

HARNESSING ARTIFICIAL INTELLIGENCE TO COMBAT ANTIBIOTIC RESISTANCE IN BACTERIA

Sarnov Roy ^a, Sreeja Chakraborty ^{b,*} Nirjhar Dasgupta ^c

^{a,b,c} Department of Biotechnology, Techno India University, Kolkata-700091, West Bengal

Abstract

Antibiotic resistance has become a growing global crisis, threatening to make once-curable infections increasingly difficult to treat and challenging the foundation of modern medicine. Bacteria have developed remarkable ways to survive antibiotic exposure, including producing enzymes that deactivate drugs, altering their target sites, reducing membrane permeability, and forming protective biofilms. Traditional methods of drug discovery and resistance detection are often slow and unable to keep pace with how quickly bacteria adapt. In recent years, artificial intelligence (AI) has emerged as a powerful tool to address this challenge. By analysing vast amounts of genomic, chemical, and clinical data, AI can predict resistance patterns, identify new antibiotic candidates, and design more effective treatment strategies. It is also revolutionizing rapid diagnostics, helping detect resistant infections within hours, and strengthening global surveillance by tracking emerging resistance trends. While challenges such as data limitations, lack of model transparency, and ethical concerns remain, the integration of AI with microbiology and clinical research offers a promising path forward. This review explores how AI is transforming our understanding of antibiotic resistance accelerating drug discovery, guiding personalized therapy, and offering innovative solutions to one of the greatest health threats of our time.

Keywords: Type your keywords here, separated by semicolons;

1. Introduction

Antibiotic resistance has become one of the most pressing global health challenges of our time, threatening to undo decades of medical progress. Infections that were once easily treatable are

becoming increasingly difficult to cure, leading to longer illnesses, higher medical costs, and rising mortality rates. The world health organization estimates that by 2050, Antimicrobial Resistance

(AMR) could cause up to ten million deaths each year if effective solutions are not implemented [1]. This alarming trend is driven by the overuse and misuse of antibiotics, unregulated access to antimicrobials, and the slow development of new drugs, combined with the extraordinary ability of bacteria to evolve and share resistance genes.

Bacteria have developed several survival strategies to withstand antibiotic pressure. They can inactivate antibiotics through enzymes, alter drug targets, reduce membrane permeability, or form biofilms that protect them from both antibiotics and the immune system [2,3]. These complex and adaptable mechanisms make traditional treatment approaches increasingly ineffective. However conventional laboratory techniques for discovering new antibiotics or detecting resistance are often slow, expensive, and unable to keep pace with how quickly bacteria evolve. During the mid-1900's, penicillin revolutionized infection treatment but its overuse led to rapid resistance in *Staphylococcus aureus*, with MRSA emerging by 1961. Subsequent decades saw resistance spread to other major antibiotics, including isoniazid, rifampin, and vancomycin, leading to VRE, VISA, and VRSA strains. Carbapenem-resistant Enterobacteriaceae and NDM-1 enzymes appeared around 2000, followed by plasmid-mediated colistin resistance (MCR-1) in 2015. By 2017, gonorrhea had become untreatable with standard dual therapy. Globally, antimicrobial resistance (AMR) now threatens multiple infections and caused an estimated 1.27 million deaths in 2019. This has created an urgent need for smarter, faster, and data-driven solutions to guide antibiotic discovery and clinical decision-making. In recent years, artificial intelligence (AI) has emerged as a powerful ally in the global fight against antibiotic resistance. By analysing vast and complex datasets—from genomic sequences and molecular structures to patient records and environmental data—AI can identify potential antibiotic candidates, predict bacterial resistance patterns, and optimize treatment strategies with remarkable precision [4,5,6]. Advanced machine

learning models are capable of uncovering hidden resistance genes, forecasting bacterial evolution, and accelerating drug development far beyond the limits of traditional methods [7]. Beyond research and discovery, AI also plays a key role in clinical care and public health. It enables rapid diagnostic systems that can detect resistant infections within hours instead of days, allowing doctors to choose the right treatment sooner [8]. Moreover, AI-driven surveillance platforms analyse real-time data from hospitals and laboratories worldwide to identify emerging resistance trends and predict outbreaks before they spread [9,10]. Despite these advances, AI is not without limitations. Challenges such as data quality, model transparency, and ethical concerns continue to restrict its widespread adoption in healthcare. Nonetheless, the integration of AI into antimicrobial research represents a turning point offering new possibilities for drug discovery, precise diagnostics, and personalized therapy.

This article provides an overview of the mechanisms of antibiotic resistance and explores how AI technologies are being applied to overcome them. It highlights AI's roles in antibiotic discovery, resistance prediction, personalized therapy, and global monitoring, while also discussing the limitations and future directions of AI in safeguarding the world against the growing threat of antibiotic-resistant bacteria.

2. Causes Of Antimicrobial Resistance

Bacteria have an intrinsic tendency to mutate rapidly due to lesser generation time and transfer its gene through horizontal gene transfer namely, transformation, transduction and conjugation. Although not significant, this essentially marks the beginning of antibiotic resistance in bacteria. This is further aggravated by bacterial adaptation and evolution as a response to inappropriate and excessive antibiotics use, [11]. As per the report published by the WHO, the causes of antibiotic resistance can be jotted down into few points.

- Prescribing antibiotics when not needed or over prescribing.
- Moreover, no requirement for prescriptions to procure antibiotics from diagnostic shops, especially in third world countries, enables patients to consume the antimicrobials even when not required.
- Patients often don't finish their treatment and tend to discontinue medications after subsidence of symptoms.
- Antibiotics are also significantly misused in case of livestock and fish farming.

- Poor control of infections in hospitals and clinics causes nosocomial infections that become even more difficult to treat.
- Lack of hygiene and poor sanitation mainly in developing countries.

These above problems are further supported by the lack of newer antibiotic development to meet the demand [12].

3. AMR: The Global Threat

During early 1940s, when World War II was in play, penicillin became the messiah of medicines, which could miraculously cure wound infections, septicaemia, pneumonia, surgical site infections, postpartum infections. As a consequence, it was used indiscriminately and extensively in both military and civilian settings. The first case of resistance of *S. Aureus* was reported in 1942. Thereafter by 1944-1945, multiple cases of *S. aureus* resistance were reported in many hospitals across the U.S and UK. By 1950, more than 50% of all *S. aureus* isolates in hospitals were penicillin resistant [13]. By 1960, this number reached 80–90% worldwide. Methicillin was introduced in 1960 to combat penicillin resistant strains. Within 1961, even Methicillin resistant *Staphylococcus aureus* (MRSA) was reported in multiple hospitals in UK. Eventually, MRSA became a global superbug [14]. As per WHO's global tuberculosis report in 1990-1993, Isoniazid and rifampin resistant tuberculosis were reported in the 1990s across Russia, India, south Africa, China, USA. Vancomycin which was the last-line antibiotic, even became resistant by 1990. vancomycin-resistant enterococci (VRE), followed by vancomycin -intermediate *S. aureus* - visa (first in Japan, 1997) and vancomycin-resistant *S. aureus* -VRSA (first in USA, 2002), hence, emerged across the hospitals in U.S and Europe [15]. Carbapenem resistant Enterobacteriaceae emerged around 2000 with a mortality rate of 50% [16,17]. New Delhi Metallo-β-lactamase was first reported in a Swedish patient who came to India for treatment in 2008. NDM-1 confers resistance to almost all β-lactam antibiotics, including carbapenems. KPC (Klebsiella pneumoniae Carbapenemase) and NDM (New Delhi Metallo-β-Lactamase) enzymes spread rapidly across continents. Colistin resistance, which is imparted by mcr-1, a plasmid-mediated gene was reported in China in 2015, which displayed rapid spread of resistance among different species, across more than 40 countries in a month [18]. In 2015, WHO included AMR in the top 10 global public health threats. By 2017, Gonorrhea became superbug by the dual therapy failure of ceftriaxone and Azithromycin [19].

The major diseases where antibiotic resistance has shown its maximum impact are namely, lower respiratory tract infections (such as

pneumonia), bloodstream infections, intra-abdominal infections, urinary tract infections, tuberculosis, skin infections, meningitis and other bacterial central nervous system infections, typhoid fever and other invasive salmonella infections, Diarrhoea, cardiac infections, bone and joint infections [20]. The same author reported that in 2019, about 1.27 million deaths were reported as a direct consequence of AMR, necessitating urgent speeding up of actions to combat AMR.

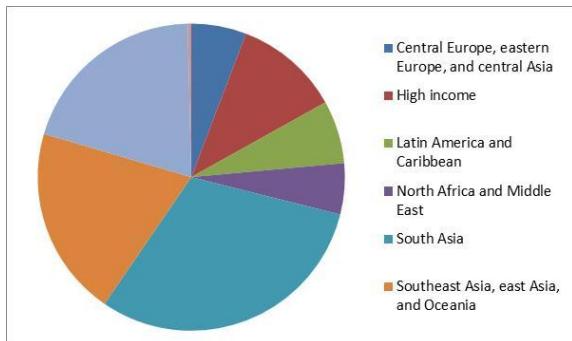


Fig. 1. Attributable deaths to antibiotic resistance in 2019.

4. Mechanisms of Antibiotic Resistance in Bacteria

Antibiotic resistance has become one of the biggest global health challenges, allowing even common infections to become harder to treat. Bacteria develop resistance mainly through genetic mutations or by acquiring resistance genes from other microbes via horizontal gene transfer [1]. These genetic changes help them survive by disabling the drug, reducing its entry, or altering the target site.

4.1 Enzymatic Drug Inactivation

One of the most widespread ways bacteria resist antibiotics is by producing enzymes that can neutralize the drug before it takes effect. These enzymes either break down the antibiotic's structure or chemically modify it, preventing it from binding to its target. For instance, β -lactamases are enzymes that destroy the β -lactam ring found in antibiotics like penicillin, rendering them useless. Similarly, aminoglycoside-modifying enzymes can attach chemical groups to aminoglycosides, stopping them from interfering with bacterial protein synthesis [2, 21, 22, 23, 24].

4.2 Reduced Drug Entry and Efflux Pumps

Bacteria can also defend themselves by limiting how much antibiotic actually reaches its target inside the cell. Some achieve this by modifying their porin channels, tiny openings in the outer membrane that normally allow molecules to pass through [25,26]. When these channels are altered or closed, antibiotics struggle to enter. Others rely on efflux pumps—

specialized proteins that act like molecular bouncers, actively ejecting antibiotics that manage to get inside. These pumps are particularly concerning because many of them can expel a wide range of drugs, contributing to multidrug resistance [27,28].

4.3 Target Modification

Another clever strategy bacteria use is altering the very site where antibiotics are supposed to bind. By slightly changing the structure of these target molecules, the drug can no longer recognize or attach to them effectively [29,30]. For example, *Streptococcus pneumoniae* can modify its penicillin-binding proteins (PBPs), which weakens penicillin's ability to interfere with cell wall synthesis [23]. Likewise, in the case of macrolide Antibiotics, bacteria can alter their Ribosomal RNA, preventing the drug from binding and stopping protein production [31,32].

4.4 Biofilm Formation and Dormant Cells

Many bacteria don't exist as single, free-floating cells instead, they form biofilms, which are dense, sticky layers that attach to surfaces like medical devices or tissues [33,34]. These biofilms act as protective shields, preventing antibiotics and immune cells from reaching the bacteria inside [35]. Within this protected environment, some cells slow down their metabolism and enter a dormant or "persister" state, allowing them to survive antibiotic exposure. Once the treatment ends, these dormant cells can "wake up" and repopulate the area, making infections especially difficult to eliminate [36].

5. How AI fits into the fight against antibiotic resistance

Artificial intelligence (AI) is rapidly emerging as a gamechanger in the fight against antibiotic-resistant bacteria. By analysing massive datasets from bacterial genomes and laboratory tests to patient records AI can predict resistance patterns with remarkable speed, enabling doctors to select the most effective antibiotics in far less time than traditional methods [37].

AI is also transforming antibiotic discovery. It can explore enormous chemical spaces, identify promising new molecules, and even suggest modifications to overcome known resistance mechanisms, significantly accelerating the search for next-generation drugs [38,39].

In the clinic, AI enhances rapid diagnostics, allowing resistant strains to be detected from genomic or imaging data within hours rather than days, which means patients receive the right treatment sooner [41]. Beyond individual care, AI supports public health surveillance by tracking emerging resistance trends and identifying hotspots, giving health

authorities an early warning to act before outbreaks spread [42].

5.1 AI in Antibiotic Discovery

Discovering new antibiotics has always been a slow, costly, and challenging process, especially as bacteria evolve resistance faster than traditional methods can keep up. Artificial intelligence (AI) is changing this landscape by rapidly analysing enormous chemical and biological datasets to identify compounds likely to work against even multidrug-resistant bacteria [37].

Beyond finding existing molecules, AI can design entirely new compounds, optimize their chemical structures, and predict how effective they will be before any lab experiments. This targeted approach saves both time and resources, making the development of promising antibiotics faster and more efficient [38,39].

AI can also mine natural product databases and suggest combinations of compounds that work together synergistically, uncovering hidden antimicrobial potential that traditional methods often miss. Already, these AI-driven strategies have led to the discovery of new antibiotics that would have been extremely difficult to identify otherwise [37].

5.2 AI in Antimicrobial Development

Artificial intelligence (AI) is reshaping the way we discover and develop new antimicrobials. Traditionally, identifying effective compounds against pathogens required years of experimentation and costly screening. Now, AI can analyse complex datasets from genomics, chemistry, and pharmacology to predict which molecules are most likely to succeed greatly speeding up the discovery process [37]. Beyond identifying candidates, AI helps refine and optimize drug properties such as stability, toxicity, and bioavailability. By simulating how molecules interact with bacterial targets before they're synthesized, researchers can focus only on the most promising compounds, saving valuable time and resources [38]. AI is also making it possible to repurpose existing drugs, revealing unexpected antimicrobial activity in compounds originally designed for other diseases. This approach not only cuts down development costs but also offers quicker solutions to fight resistant infections [40]. In essence, AI brings precision and speed to antimicrobial development turning what once took years into a process that can unfold in months, and offering new hope in the global effort to overcome antibiotic resistance.

5.3 AI for Predicting Resistance Mechanisms

Artificial intelligence (AI) is transforming how scientists understand and predict bacterial resistance.

Instead of relying solely on traditional lab methods, researchers can now use AI to analyse huge amounts of genomic, proteomic, and clinical data to pinpoint the genes, mutations, and molecular pathways responsible for antibiotic resistance [7,43]. Machine learning models can even predict whether a bacterial strain will resist a particular drug just by examining its genetic sequence. This allows doctors to choose the most effective antibiotic early on, reducing the misuse of broad-spectrum drugs that often worsen resistance [11].

What makes AI especially powerful is its ability to uncover hidden resistance mechanisms subtle genetic patterns or mutations that might escape human analysis. Deep learning models can recognize these complex relationships and reveal how bacteria adapt to survive under drug pressure, offering new insights for developing stronger and more targeted therapies [44]. Ultimately, AI doesn't just help us detect resistance it helps us stay one step ahead of it. By anticipating how bacteria evolve, AI supports faster diagnostics, smarter antibiotic use, and more effective drug design in the ongoing fight against antimicrobial resistance.

5.4 AI for Personalized Therapy

Artificial Intelligence (AI) is transforming antibiotic treatment by making it more personalized and precise. Instead of relying on broad-spectrum prescriptions, AI allows doctors to tailor therapy to each patient's unique infection and health profile. By analysing clinical records, bacterial genomes, and patient-specific factors, AI can predict which antibiotic and dosage will be most effective, helping to avoid ineffective treatments and limit resistance [45]. Machine learning models also take into account individual variations such as immune strength, gut microbiome balance, and existing medical conditions. These insights help clinicians design customized antibiotic regimens that not only target the infection effectively but also reduce side effects and the chances of resistance emerging [46]. In hospitals, AI-driven diagnostic systems can continuously monitor patients in real time, using data from lab tests, imaging, and electronic health records. They can detect early signs of treatment failure or infection recurrence and recommend timely adjustments to therapy, ensuring each patient receives the right care at the right moment [47].

Ultimately, AI is reshaping infectious disease management by turning antibiotic use into a precision-guided process where treatment is smarter, safer, and personalized for every patient.

5.5 Application of AI against antibiotic resistance

Antibiotic resistance has become one of the biggest global health threats of our time. As bacteria continue

to evolve faster than new drugs can be developed, traditional research methods alone can no longer keep up. In this growing crisis, artificial intelligence (AI) has emerged as a powerful ally transforming how scientists discover, design, and use antibiotics.

For decades, antibiotic discovery has been slow and expensive. AI now changes that by analysing massive chemical and biological datasets to spot patterns that humans might miss. Machine learning models can predict how molecules interact with bacterial targets and even design entirely new antibiotics that can overcome resistant strains [37]. AI also helps scientists refine drug candidates before they even reach the lab predicting their safety, stability, and effectiveness. This saves valuable time and resources that would otherwise be spent on trial-and-error experiments [38]. Moreover, AI can repurpose existing drugs, uncovering hidden antimicrobial properties in compounds originally meant for other diseases. This strategy accelerates treatment options while lowering development costs [40].

Understanding how bacteria develop resistance is key to stopping it. AI can analyze genomic and proteomic data to identify resistance genes, mutations, and biochemical pathways linked to antibiotic failure [7]. By predicting which bacterial strains are likely to resist a specific drug, AI enables doctors to make quicker and more accurate treatment decisions. Beyond the clinic, AI helps researchers uncover previously unknown resistance mechanisms, guiding the creation of next-generation antibiotics that remain effective longer [48].

AI is also transforming the speed and accuracy of diagnostics. By processing genomic data, medical images, or lab results, AI-powered tools can detect resistant infections within hours a process that used to take days [41]. Faster diagnosis means patients receive the right antibiotic sooner, reducing misuse of broad-spectrum drugs and improving survival rates. Every infection and every patient is different. AI brings precision to antibiotic therapy by tailoring treatments to an individual's infection type, genetics, and medical history. Machine learning models can recommend the best antibiotic and dosage for each case, minimizing side effects and resistance risks [48]. AI can also monitor patient data in real time, adjusting treatment as needed. This dynamic approach ensures that therapies remain both safe and effective [46,47].

On a larger scale, AI supports global surveillance of antibiotic resistance. By analysing hospital, laboratory, and environmental data, AI can identify emerging resistance hotspots and predict future outbreaks [9]. This early warning system helps public health authorities respond before resistance spreads widely.

6. Limitations Of AI Against Antibiotic Resistance

AI systems rely heavily on large and high-quality datasets, including bacterial genomes, lab results, and patient records. If the data is incomplete, inconsistent, or biased, the predictions can be misleading or inaccurate, which may limit clinical usefulness [47].

AI models trained on data from a specific population, bacterial strain, or region may not perform well when applied elsewhere. This means predictions may be less reliable for new strains or in different geographical settings [37]. Many AI algorithms, especially deep learning models, act as "black boxes," making it hard for clinicians to understand how decisions are made. Lack of transparency can reduce trust and slow adoption in clinical practice [48]. AI can suggest potential antibiotics, predict resistance, or propose treatment plans, but all predictions require laboratory or clinical validation. Without experimental confirmation, AI insights alone are not sufficient for safe clinical use.

Using patient data raises important ethical questions, including privacy, consent, and adherence to regulations like HIPAA or GDPR. Mismanagement could lead to data breaches or misuse of sensitive medical information [48].

Effective AI deployment requires high-performance computing, robust IT systems, and trained personnel. Many low-resource or developing regions may struggle to implement AI solutions, limiting their global impact [47].

AI can inherit biases present in training data, potentially favouring certain populations or pathogen types. Such biases can compromise fairness and accuracy, particularly in treatment recommendations [41]. Bacteria evolve quickly, sometimes faster than AI models can be updated. Without constant retraining and access to real-time data, predictions can become outdated or less effective over time [45].

7. Conclusion

Artificial intelligence (AI) is reshaping how we confront one of the greatest medical challenges of our time antibiotic resistance. What was once a slow, trial-and-error process of discovery has evolved into a dynamic, data-driven effort powered by machine intelligence. AI allows us to see patterns that were previously hidden, analysing massive genomic, molecular, and clinical datasets to identify potential antibiotics, predict emerging resistance, and repurpose existing drugs for new therapeutic use. It brings speed and precision to every stage of the process from drug discovery to diagnostics helping detect resistant infections within hours, rather than days. In clinical care, AI supports truly personalized therapy by recommending the most effective

antibiotic and dosage for each patient, reducing unnecessary drug use and preventing the further spread of resistance. Beyond the hospital, AI-driven surveillance systems continuously monitor global resistance trends, giving scientists and public health agencies the ability to respond before small threats become large-scale outbreaks. However, the success of AI depends on the systems and values that guide it—high-quality, unbiased data; transparent and interpretable models; and ethical integration into healthcare. Challenges such as data inconsistency, infrastructure limitations, and the need for clinical validation must be overcome through collaboration between data scientists, microbiologists, and clinicians.

Ultimately, AI is not a replacement for human expertise but a powerful extension of it. When combined with scientific knowledge and clinical judgment, AI gives us the means to outpace bacterial evolution and restore control over infections that once seemed unbeatable. By embracing this partnership between human intelligence and machine learning, we can preserve the life-saving power of antibiotics and move toward a future where infections are treated faster, smarter, and more safely than ever before.

Acknowledgments

We would like to thank the honorable Chancellor and the Vice Chancellor of Techno India University, West Bengal; for providing us the infrastructure to carry out this work.

Reference

- [1] J. Davies, D. Davies, Origins and evolution of antibiotic resistance, *Microbiol. Mol. Biol. Rev.* 74 (2010) 417–433.
- [2] N.I. Zahari, E.N. Engku Abd Rahman, A.A. Irekeola, N. Ahmed, A.A. Rabaan, J. Alotaibi, S.A. Alqahtani, M.Y. Halawi, I.A. Alamri, M.S. Almogbel, A.H. Alfaraj, A review of the resistance mechanisms for β -lactams, macrolides and fluoroquinolones among *Streptococcus pneumoniae*, *Medicina* 59 (2023) 1927.
- [3] P. Rajput, K.S. Nahar, K.M. Rahman, Evaluation of antibiotic resistance mechanisms in gram-positive bacteria, *Antibiotics* 13 (2024) 1197.
- [4] J.M. Stokes, K. Yang, K. Swanson, W. Jin, A. Cubillos-Ruiz, N.M. Donghia, C.R. MacNair, S. French, L.A. Carfrae, Z. Bloom-Ackermann, V.M. Tran, A deep learning approach to antibiotic discovery, *Cell* 180 (2020) 688–702.
- [5] C. Tse, Artificial intelligence in drug discovery and development, (2020).
- [6] A. Zhavoronkov, Artificial intelligence for drug discovery, biomarker development, and generation of novel chemistry, *Mol. Pharm.* 15 (2018) 4311–4313.
- [7] G. Arango-Argoty, E. Garner, A. Pruden, L.S. Heath, P. Vikesland, L. Zhang, DeepARG: a deep learning approach for predicting antibiotic resistance genes from metagenomic data, *Microbiome* 6 (2018) 23.
- [8] A.A. Rabaan, S. Alhumaid, A.A. Mutair, M. Garout, Y. Abulhamayel, M.A. Halwani, J.H. Alestad, A.A. Bshabshe, T. Sulaiman, M.K. AlFonaisan, T. Almusawi, Application of artificial intelligence in combating high antimicrobial resistance rates, *Antibiotics* 11 (2022) 784.
- [9] J. Kaur, J. Kaur, A.S. Dhama, S. Jindal, K. Walia, H. Singh, Strengthening the surveillance of antimicrobial resistance in India using integrative technologies, *Front. Public Health* 10 (2022) 861888.
- [10] S. Pillay, D. Calderón-Franco, A. Urhan, T. Abeel, Metagenomic-based surveillance systems for antibiotic resistance in non-clinical settings, *Front. Microbiol.* 13 (2022) 1066995.
- [11] D.I. Andersson, N.Q. Balaban, F. Baquero, P. Courvalin, P. Glaser, U. Gophna, R. Kishony, S. Molin, T. Tønrum, Antibiotic resistance: turning evolutionary principles into clinical reality, *FEMS Microbiol. Rev.* 44 (2020) 171–188.
- [12] F. Branda, F. Scarpa, Implications of artificial intelligence in addressing antimicrobial resistance: innovations, global challenges, and healthcare's future, *Antibiotics* 13 (2024) 502.
- [13] M. Barber, Staphylococcal infection due to penicillin-resistant strains, *Br. Med. J.* 2 (1947) 863.
- [14] M.P. Jevons, "Celbenin"-resistant staphylococci, *Br. Med. J.* 1 (1961) 124.
- [15] K. Hiramatsu, H. Hanaki, T. Ino, K. Yabuta, T. Oguri, F.C. Tenover, Methicillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility, *J. Antimicrob. Chemother.* 40 (1997) 135–136.
- [16] H. Yigit, A.M. Queenan, G.J. Anderson, A. Domenech-Sánchez, J.W. Biddle, C.D. Steward, S. Alberti, K. Bush, F.C. Tenover, Novel carbapenem-hydrolyzing β -lactamase, KPC-1, from a carbapenem-resistant strain of *Klebsiella pneumoniae*, *Antimicrob. Agents Chemother.* 45 (2001) 1151–1161.
- [17] P. Nordmann, G. Cuzon, T. Naas, The real threat of *Klebsiella pneumoniae* carbapenemase-producing bacteria, *Lancet Infect. Dis.* 9 (2009) 228–236.
- [18] Y.Y. Liu, Y. Wang, T.R. Walsh, L.X. Yi, R. Zhang, J. Spencer, Y. Doi, G. Tian, B. Dong, X. Huang, L.F. Yu, Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China, *Lancet Infect. Dis.* 16 (2016) 161–168.
- [19] M.J. Cole, M. Day, S. Jacobsson, A.J. Amato-Gauci, G. Spiteri, M. Unemo, et al., The European response to control and manage multi- and extensively drug-resistant *Neisseria gonorrhoeae*, *Euro Surveill.* 27 (2022) 2100611.
- [20] C.J.L. Murray, K.S. Ikuta, F. Sharara, L. Swetschinski, G.R. Aguilar, A. Gray, et al., Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, *Lancet* 399 (2022) 629–655.
- [21] K. Bush, G.A. Jacoby, Updated functional classification of β -lactamases, *Antimicrob. Agents Chemother.* 54 (2010) 969–976.
- [22] G.D. Wright, Bacterial resistance to antibiotics: enzymatic degradation and modification, *Adv. Drug Deliv. Rev.* 57 (2005) 1451–1470.
- [23] J. Davies, D. Davies, Origins and evolution of antibiotic resistance, *Microbiol. Mol. Biol. Rev.* 74 (2010) 417–433.
- [24] T. Palzkill, Metallo- β -lactamase structure and function, *Ann. N. Y. Acad. Sci.* 1277 (2013) 91–104.
- [25] A.H. Delcour, Outer membrane permeability and antibiotic resistance, *Biochim. Biophys. Acta* 1794 (2009) 808–816.
- [26] H. Nikaido, Multidrug resistance in bacteria, *Annu. Rev. Biochem.* 78 (2009) 119–146.
- [27] X.Z. Li, H. Nikaido, Efflux-mediated drug resistance in bacteria: an update, *Drugs* 69 (2009) 1555–1623.
- [28] J.M. Pagès, M. Masi, J. Barbe, RND-efflux system: AcrAB–ToIC and MexAB–OprM efflux-pump archetype, *Trends Mol. Med.* 11 (2005) 382–389.
- [29] M. Archambault, J. Harel, J. Gouré, Y.D. Tremblay, M. Jacques, Antimicrobial susceptibilities and resistance genes of Canadian isolates of *Actinobacillus pleuropneumoniae*, *Microb. Drug Resist.* 18 (2012) 198–206.
- [30] J. Lin, K. Nishino, M.C. Roberts, M. Tolmacy, R.I. Aminov, L. Zhang, Mechanisms of antibiotic resistance, *Front. Microbiol.* 6 (2015) 34.
- [31] B. Vester, S. Douthwaite, Macrolide resistance conferred by base substitutions in 23S rRNA, *Antimicrob. Agents Chemother.* 45 (2001) 1–2.

[32] J.M. Munita, C.A. Arias, Mechanisms of antibiotic resistance, in: *Virulence Mechanisms of Bacterial Pathogens*, (2016) 481–511.

[33] L. Hall-Stoodley, J.W. Costerton, P. Stoodley, Bacterial biofilms: from the natural environment to infectious diseases, *Nat. Rev. Microbiol.* 2 (2004) 95–108.

[34] H.C. Flemming, J. Wingender, U. Szewzyk, P. Steinberg, S.A. Rice, S. Kjelleberg, Biofilms: an emergent form of bacterial life, *Nat. Rev. Microbiol.* 14 (2016) 563–575.

[35] K. Lewis, Persister cells and the riddle of biofilm survival, *Biochemistry (Moscow)* 70 (2005) 267–274.

[36] J.W. Costerton, K.J. Cheng, G.G. Geesey, T.I. Ladd, J.C. Nickel, M. Dasgupta, T.J. Marrie, Bacterial biofilms in nature and disease, *Annu. Rev. Microbiol.* 41 (1987) 435–464.

[37] J.M. Stokes, K. Yang, K. Swanson, W. Jin, A. Cubillos-Ruiz, N.M. Donghia, et al., A deep learning approach to antibiotic discovery, *Cell* 180 (2020) 688–702.

[38] C. Tse, Artificial intelligence in drug discovery and development, (2020).

[39] A. Zhavoronkov, Artificial intelligence for drug discovery, biomarker development, and generation of novel chemistry, *Mol. Pharm.* 15 (2018) 4311–4313.

[40] T. Ali, S. Ahmed, M. Aslam, Artificial intelligence for antimicrobial resistance prediction: challenges and opportunities towards practical implementation, *Antibiotics* 12 (2023) 523.

[41] S.M. Mandal, Preventative strategies to stop the spread of antibiotic resistance, *Front. Antibiot.* 2 (2023) 1283336.

[42] A.A. Rabaan, S. Alhumaid, A.A. Mutair, M. Garout, Y. Abulhamayel, et al., Application of artificial intelligence in combating high antimicrobial resistance rates, *Antibiotics* 11 (2022) 784.

[43] X. Yin, X.T. Jiang, B. Chai, L. Li, Y. Yang, J.R. Cole, J.M. Tiedje, T. Zhang, ARGs-OAP v2.0 with an expanded SARG database and hidden Markov models, *Bioinformatics* 34 (2018) 2263–2270.

[44] J.M. de la Lastra, S.J. Wardell, T. Pal, C. de la Fuente-Nunez, D. Pletzer, From data to decisions: leveraging artificial intelligence and machine learning in combating antimicrobial resistance, *J. Med. Syst.* 48 (2024) 71.

[45] A. Howard, N. Reza, P.L. Green, M. Yin, E. Duffy, H.C. Mwandumba, A. Gerada, W. Hope, Artificial intelligence and infectious diseases: tackling antimicrobial resistance, from personalised care to antibiotic discovery, *Lancet Infect. Dis.* (2025).

[46] P. Rajpurkar, E. Chen, O. Banerjee, E.J. Topol, AI in health and medicine, *Nat. Med.* 28 (2022) 31–38.

[47] E.J. Topol, High-performance medicine: the convergence of human and artificial intelligence, *Nat. Med.* 25 (2019) 44–56.

[48] J.M. de la Lastra, S.J. Wardell, T. Pal, C. de la Fuente-Nunez, D. Pletzer, From data to decisions: leveraging artificial intelligence and machine learning in combating antimicrobial resistance, *J. Med. Syst.* 48 (2024) 71.