safety and the microbiome is that microbiomes are very diverse; for example, in the oral microbiome, the goal is to disturb dental biofilms, and leaving the microbiome without intervention can lead to disease [4]. Additionally, within a microbiome, there can be very different environments; for example, different areas of the skin may be dry or oily. This makes it challenging to come up with generalised guidance that applies to these distinct environments. Furthermore, there is currently no definition of a 'healthy' microbiome. What is healthy in my gut, is not necessarily healthy for someone else. Whilst there are differences in the microbial makeup of each microbiome, there may be some functional overlap, which could be measured to ensure that a product is not impacting the beneficial functions of a microbiome, such as butyrate production for the host [5].

Modulating the microbiome may lead to currently unidentified off-target effects, and therefore efforts to determine safety should also include assessing these effects. At the workshop, it was generally agreed that if the host is not being negatively impacted (such as an increase in inflammation, for example), a change in microbiome makeup may be acceptable. Ultimately, when determining the safety around microbiome-based products, there should be a risk analysis framework that helps to identify any short-term and long-term safety risks in both healthy and vulnerable populations. This allows researchers to measure these risks and determines if these risks are acceptable when weighed against potential benefits of the product. Measuring long-term risk is particularly challenging in humans, and retrospective studies may be useful to address this. Additionally, using a citizen science approach could be powerful, where an optional pharmacovigilance scheme for microbiome products could allow for the tracking of long-term causal effects, especially if many people participated in it.

It was great to be a part of this Society-led workshop, in partnership with Unilever, and to hear from such a diverse range of backgrounds about what microbiome safety means to them.

The main messages from this workshop will be shared with the scientific community more formally soon in one of the Society journals – *Microbial Genomics* – and this will enable the field to begin to outline best practice for measuring microbiome safety. Moving forward, the organisers of the workshop hope to build upon these discussions and include safety with respect to other members of the microbiome like fungi and viruses, and other microbiomes such as the lung/vagina, and they are interested in hearing from anyone interested in collaborating; please get in touch at **info@microbiologysociety.org**.

The workshop was co-organised by Professor Lindsay Hall (University of Birmingham), Dr Aline Metris (Unilever's Safety and Environmental Assurance Centre), Dr Gabriela Juarez Martinez (Innovate UK-KTN), Dr Jay Tiesman (P&G) and by the Microbiology Society.

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The Complex Landscape of Emerging Fungal Challenges in Public Health

In this piece, *Journal of Medical Microbiology* Editor and public health researcher, Lysangela Alves, examines the landscape of emerging fungal challenges.

Fungal infections remain a significant challenge in clinical and public health settings, presenting a growing threat to global well-being. While bacteria and viruses are often in the spotlight, fungi quietly infiltrate communities, causing infections ranging from superficial skin conditions to life-threatening systemic diseases. In recent years, the medical community has become increasingly alarmed by emerging fungal threats, demanding heightened attention, research and practical strategies for prevention and treatment.

Understanding the dynamics of fungal threats

Fungi are ubiquitous in our environment, and most are harmless to humans. However, certain species have evolved to exploit weaknesses in the human immune system or adapt to medical interventions, leading to infections that are difficult to treat. As the use of immunosuppressive therapies, broad-spectrum antibiotics and invasive medical procedures becomes more common, the risk of fungal infections escalates. In addition, treating such infections relies heavily on only four classes of antifungal drugs: polyenes, azoles, echinocandins and the pyrimidine analog 5-flucytosine.

Data from the Global Action Fund against Fungal Infections (GAFFI) indicate that more than 300 million people worldwide suffer from severe fungal infections annually, resulting in around 2 million deaths annually (**gaffi.org**). These statistics are comparable to those observed for malaria and tuberculosis, which cause 1.2 and 1.4 million deaths yearly, respectively [1].

The spread of drug-resistant fungi in nature and healthcare settings has prompted international funding bodies to address antifungal resistance. Public health agencies worldwide, such as the GAFFI and the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), recently started programmes to address the fungal threat, which includes antifungal resistance, emphasising a comprehensive One Health framework. The World Health Organization (WHO) launched a pilot *Candida* surveillance scheme in 2018, which was later included in the Global Antimicrobial Resistance Surveillance System GLASS (**www.who.int/initiatives/glass**). In 2022, the WHO launched the WHO Global Fungal Priority List (FPPL) initiative, representing the first worldwide initiative to systematically prioritise fungal pathogens, acknowledging their unmet research and development (R&D) needs and perceived significance in public health. The primary goal of the FPPL is to concentrate efforts on research and policy interventions, fortifying the global response to fungal infections and antifungal resistance. Centred on various factors such as antifungal resistance, deaths, evidence-based treatment and access to diagnostics, the critical threat organisms identified were *Cryptococcus neoformans*, *Candida auris*, *Aspergillus fumigatus* and *Candida albicans*. Seven fungal species were identified as high-priority pathogens, and another eight were categorised as medium priority [1].

Research and innovation

Investment in research and innovation is paramount in addressing emerging fungal threats. A better understanding of fungal biology, genetics and pathogenesis can lead to more effective diagnostics, treatments and preventive strategies. Collaborative efforts between clinicians, researchers and the pharmaceutical industry are essential to generate knowledge and products to accelerate progress in this field. Public health workers, politicians and the public are also essential for advancing policies to address fungal threats. For instance, the challenges of developing antifungal drugs are evident due to the high costs, time and risks associated with the process. For example, the development of Cresemba (isavuconazole) took 13 years and around US $130 million.

Nevertheless, a newly approved drug, ibrexafungerp, works through the non-competitive inhibition of β-1,3-D-glucan synthase. In addition, new antifungal classes are currently in late-stage clinical development: fosmanogepix inhibits the GWT1 protein, which is involved in cell wall localisation of GPI-anchored mannoproteins); olorofim, being developed for invasive infections, inhibits dihydroorotate dehydrogenase enzyme (DHODH), involved in pyrimidine biosynthesis; opelconazole is a triazole being designed for inhalation; and rezafungin is from the echinocandin family) [2]. As we cannot separate environmental settings from human health, the extensive antifungal use in agriculture and animal husbandry directly affects One Health. For example, in agricultural settings, widespread antifungal applications on crops are responsible for high rates of azole-resistant *A. fumigatus* infections [3]. These drugs share structural similarities with medical triazoles and are used indiscriminately worldwide, leading to environmental contamination. Like olorofim, DHODH-targeting compounds are in advanced development as herbicides, and their application in agriculture is expected to drive resistance in human fungal pathogens. While removing azoles or other human-biosimilar antifungals from agriculture is challenging due to their impact on global food production, there is an urgent need for a divergence between fungicides for agriculture and antifungals for pharmaceutical use.

Conclusion

The increasing prevalence of emerging fungal threats poses a multifaceted clinical and public health challenge. As these infections become more resistant and widespread, it is essential to prioritise research, raise awareness and implement strategies for prevention and treatment. The collaboration of global health organisations, governments and the scientific community is essential to mitigate the impact of fungal infections and safeguard the well-being of individuals and communities worldwide.

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Champions Q&A with Blanca Perez-Sepulveda and Arindam Mitra

We spoke to two of our Champions – Blanca Perez-Sepulveda from the University of Liverpool, UK, and Arindam Mitra from Adamas University in Kolkata, India – about the emerging threats associated with lack of international collaboration and why this is so important.

Where are you currently based and what is your role?

Blanca: I work as a Postdoctoral Research Associate at the University of Liverpool, UK.

Arindam: I am the Department Head and Professor of Biological Sciences at Adamas University located in Kolkata, India. As the departmental head, I am responsible for overseeing both the academic and administrative duties of the department, with the help of exceptional colleagues and staff. My area of research focuses on infectious diseases, biofilms and vaccine development. We are currently developing an eco-friendly plant-based strain. My long-term goals are to enhance teaching and research standards and to foster an interactive and collaborative learning environment for students and learners.

Why did you decide to become a Microbiology Society Champion?

Blanca: I joined the Microbiology Society as a PhD student and have experienced the impact the Society has on its members and the wider community. I have seen the Society's commitment to changing culture, which motivated me to get more involved.

Arindam: My strong interest in and passion for microbiology aided me in my decision to take on the role of Champion to actively support and promote the field's advancement. In my experience, the Champions Scheme offers a fantastic opportunity to organise events locally and internationally, and by supporting these events, the Scheme facilitates collaboration and network among scientists and Society members, which is important to me. Organising these events/talks has also given me a chance to improve the awareness of the role of microbes and the field of microbiology in diverse fields. For me, volunteering for the Society is a means of giving back to the microbiology community.

You have led an international project, could you tell us more about this project and how/why you got involved with it?

Blanca: The 10,000 *Salmonella* Genomes (10KSG) project was funded by the Global Challenges Research Fund (GCRF), to sequence isolates from Low- and Middle-Income Countries (LMICs). The project required establishing collaborations with colleagues in research and reference labs from various countries, which initially caught my interest. I joined my current lab when funding for the 10KSG project had just been secured and I quickly started taking the lead as I got more involved. I realised that my mother tongue was valuable for connecting and creating strong collaborations with colleagues in Spanish-speaking countries.

Arindam: I have been involved with multiple international collaborations, some with other international members and some with Champions of the Society. One such collaborative effort was Champions Talk, a series of international webinars with Microbiology Society Champions during the pandemic. Society Champions delivered the talks, whilst the Department of Microbiology at Adamas University, India, hosted the webinar. This webinar series convened Microbiology Society Champions to exchange their research findings, pedagogy and experience in the discipline of microbiology and other allied fields.

Why do you think collaborating internationally is important?

Blanca: International collaboration opens the possibility of understanding the global picture; although we generally focus research on a particular micro-organism in a defined environment, nothing happens in isolation, and there are not only physical and chemical variables but also a cultural and economic background. By fostering international collaborations, we can place biological research in a wider context and take the action needed to change, rather than to solely collect data points.

Arindam: Collaborating internationally is important because it brings together different scientists with diverse perspectives, knowledge and skill sets, which is crucial to address/solve global health challenges, such as antimicrobial resistance or a pandemic like COVID-19. The Microbiology Society also developed the initiative 'Knocking out AMR' which brings together experts with a variety of skills to formulate strategies on diagnostics, surveillance, vaccines, therapeutics and policies for antimicrobial resistance. I believe that international collaboration can create new opportunities, innovation and sustainable solutions.

Do you think there are risks to a lack of international collaboration?

Blanca: In recent years, during the COVID-19 pandemic, we have first-hand experience of the power of international collaboration. Without international collaboration, there is a great risk of delayed detection and inadequate response to pathogens, as well as slow scientific innovation and higher economic costs.

Arindam: Yes. A lack of or limited international collaboration can impair or halt research on issues that require international cooperation. A lack of international collaboration can also halt exchange of ideas and innovation, where integrating perspectives of both local and international scientists can impact or make a difference to our economy and bring peace among countries.

What advice would you give to other microbiologists looking to get involved with international collaborations?

Blanca: I would encourage anyone wanting to engage with colleagues in other countries to be conscious of the kind of collaboration that will be established and agree to the terms at the beginning to avoid the collaboration being unintentionally one-sided. I think it is fundamental to value local knowledge and experience, consider the cultural, social and economic context of all parties, be honest and manage expectations based on what is feasible.

Arindam: International collaboration offers numerous potential opportunities for microbiologists, especially in the advancement of innovative solutions to global challenges. Such associations can facilitate networking, development of research projects, organising events, training and scholarly publications. As the Microbiology Society's Annual Conference brings together an international gathering of microbiologists, industry professionals, researchers and other experts in the field of microbiology, participation in the Annual Conference can also help networking with peers and international experts. By volunteering for various events, schemes and activities at the Society, international collaborations with fellow microbiologists can be facilitated.

GET INVOLVED

Interested in expanding your network and championing the importance of microbiology? Get involved! The next round of recruitment for the Champions Scheme will take place from 2 September to 31 October 2024. More details are available on our Society Champions webpage: microb.io/3wDD7eC.

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Artificial Intelligence: Should You Be Worried?

Lucy Nixon

Artificial intelligence – generative AI (GenAI) in particular – leapt into the public consciousness with the launch of ChatGPT. As with all revolutionary technology, people responded either with great enthusiasm or with deep concern, pointing to what could go wrong – everything from job losses to the end of the world.

Undoubtedly, AI is already making changes to the way that people work, and many, if not most, big organisations are developing new policies and procedures to integrate AI into their operations.

On the other hand, governments – and others – are expressing concerns and are looking at how to govern AI to reduce the risks that come with this new technology.
So, should you be worried?

To understand the risks that GenAI brings, we should first cover – at a high level – how GenAI works.

What is generative AI?

GenAI can produce text that looks as if a human wrote it as well as code, images, music and videos – and even non-coders can now create tailored versions of ChatGPT to help with specific tasks.

GenAI uses complex algorithms that generate something new based on twofold input: the training data used to train the AI, and the prompts, which are the questions and additional information used to trigger the output (figure 1).

Large quantities of input data are collected and used to train the software. For a text GenAI, the training data is collated from online content, such as webpages, online books and other texts, and social media. Based on this information, the algorithms learn to predict what the next letter or word will be, using the patterns and structures inherent in the training data. GenAI does not understand the information in any way – the trainer tweaks the algorithm until the output reliably makes sense.

For specialist GenAI models, additional specific data is likely to be used to fine tune the AI for its intended purpose.

Prompting a GenAI tool to provide a response can range from a simple question or instruction (such as 'what is...' or 'create a...') to a complex series of questions and provision of additional information. This isn't always as easy as it sounds, and a new job title has emerged: prompt engineer.

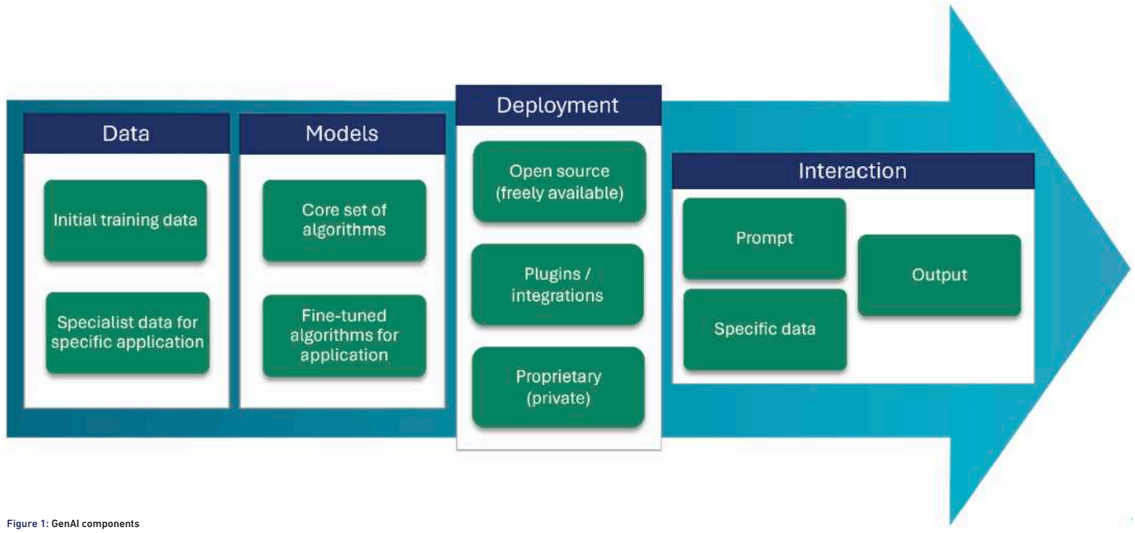

Figure 1: GenAI components

What are the general risks posed by AI?

AI will almost certainly increase the quantity and impact of cyber attacks. Using AI to, for example, craft high-quality phishing emails makes attacking easier for novice hackers and commoditisation of AI-enabled capability will make attacks easier for cyber-criminals and state actors.

AI could be (and in some cases is) being used with malicious intent, for:

- Criminal purposes, such as deepfakes, phishing and stalking.
- Terrorism (such as manipulating driverless cars or attacking AI-controlled systems).
- Disinformation: manipulating public opinion using fake news.

> **There are many examples of ways in which AI can be used for good, perhaps especially in science, but it is a dual-purpose tool and could become a threat.**

Other general societal risks include:

- Unintended societal upheaval due to changes in job roles and availability.
- An effect on climate change because AI needs a lot of computing power.
- A widespread loss of privacy across the population because of the speed at which the volume of existing data can be scanned to extract information.

Is GenAI a specific threat to science?

Because GenAI's purpose is to generate new output, it can be, and already is being, used to collate, search and summarise large volumes of data, synthesise research papers, design drugs, spot potential health problems on scans, write articles, devise solutions to problems, and so much more.

There are many examples of ways in which AI can be used for good, perhaps especially in science, but it is a dual-purpose tool and could become a threat. It could be used with bad intent, or – given how rapidly it is developing – contain systemic error. And, of course, it can itself be attacked.

Personal data and financial data must be protected. Research data will also be of interest – criminal cyber attackers may be interested in confidential and sensitive data, and state actors may be interested in intellectual property (IP). It is vital that sensitive research data and IP are protected, not only to get ethical approval for research, but also to ensure that the results of studies are valid, and to protect the commercial interests of the organisation.

There are potential issues in every GenAI component (figure 2):

1. Input data quality. The quality of the articles GenAI can write is dependent on the quality of the input data.
2. Input data bias. The input data could be biased, whether intentionally or not. Bias in early AI systems has been demonstrated, but even if you are controlling your own input data, the potential for bias should be considered.
3. Algorithms and mistakes. All software contains bugs and can make mistakes. GenAI has been known, for example, to convincingly reference legal cases that do not exist. There is a risk of references to fake scientific studies being produced – clearly a misleading result – which also results in a recursive risk: these being resubmitted as fake input data.
4. Algorithms and transparency. There is a lack of transparency about how the output is achieved. Unlike the scientific process, the results may not be repeatable.
5. Deployment. Any software – including third-party software – may be vulnerable to cyber attack.
6. Prompt intentions. If AI can generate, for example, drugs intended for beneficial medical purposes, it can also be asked to generate designs for poisonous substances.
7. Output. There is a risk of sensitive information disclosure, of reverse engineering to acquire information about IP, and of poorly validated output facilitating cyber-attack.

And, taking a broader perspective, the risk of AI being used to manipulate public opinion means that it may also be used to instill a distrust in society of science and of experts in general.

So, should you be worried?

As the scope of what AI can do increases, there will be many things that AI can do more efficiently and more accurately than we can – and this will, overall, be to our benefit. The revolution that AI will engender is inevitable; the issue will be understanding the potential risks and impact of AI and putting in place controls to manage it.

At a macro level, governments around the world are working to put governance in place and reduce AI risks. The EU AI Act should foster responsible AI development and safeguard fundamental rights, and the UK Government will fund AI research hubs and train regulators.

At a local level, both within your organizations and personally, it's crucial to grasp the scope and purpose of AI implementation. This involves understanding where AI is utilised and the rationale behind its usage. Furthermore, it's essential to assess how AI impacts existing policies such as acceptable use policies and processes such as security awareness training. If you are developing an AI-specific policy, it should include guidelines on protection of sensitive data and for fact-checking information generated by AI. When choosing third-party software to manage data, considering AI implications is imperative.

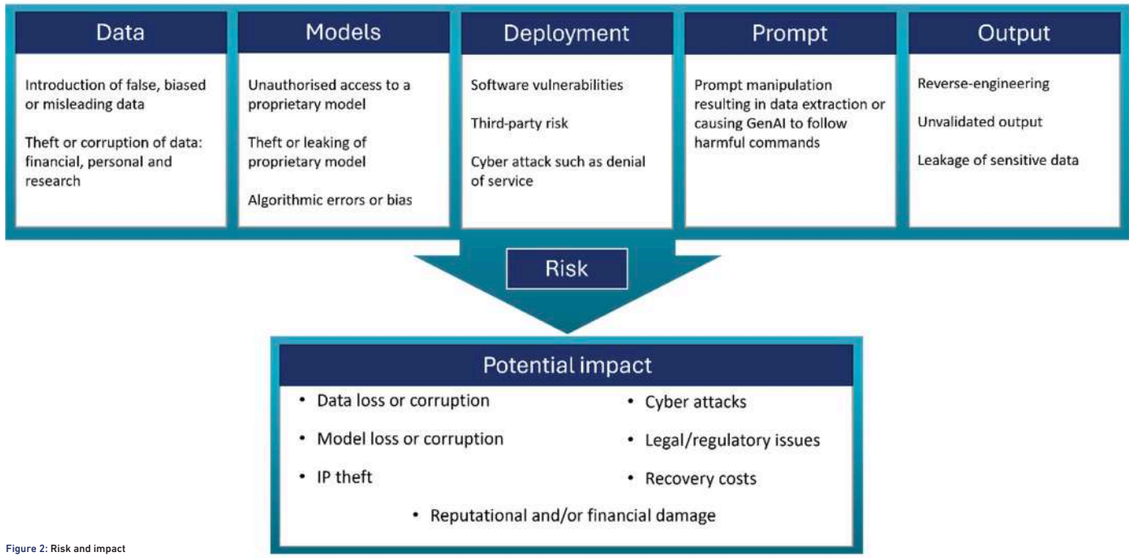

Figure 2: Risk and impact

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Things are changing fast – and AI will be trained to do more things, faster, and become ever more embedded in our work and daily lives. It's going to be interesting...

Biography

Lucy has worked as a consultant in IT systems implementation and IT strategy for UK Government departments, and in digital strategy for listed companies. She now works as an information security consultant for CSP, with a particular interest in AI, secure software development, software supply chain security and business continuity.

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The Re-emerging Threat of Measles

Jessica Swanson

As an early career researcher born after the introduction of the measles vaccine, I have never experienced measles infection, nor know anyone who has had measles, thanks to childhood vaccinations. However, when I mentioned to my parents that I was writing this article, they both had anecdotes from their childhood about measles. Unfortunately, there has been a recent fall in vaccination rates and there has been a surge in the number of measles cases, not just at home in the UK, but globally; and the risks of this preventable infection are becoming more apparent.

Measles disease is caused by measles virus, a highly infectious pathogen. Anyone can be infected by measles virus; however, it is most dangerous in children under five and adults over 30, as complications are more likely to occur. Measles infections are also dangerous for pregnant women and can cause issues such as premature birth of the baby.

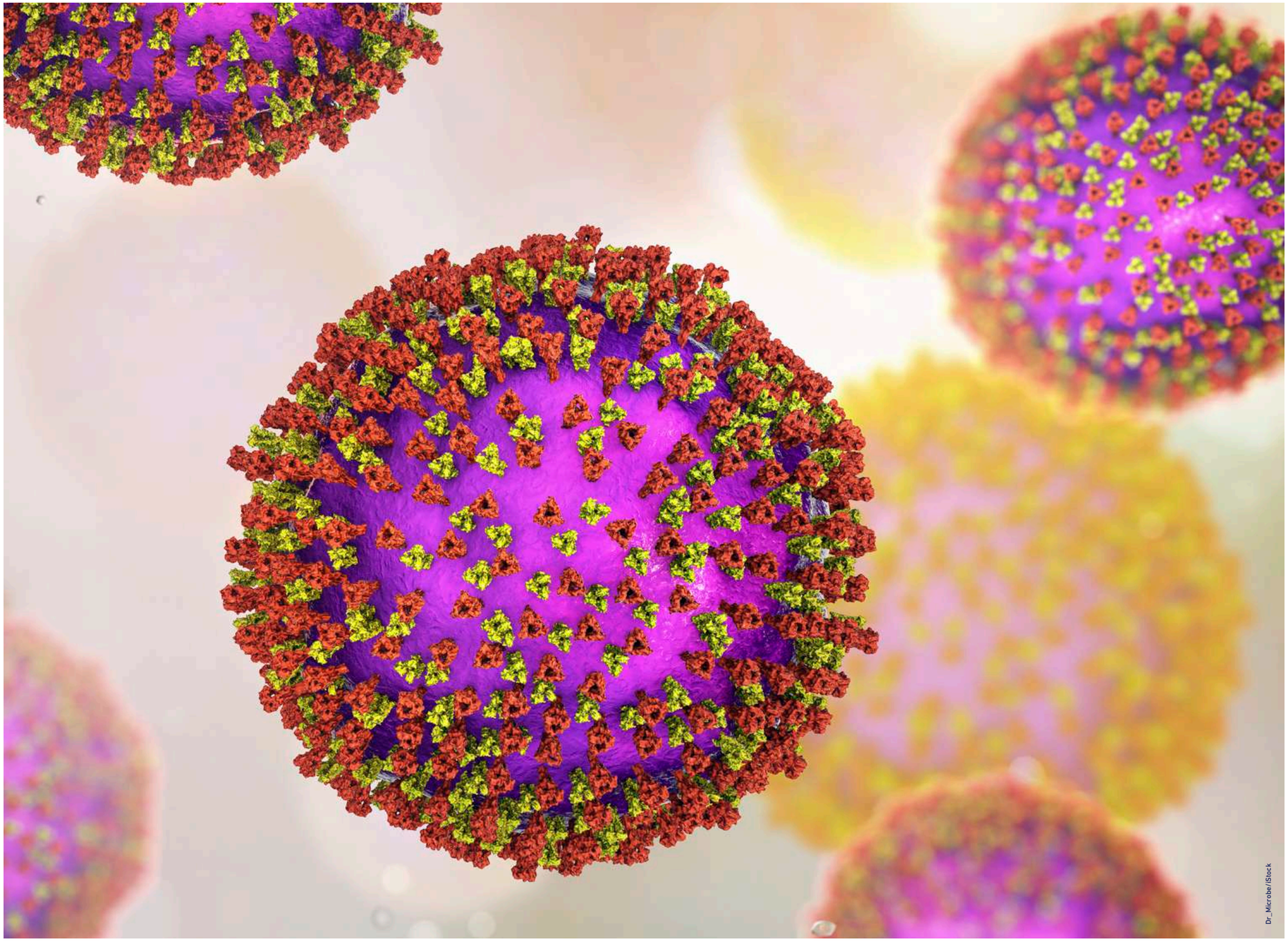
The most obvious symptom of infection is the development of an itchy rash which starts on the face and head and can last several days. Other symptoms are a cough, sore throat, red watery eyes, and the presence of small white spots on the inside of the cheeks. The virus can be passed on from an infected individual about four days before development of the itchy rash and then continue to be transmitted for about four days after the rash started.

While these milder symptoms can be manageable, complications can occur during infection such as blindness, encephalitis, diarrhoea, ear infections and pneumonia. One in five children who get ill will need to be hospitalised because of infection. The virus can also affect the immune system of an infected individual, and this can leave people vulnerable to further infections.

Measles is an airborne virus and can be transmitted by coughing or sneezing by infected individuals. Infectious particles from coughs and sneezes can then stay infectious on surfaces for up to two hours. This can result in infections caused by contact with contaminated surfaces.

Measles is one of the most infectious viruses we know of and a single infected person can go on to infect an average of 12–18 people within a susceptible population. In comparison, a person infected with SARS-CoV-2, the virus responsible for the COVID-19 pandemic, went on to infect 2–3 susceptible people.

Unfortunately, there has been a recent fall in vaccination rates and there has been a surge in the number of measles cases, not just at home in the UK, but globally; and the risks of this preventable infection are becoming more apparent.



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The highly infectious nature of measles makes vaccination a challenge as high levels of vaccine coverage are needed to prevent spread, and the World Health Organization (WHO) recommends a vaccination rate of at least 95% to prevent spread and protect those at risk.

Before the introduction of the measles vaccine this common childhood disease is estimated to have caused 2.6 million deaths per year worldwide. However, thanks to the development of an effective vaccine, this has dropped substantially, and the WHO estimated that measles vaccination prevented 56 million deaths globally between 2000 and 2021.

The current measles vaccine is an attenuated vaccine, which means the vaccine contains a small amount of weakened virus. This weakened virus introduces the body's immune system to the virus and allows the immune system to mount an effective response to the pathogen. Unfortunately, one dose is not always sufficient to induce immunity, so it is essential that a second dose is received. Two doses of measles vaccine results in about 99% of people being protected from measles.

The most common method of vaccination is receiving the measles vaccine as part of routine childhood vaccination with the measles, mumps and rubella (MMR) vaccine. Use of the combination vaccine has the added benefit of protection against two other dangerous infections and reducing the number of individual vaccinations a child needs to receive. There is also a measles-only vaccine; however this is not as widely used as the combination vaccine offers these additional benefits.

As with all vaccines, some common side effects, such as soreness around the injection site, can be experienced when receiving these vaccines. In addition, as the measles vaccine is a weakened form of measles virus, it is possible that a vaccinated child will get a very mild version of measles and feel unwell for two or three days. If this occurs, the child is not infectious and will recover quickly. While this can be worrying to parents of vaccinated children, it is important to compare these side effects with the risks associated with a full measles infection, which can be fatal or have long-lasting consequences such as blindness.

Despite the success of the measles vaccines there has been a decline in vaccination rates globally, and there were about 128,000 deaths globally caused by measles in 2021. These deaths were mainly in children under the age of five and may have been preventable with use of the available vaccines. The WHO reported that globally in 2022, only 83% of children received one dose of vaccine before their first birthday, which is the lowest vaccine uptake since 2008.

Within the UK there has been an increase in laboratory-confirmed cases of measles, with the UKHSA reporting 368 cases from 1 January to 31 December 2023. Of these cases, 160 were reported in the West Midlands and 122 in London. The increased prevalence of measles has recently resulted in the death of an adult in Ireland, highlighting that measles is a concern for all age groups, especially in adults who were not vaccinated as children and are now at risk as protective vaccine coverage decreases.

In the UK, the NHS estimates there are more than 3.4 million children under the age of 16 that have either missed both or one dose of MMR and therefore are at risk of infection. The NHS has responded by contacting carers of children that have missed routine MMR vaccines and encouraging more vaccine uptake. In areas such as the West Midlands and London, where there have been the most cases, people aged 11–25 are also being encouraged to get any missed MMR doses to ensure they are protected.

The low vaccination rates for measles presents a risk of measles outbreaks within communities. While there is a preconception that measles just causes a nasty rash, the reality is that this is a serious infection that can cause severe complications and be fatal. The maintenance of a 95% vaccination rate is essential to protect vulnerable members of the community, such as those with underlying health conditions, and to prevent spread of infections.

While the return of measles is concerning, it is important to remember that measles isn't currently endemic in the UK, as the WHO announced the UK had eliminated measles in 2017. This means measles is not currently circulating in the UK. However, there is still a risk of introduction of cases from countries where measles infections are more common or where vaccine uptake has been low. Outbreaks can only occur when an infection is brought into a community with vaccination coverage lower than 95%, allowing spread amongst unvaccinated individuals. This means that with an increase in vaccine uptake, ideally reaching a vaccination rate of 95%, it is possible to prevent further outbreaks.

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Biography

Jessica Swanson completed her PhD designing virus-like particle vaccines for foot-and-mouth disease virus using the hepatitis B core as a vaccine scaffold. Since then, she has worked on other viruses and other VLP-based vaccines and is passionate about the importance of vaccines.

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Drug Combinations to Counter the Threat of Alphaviruses

Leen Delang, Grace Roberts, Judith M White and Stephen J Polyak

Over the past 20 years, the world has experienced multiple epidemics of diseases caused by mosquito-transmitted viruses. These include Dengue, Zika and Chikungunya viruses. There are over 70 different mosquito-transmitted viruses that are known to cause disease in humans, resulting in millions of infections each year, inducing health and economic burdens. Geographically, the reach of these viruses is ever increasing due to global travel, global warming, trade and urbanisation. Viruses that were previously restricted to tropical/equatorial regions are now spreading further, causing issues in previously unexposed populations – including the USA and Europe.

Of the mosquito-borne viruses, alphaviruses in particular are regularly causing localised outbreaks across the globe. Chikungunya virus (CHIKV) is one of the most widespread alphaviruses. CHIKV is transmitted by two species of mosquito: *Aedes aegypti* (also known as the 'yellow fever mosquito') and *Aedes albopictus* (also known as the 'tiger mosquito'). Since 2004, CHIKV has caused millions of infections in the Indian Ocean region and emerged in Europe and Latin America, resulting in more than 2.1 million cases. CHIKV infection typically causes a short disease with high fever, headache, rash, myalgia and painful arthritis, usually resolving within one week. However, in up to 50% of infections, CHIKV can develop into long-term severe rheumatic disease, with patients experiencing severe, often debilitating, joint pain for years. This chronic arthritis-like illness poses a substantial economic burden and a significant decrease in quality of life. Between 2010 and 2019, CHIKV caused an estimated average yearly loss of over 106,000 disability-adjusted life years, which captures years of life lost due to premature mortality and disability.

***Aedes aegypti* mosquito.** frank600/iStock

Of the other alphaviruses, Mayaro virus (MAYV) is a lesser-studied virus which has caused significant outbreaks in South America and is also associated with long-term debilitating joint pain. Sindbis virus (SINV) is widespread in Africa, Asia, Europe and Australia, and is mainly transmitted by *Culex* species of mosquitoes, although it has also been detected in other mosquito species. SINV has presented as arthritis, rash and fever in Finland, Sweden and Russia. Of the different equine encephalitis viruses, eastern equine encephalitis virus (EEEV) has an extremely high mortality rate, with 30% of infections resulting in death, with individuals that do survive developing severe neurological issues. Venezuelan equine encephalitis virus (VEEV) has a much lower mortality rate of <1% but causes neurological symptoms in 14% of infected individuals. Recurrent epidemics of both EEEV and VEEV have occurred since 2000. Western equine encephalitis virus (WEEV) has also caused multiple outbreaks including one in Argentina in 2023.

Currently, despite the significant health and economic burden, and the proven ability of alphaviruses to cause rapid outbreaks globally, there are no antiviral drugs to treat alphaviruses.

Currently, despite the significant health and economic burden, and the proven ability of alphaviruses to cause rapid outbreaks globally, there are no antiviral drugs to treat alphaviruses. Whilst many of the alphaviruses cause a limited, self-resolving disease, targeted antiviral drugs could prevent the long-term complications seen in a small but significant proportion of patients. In addition, if antivirals were taken early in infection, it would reduce the amount of virus in the individual, which reduces the chances of chronic sequelae and of mosquitos spreading the virus further. In an ideal situation, antivirals for alphaviruses would be used prophylactically, with people who live in, or travel to, areas with high levels of these viruses taking antivirals to prevent infections in the first place, similar to the standard use of anti-malarials for travellers visiting endemic countries.

One approach to finding antivirals is to assess the potential antiviral effects of drugs in clinical use for other uses, often referred to as 'drug repurposing'. This speeds up the process of getting these treatments to patients as all drugs in clinical use will have passed rigorous safety testing. However, this approach was done extensively, yet unsuccessfully, for the SARS-CoV-2 pandemic. Early in the pandemic, there was a frantic search for approved agents that may have activity against the virus. This process was limited for multiple reasons. One issue being that prior studies conducted on these drugs were often restricted in terms of the types of cells they were tested in, making it harder for the repurposing process to be effective in physiologically relevant tissues (e.g. lung for SARS-CoV-2). In addition, use of approved drugs for SARS-CoV-2 was pursued without consideration of how the drugs behave in a person compared with the laboratory. Many drugs that show antiviral activity in cells in a lab are not potent enough to induce the same protective effect in humans, due to how the body processes the drug, and how the drug then disseminates and behaves in the body.

Drug resistance is also an important consideration, since viruses (particularly RNA viruses, which alphaviruses are) can quickly evolve to become resistant to drugs. If antivirals are administered sub-optimally, for example at low doses or at infrequent intervals, viruses have more opportunity to mutate to become resistant. This issue is more common in chronic infection, such as with hepatitis C virus (HCV) or HIV where infections persist for a lifetime. However, resistance has been observed in viruses that cause acute infections such as influenza (flu), polio and SARS-CoV-2. This is more commonly seen in patients who have compromised immune systems, for example the elderly, or those taking medication to suppress the immune system (e.g. transplant patients).

***Aedes albopictus* mosquito sucking human blood.** frank600/iStock

Treating patients with combinations of antivirals has two advantages over monotherapies. Firstly, combination therapy reduces the chance of viruses evolving drug resistance, particularly when the drugs administered target different parts of the virus. Secondly, some drug combinations can produce a synergistic effect – where the activity of each drug is more potent in the presence of the other – which can allow for reduced doses to be administered. A reduction in doses, whilst still retaining potent anti-viral activity, can reduce potential side effects of the treatment. Combination therapy is already the standard procedure for some chronic RNA virus infections including HIV and HCV and has been hugely successful in the treatment of these patients.

With this in mind, drug repurposing for emerging viruses could be highly improved by testing combinations of drugs. Whilst designing and testing drugs that specifically target viral proteins (e.g. direct-acting antivirals – DAAs) are clearly necessary and important, testing these drugs in combination with drugs that target host functions (host-targeting antivirals – HTAs) is highly worthwhile. Our group has shown that certain combinations of DAAs and HTAs are synergistic against SARS-CoV-2. For alphaviruses, little is known about DAA–HTA combinations in relevant laboratory-based models for alphaviruses.

We have also shown that a combination of approved DAAs can confer antiviral synergy against viruses that have pandemic-causing potential including Ebola, Lassa and SARS-CoV-2. In our laboratory, we have shown that a combination of molnupiravir, originally developed for use against influenza, and nirmatrelvir (the active component of the drug paxlovid), originally developed for SARS-CoV-1, work synergistically to suppress SARS-CoV-2 infection in human lung cells, and others have shown a benefit in primates.

Given the toll of the COVID-19 pandemic on the global population and economy, concerted investments in viral pandemic surveillance and response, including for alphaviruses, must become and remain a priority. The time to act is now so we can be better prepared for the next virus spillover into humans, which history has taught us will most certainly occur. Research into drug combination therapies is a key aspect of global pandemic preparedness.

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Biographies

Leen is a Professor at the University of Leuven in Belgium. The research of her team focuses on understanding interactions between mosquito-borne viruses, their mosquito vectors and the mammalian host, and on translating these insights into new antiviral strategies.

Leen Delang

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Grace, currently a scientific officer at the University of Leeds, UK, delivers practical teaching in the School of Biomedical Sciences. Previously, her postdoctoral and PhD research focused on various viruses including Chikungunya virus (CHIKV), respiratory syncytial virus (RSV) and hepatitis C virus (HCV).

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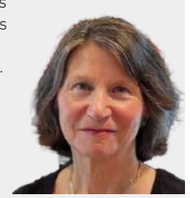
Judith is an Emeritus Professor of Microbiology and Cell Biology based at the University of Virginia. Her research has focused on mechanisms of viral entry into cells, with a special emphasis on viral membrane fusion proteins. In recent years she has spear-headed efforts to identify drug combinations with utility against viruses that cause acute infections including Ebola, Lassa and SARS-CoV-2.



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Steve is a Professor at the University of Washington in Seattle whose research focuses on oral drug combinations for viral pandemic response and preparedness. He is also actively engaged in undergraduate and graduate education.

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Comment: The Emerging Threat of Antifungal Resistance

Gillian Kiely

monzoff/iStock

The global burden of fungal infections is rising, with recent estimates suggesting approximately 2.5 million deaths per year are directly attributable to these infections. This alarming reality is compounded by the fact that the largest contribution to deaths comes from undiagnosed cases [1]. Medical mycology is often considered a 'niche' area of medicine; however, it is clear from the scale of these numbers that this perception needs to change [2].

Clinically, the diagnosis of fungal infections is challenging due to limited sensitivity of diagnostics and often only a 'possible' or 'probable' diagnosis is achieved [3]. Treatment options are also limited, with only four classes of antifungals licensed for clinical use and only one of these available in oral formulations [4]. The lack of treatment options highlights the significant threat antifungal resistance (AFR) poses to human health.

Recognising this threat, in 2022 the World Health Organization (WHO) published its first Fungal Priority Pathogen List. The aim of this list is to raise public awareness of fungal disease and AFR and to drive global action, including the research and development of diagnostics and antifungal treatments [5].

The drivers of AFR are complex, and there are parallels with antibiotic resistance. As with the exposure of bacteria to antibiotics, AFR can emerge in both yeast and moulds in patients during antifungal treatment. Additionally, environmental pressures can drive AFR when fungi are exposed to fungicides in nature [6]. Intensive farming methods, particularly for crops, often require the use of fungicides, some of which have the same mechanism of action (MoA) as antifungal treatments used in humans and can cause resistance in humans [7, 8].

On a positive note, there are at least five antifungal medicines in late-stage clinical development. However, only two of these molecules have novel MoAs with evidence to suggest they can target critical priority pathogens: *Candida auris* (a sometimes pan-resistant species of *Candida* that emerged in 2009) and azole-resistant *Aspergillus fumigatus* [9, 10]. Worryingly, agri-chemical companies are already developing fungicides with MoAs that have the potential to select for resistance against these much-needed new medicines before they can be used in humans [11]. This could mean that even if promising late-stage candidates do succeed they may only be of limited use in the treatment of resistant fungal infections.

A broken model fixed only for antibiotics?

Legitimate efforts to reduce the development of resistance often lead to tight restrictions being imposed on new antimicrobials. This can limit financial returns and disincentivise research and development, leading to market failure.

Progress is being made to redress this; in July 2022, NHS England (NHSE) and NICE launched a pilot scheme trialling an innovative reimbursement model whereby companies are paid a fixed annual fee for antimicrobials, based on appraisal of their value to the NHS, as opposed to volumes used (i.e. subscription-based contracts) [12]. While current proposals to broaden this scheme do not include antifungals, there is a recognition by NICE and NHSE that the same challenges exist for antifungals as antibacterials and a similar approach should be considered. Prioritising the inclusion of antifungals in this model could be the driver needed not only to get novel agents in development to market, but also to incentivise companies to continue innovating and investing in R&D to ensure a healthy pipeline for the future.

For this model, appropriate criteria must be developed to appraise the critical value of antifungals to modern medicine and to do so accurately will mean the challenges in diagnosis, susceptibility testing and the overall lack of systematic surveillance of fungal infections beyond candidaemia will need to be addressed. In addition, the impact of fungicide use on AFR must be considered. What's clear is that to tackle AFR we need continued innovation and a strategic One Health approach.

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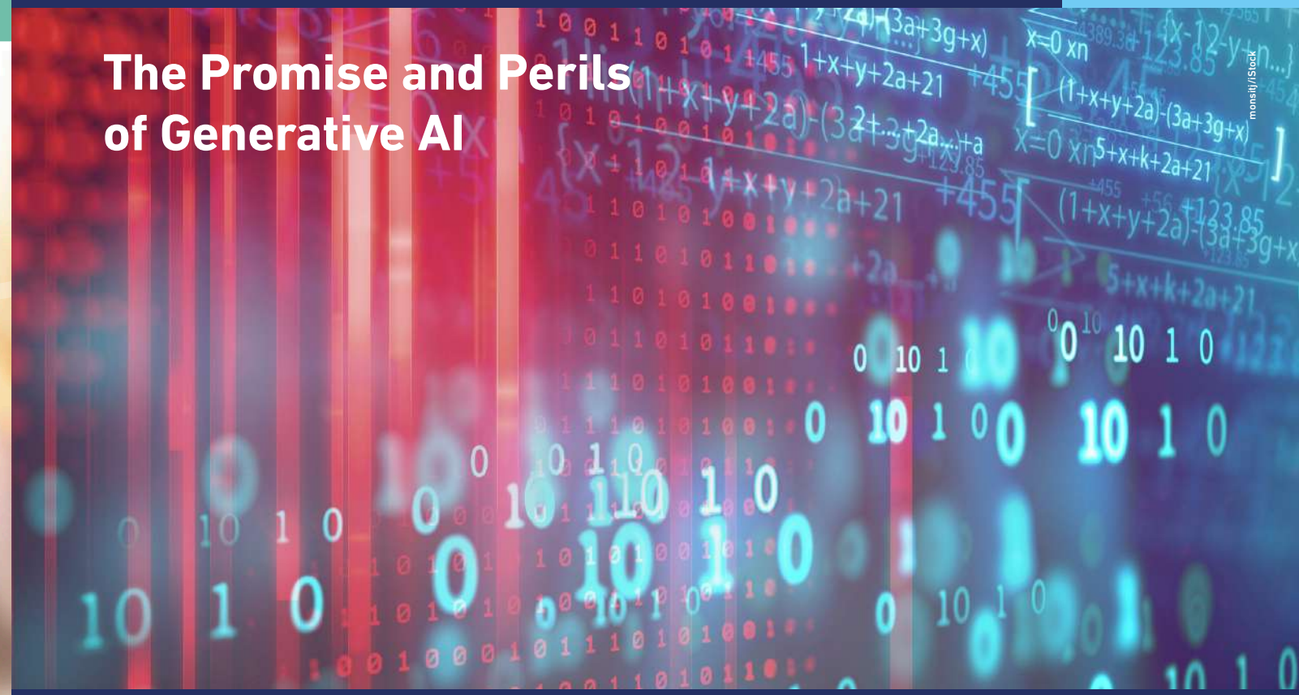
The Promise and Perils of Generative AI



Chelsea Brown from University of Groningen, Netherlands, and winner of the 2023 Young Microbiologist of the Year Competition, shares her perspective on the use of artificial inteligence within biological research and the associated threats.

Anyone who asks me about my research will inevitability hear about how powerful I think computational tools can be in helping with tackling important questions in biology. Information on interactions and dynamics on a very small timescale or with extremely high resolution can be gained, and these can help direct more traditional wet lab experiments. But, along with the benefits of computational research, it is imperative that we acknowledge the pitfalls we can face, especially in fast-growing areas such as artificial intelligence (AI).

AI uses machine learning to perform a series of tasks that the user does not need to directly tell the program to do. AI can even generate outputs ranging from words to pictures and chemical structures, and this is specifically called generative AI.
A rapidly growing area of generative AI is the use of large multi-modal models (LMMs), which can produce data in a different form from the input data (for example pictures to words). The World Health Organization (WHO) predicts that these programmes will be widely used in scientific research (including drug development) and healthcare/public health.

Generative AI is intrinsically biased by the data it is trained on. One example that is in the forefront in structural biology is how AlphaFold (a model to predict protein secondary structure) struggles with some membrane proteins and intrinsically disordered domains. As the model is not trained on many examples of these, the program sometimes does a very poor job at accurately predicting these. But this pitfall in AI models can have a more sinister impact than incorrectly predicted protein structures. A recent warning produced by the WHO highlighted how AI used in healthcare technologies can be 'dangerous' for people in lower-income countries. If the populations are not well represented in the training data for these models, the outcome in treatment could potentially be harmful.

Only at the start of this year, the WHO had to update their guidelines on AI ethics which was originally published three years prior. This demonstrates how quickly the landscape is changing with these technologies. The main warnings are against being overconfident in the output, without giving appropriate thought to the accuracy, safety and useability of these models.

Everything is growing quickly; caution should be used so we fully understand the drawbacks of the technology before relying on it too heavily. A good amount of scepticism should be used as new models are produced, looking into the data they are trained on and ways they could go wrong before trusting that they are providing the right results.

Further reading

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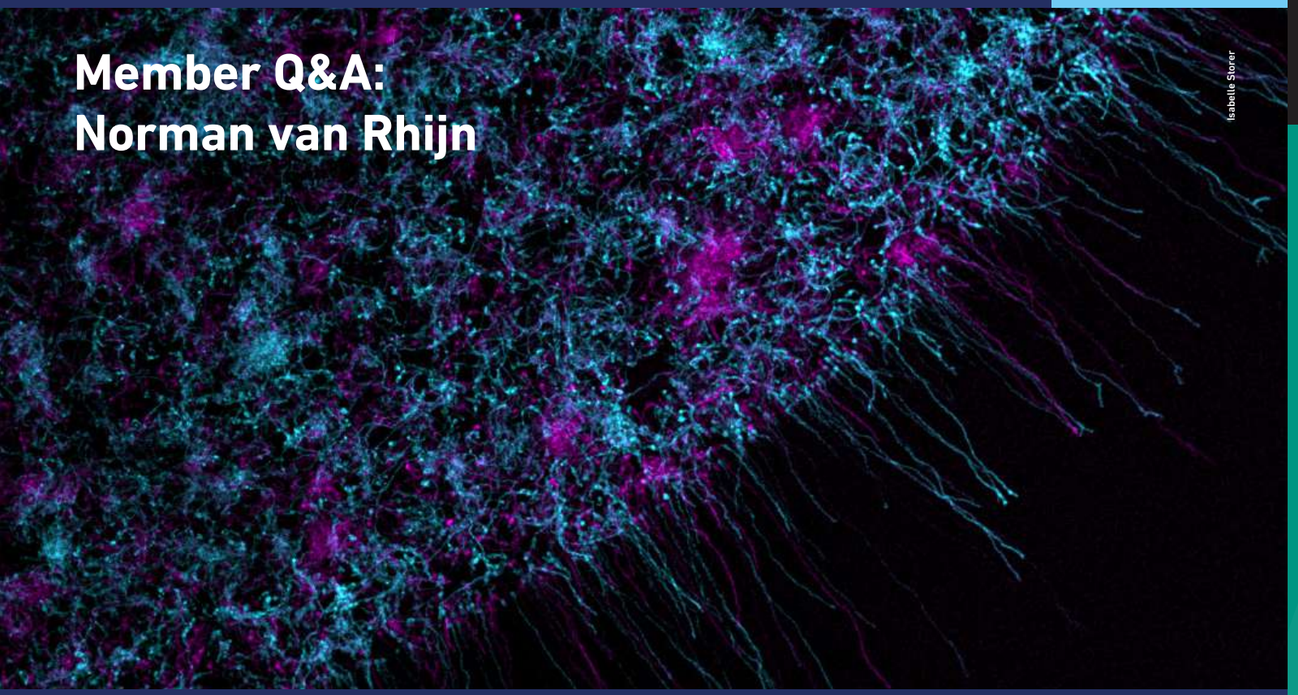
Member Q&A: Norman van Rhijn



This is a regular column to introduce our members. In this issue, we're pleased to introduce Norman van Rhijn.

Where are you currently based and what is your role?
I am currently based in Manchester, United Kingdom. I am currently a Wellcome Trust funded Research Fellow at the University of Manchester, based in both Microbial Evolution Research Manchester and the Manchester Fungal Infection Group.

What area of microbiology do you specialise in?
I specialise in mycology, antimicrobial resistance and One Health. In particular, I'm currently focused on how climate change will affect fungal pathogens in the environment and how different factors will select and drive the evolution of potential pathogenic traits in fungi.

When and why did you first become interested in microbiology?
I was quite late to the party; only really in the second year of my undergraduate (Biology) I became interested in microbiology. My interest was sparked by a unit on genetics where we cloned a drug resistance marker into a fungus and showed it became resistant to certain therapies. The ability to construct new elements and transform them into a genome fascinated me.

As an Early Career (EC) microbiologist, what are some of the professional challenges you face and how do you overcome these?
Balancing progressing my own career and supporting the career of others. Being in science can sometimes promote being selfish, using personal metrics and goals to reach. However, furthering science as a team is not only much more satisfying, it is actually more productive and better for your wellbeing as well.

Do you have any role models, if so, who?
I've always been a fan of Beatrix Potter. While she is mostly known for the Peter Rabbit stories, she was an avid mycologist and has drawn some of the most fascinating fungi. She combined her science with her love of nature; preserving farms, keeping sheep and protecting the Lake District – an area which is very close to my heart.

If you hadn't gone into science, what career path do you think you would you have chosen?
I probably would have opened my own pizzeria. I used to work part time in a pizzeria with my brother and friends. Giving people the joy of good food and service is incredibly gratifying.

What has been the highlight of your career so far?
The end of last year, our research was used in the House of Lords as the basis for a debate on fungicide use in the environment. Watching a live debate where your work is mentioned and discussed on a country-level shows that the work we do can actually make a difference.

What do you hope to achieve in your career in the future?
In the future I hope to achieve scientific development and significant research that contributes to positive change and impacts health. Also, establishing a supportive environment for students to thrive in. And lastly, a lot of fun in science!

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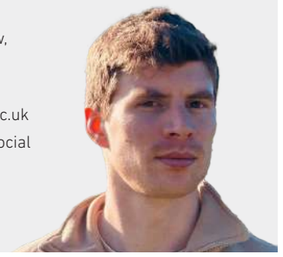

Coccus Pocus 2023: The Microbiology-Inspired Scary Story Competition About Biofilms and Antimicrobial Resistance Was Back!

In September 2023, the Centre for Biomedicine at Hull York Medical School launched an exciting scary story competition for Halloween, Coccus Pocus 2023!

The competition was supported by the National Biofilms Innovation Centre as part of their #BiofilmAware campaign, which is all about helping people to understand what biofilms are and why biofilms are so important.

A growing network of fifteen creative academics and researchers from around the world kindly offered to act as Coccus Pocus Ambassadors, communicating the event at their institutions. This was the fourth year that the competition was run and has attracted a large number of fascinating entries from the UK and beyond!

The contestants were encouraged to write a short horror sci-fi story between 500 and 2,000 words, including antimicrobial resistance and/or microbial biofilms. The story evaluation committee ranked the stories according to the intrigue of their plot, use of language, character description and scientific soundness.

The winners from the 18+ group were:

The first prize (a £100 Amazon voucher) was awarded to **Neelabh Datta** from Asutosh College (affiliated to University of Calcutta, India) for his thrilling story *Resistant Horror*. It is about a freakish mutant *Francisella tularensis* biofilm that led to death and destruction!

2nd place: Megan Poxon from the University of Warwick for her story *Police Report* (awarded a £30 Amazon voucher).

3rd place: Mohamed Nasleem Yoosuf from Sheffield Hallam University for his story *The Whispering Biofilm: A Tale of Science and Monstrous Ambition* (awarded a £20 Amazon voucher).

The winners from the 12–17 group were:

The first prize (a £100 Amazon voucher) was awarded to **Rebecca Balbes**, for her amazing tale *Parasitic*. It is about a creepy bacterial biofilm that required use of the notorious Disinfectant Gun!

2nd place: Patrick Renton for his story *Long Forgotten Lingerers* (also awarded a £30 Amazon voucher).

3rd place: James Finn for his tale *Biofilm Monster* (also awarded a £20 Amazon voucher).

All this year's winners in this group were from St Peter's Catholic College, Surrey. We are grateful to their enthusiastic science teacher, Ms Tara Byrne, for motivating them!

Read all winning stories at: **biofilms.ac.uk/coccus-pocus-2023-winning-stories**.

Coccus Pocus will run again in September 2024!
Can you think of any biofilm- or AMR-related scary stories?
Would you like to be one of our Coccus Pocus Ambassadors?
And... which university or school will claim our next trophy?

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