

## Inauguration Ceremony of the 2024-2025 Academic Year Commemorating the 25th Anniversary of the University of Foggia Address by the Director of Medical and Surgical Sciences Department Gaetano Serviddio

## Artificial Intelligence and the Art of Healing: Contradiction or Revolution?

Every now and then, human history makes extraordinary leaps, moments in which technical and scientific progress throws open doors that only a short time before seemed inaccessible. In the last ten years, medicine has gone through one of these epochal turning points. Today, it is no longer just a matter of treating diseases but also of understanding them in depth, of preventing them before they appear and, in some cases, even of rewriting the very rules of biology.

Let's imagine a world in which medicine is no longer limited to treating symptoms, but actively works to deeply understand the mechanisms behind how a disease develops and manifests itself, with the aim of understanding the individual in their essence, scrutinizing the secrets of their genetic code, analyzing the hidden signals of proteins and deciphering the intricate language of their cells.

This world is no longer a distant dream: it is the realm of the omic sciences that reveal the hidden fabric of life and of Artificial Intelligence (AI), the brilliant ally that helps us interpret this enormous complexity.

Together they are giving life to a new paradigm: precision medicine, a tailored approach that looks at the patient no longer as a clinical case, but as a unique individual. Imagine observing an infinite musical score, a web of notes that unfolds in complex and unpredictable harmonies: this is human biology seen through the sciences of omics. Genomics has paved the way: decoding DNA means reading the instruction manual of our body, discovering which genes predispose to diseases, how they interact and are inherited, which ones protect and how to intervene to modify their destiny. Genomics is the book of life, an infinite tome written with an alphabet made up of only 4 letters:

A, T, C and G, the nitrogenous bases that make up DNA. It is science that has allowed us to decode and rewrite this extraordinary code, where each letter and sequence tells the unique story of an organism, from its physical traits to its vulnerability to disease. The genome is a vast and complex network of genes, molecular switches, and biological destinies. Each gene is a door to a room of life, and each genetic variant is a variation on a theme that makes an individual unique.

The genome includes 3 billion nitrogenous bases which were fully sequenced in the Human Genome Project (HJP): 20 research centers among the most renowned in the world, 18 countries and the work of 10,000 researchers took 13 years to complete it.

In 2003, Bill Clinton and Tony Blair announced to the world the availability of the first draft of human genome. Since then, genomics has evolved, and today genomics studies the genetic variance among individuals and populations, as well as the interactions between genes and environment and, lastly, how these can influence the development of diseases. But genomics is just the beginning. If DNA is the project and RNA is its messenger, proteins are the executors of the biological destiny. Proteomics studies the world of proteins, it explores how the instructions of genes become cellular functions. Twenty thousand genes code over 1 million proteins which constitute a "proteome", a flexible complex that changes in response to environment conditions, stimuli and diseases. DNA defines the "what", but it is proteins to define the "how" and the "why". The degrees of complexity are not finite: genes and proteins and evolution, of conscious mutations which make the human being, from generation to generation, different and more efficient in facing the new challenges of the surrounding environment.

The human biological machine always knows what to do, with a wealth of 70,000 years. And what it does, in every single moment, is written in metabolites (metabolites are sugars, hormones, vitamins, fats and amino acids, as well as the waste products of toxic substances, foods, and drugs). Studying the whole, along with metabolomics allows us to analyze the hidden equilibria of our body, revealing the secrets of metabolism. Today we are able to analyze more than 100,000 metabolites simultaneously; a tridimensional analysis which reveals the chemistry of life thanks to which we are in the process of rewriting human biology defining precisely the processes that distinguish us from one another.

If all this may seem complicated, try to add to each of these worlds the infinite relations between them: microbiomics, which studies the community of microorganisms (a

trillion bacteria and viruses, which live with the man); epigenomics, which studies the influence of the environment on the human genome; interactome, which studies the set of interactions between proteins, DNA and biomolecules; and yet, phenomics, lipidomics, glycomics and many others.

The advent of these new technologies has introduced a real shift in approaching the study of human sciences. Omics, in face, studies the set: it decodes the relations among systems, it maps complex processes, it describes both common and individual responses and is, therefore, able to outline not only the general explanations but above all individualized profiles.

Thanks to omic sciences, medicine is transforming into a "tailor-made" type of discipline, where there are no longer any "one-size-fits-all" treatments. These new sciences have paved the way to a revolutionary concept, personalized medicine, which does not examine a disease as a generic entity but as a patient as an exclusive universe. Through an innovative approach, personalized medicine aims at providing "tailor-made" healthcare, adapted to the biological, genetic, environmental and clinical characteristics of each individual.

Unlike traditional medicine, which resorts to standardized protocols to treat groups of patients, personalized medicine recognizes that every person is unique and it develops therapeutic strategies which take into account this uniqueness.

Even today, the doctor seeks a small number of blood tests, observes X-rays on a screen, compares microscopic data and, lastly, entrusts to experience. This is done with the aim of integrating familiarity, sex, age, and physical constitution to suggest a probably effective therapy, as it was previously tested in similar populations.

Let's ask ourselves what would it happen in a world in which a doctor had access to a virtual archive that stores billions of medical, genetic and metabolic histories, originating from different parts of the world? The doctor may, not only identify the disease, but also understand how it develops in the context of that patient. All this data represents an infinite mosaic composed of billions of colorful tiles, each of which represents a fragment of information: heart rate, the sequence of a gene, blood sugar levels recorded at a specific moment, stress levels, radiological images, adverse reactions, intolerances. Separately, these fragments are insignificant and chaotic, but united, they create a vivid and complex image, that of human health. This data will allow us to predict not only what treatment will work better, but also what dosage will be optimal to minimize side effects.

This level of complexity exceeds the human analysis capability and that of traditional calculations. Only with the use of AI, the data gathered may be analyzed in ways you have never imagined: AI is the tool that allows their interpretation as it does not just process information, but it "learns", analyzing complex patterns and forecasting based on correlations that are invisible to the human eye.

AI represents one of the most revolutionary advancements of our time.

Born from the desire to replicate the human ability to learn, discuss and solve problems, AI answers three great needs today: automize complex tasks – that is streamline calculations and decisions which would, otherwise, require enormous human efforts; address unsolvable problems; analyze a quantity of data and models that go beyond the human cognitive capability and increase efficiency of operations, making operations faster and more precise, which would, otherwise, be slow and prone to errors if done manually. We should think of the first human genome which required 13 years of work and three billion dollars. Today, thanks to AI, the sequencing of the human genome requires less than 24 hours at the cost of a few hundred euros.

The use of AI is necessary as the use of new sciences on large scale generates an impressive amount of data: in the European "Cancer Genome" project, genetic and clinical data have been collected generating 20 petabytes of data, that is 20 million gigabytes. Considering that a petabyte can hold 200,000 HD movies, it would be like watching movies for 400 consecutive years.

AI has already entered our lives forcefully for a few years. Analyzing data on news, travel movements and real time health reports, the Canadian platform BlueDot, was one of the first to report an unusual outbreak of pneumonia in Wuhan, China, in December 2019. It would later become the largest pandemic of the modern era. In the midst of the pandemic, AI has, then, supported the development of vaccine, accelerating the design of lipid nanoparticles that carry mRNA. Still, AI has been used to predict the distribution of respirators in a geographically affected area to avoid wasting valuable resources; an AI-based ChatBot has helped thousands of people in the rural areas of Korea to decide if the symptoms required hospitalization and, to stay closer to us, the IMMUNI app was based on an AI model.

It becomes evident that AI is much more that a new medical technology: it is a bridge between the complexity of biology viewed as a whole and the simplicity of personalized treatments.

A futuristic example: molecular hospital

Let's imagine a future not too far away in which a person with a genetic predisposition to diabetes will no longer have to wait to develop the disease. After a simple blood test, a genomic and proteomic scan, and an algorithm based on metadata, an individual profile could be built to compare with millions of similar profiles in a few minutes. If, despite everything, early alterations in metabolism occur, so that the onset of diabetic disease can be identified, a "molecular laboratory" could collect a sample to monitor changes in real-time. Every therapeutic decision could be adjusted based on the body responses ensuring prompt and highly targeted interventions. Looking forward, the future of biology seems to be hanging between science and imagination: the next frontier will be synthetic biology with the ability to design artificial cells and tissues in order to regenerate damaged organs or treat incurable diseases and, why not, the application of omic sciences in the space where astronauts could receive personalized treatments to face the effects of the absence of gravity.

## Is IA human and democratic?

Over the last century, modern healthcare systems have represented one of the most important achievements for the humanity, transforming health into a universal right. However, this aspiration nowadays clashes with a complex reality: the progressive increase in costs, growing disparities, and the pressure of new global challenges such as population ageing and climate crisis. The deep crisis that healthcare systems are going through is not only economic but also structural, ethical and technological. Therefore, priorities and strategies for the future need to be rethought.

In 1978, when Tina Anselmi submitted to the Houses the project of a new national healthcare system, she described the principles on which modern medical care would be based on: comprehensiveness of services, universality of recipients, equality of treatments, respect for dignity and freedom of the person. That system has entered into a crisis.

The first and most evident critical factor of the generalist systems is the ageing of the population. In developed countries, the increase in life expectancy has led to an exponential increase in chronic diseases, such as diabetes, Alzheimer and cardiovascular diseases. These conditions require long-term treatments and a financial and organizational effort that healthcare systems, which are often designed to manage acute conditions, are not equipped to address. Today the elderly consume a significant share of the healthcare resources of industrialized countries, in some cases up to 60%. In addition to this, there is the explosion in technological innovation costs. Gene therapies, biological drugs and personalized medicine promise increasingly effective treatments, but with costs that can reach unimaginable figures.

This scenario creates an ethical dilemma: how to distribute limited resources equally without sacrificing the access to treatment for most of the population? Moreover, pharmaceutical companies, which are often driven by the logic of profit, make it more and more difficult to balance innovation and accessibility.

A tangible example is represented by the spinal muscular atrophy therapy, a genetic neuromuscular disorder that begins in the first months of life and has dramatically disabled effects. Genomics has allowed to identify the defective gene, transcriptomics has explained what was the deficient protein, interactomics and proteomics have clarified the function of the missing protein in the motor function. AI has developed models of interaction, has led the modifications to the experimental protocol, and has defined safety profiles of gene manipulation therapy accelerating the achievement of an effective treatment in a very short time. Treatments today are highly effective and available. We only need one phial to cure these children but ...it costs 2 million euros! So, how is it possible to reconcile new medical technologies with exponential costs of therapies?

The increase in inequalities in access to healthcare is evident to all. While in more industrialized countries the availability of advanced therapies is increasing, in many parts of the world access to basic services is still lacking. Maternal and infant mortality, preventable diseases and the absence of adequate healthcare infrastructures are daily problems for billions of people. However, inequalities are also increasing within developed countries: despite the promise of universality, populations in the southern regions of Italy, immigrant populations, and generally citizens with lower income levels must overcome enormous barriers in accessing services.

Addressing the crisis of modern healthcare systems has required a combination of innovation, political will and global collaboration. One of the priorities should be investment in prevention, which offers high economic and social return. Programs of health education, early diagnosis and promotion of healthy lifestyles can significantly reduce the burden of chronic diseases.

Technology is often seen as a source of costs, instead it can be part of the solution. Telemedicine and AI offer opportunities to improve efficiency, reduce costs and ensure broader access to healthcare services. However, it is necessary to ensure that these innovations are distributed equally and do not create further barriers to more vulnerable populations.

A mindful approach to AI usage in medicine requires a careful reflection that embraces the fundamental values of medical practice and the implications of technology in society. One crucial aspect concerns the respect for the principles of autonomy, justice and solidarity. AI should never replace human decision-making ability, neither that of the doctor nor that of the patient, but rather it should act as a tool that expands the cognitive and operational capabilities of human beings. This implies that any decision taken with the help of an algorithm must be transparent, comprehensible and subject to the critical judgment of aqualified healthcare professional that can guarantee the centrality of the person in the entire treatment process.

Second, transparency of algorithms is another strategically important issue. Many AI systems, specifically those based on deep-learning, operate as "black boxes". This means that decision-making processes whose internal logics are not easily comprehensible, not even by the developers themselves. This opacity raises questions about trust that we can place in a diagnosis or in a recommendation generated by a machine. It is not ethically acceptable for a technology, no matter how advanced, to impose on the patient or the doctor to place blind trust in it. For this reason it is essential to promote the adoption of global standards that oblige producers of AI systems not only to document and explain clearly what are the criteria used by the algorithms to make decisions, but also subject them to independent controls and audits.

Third, one additional challenge is represented by the tendency of algorithms to reproduce the errors present in the data with which they were trained. It is well known that many datasets used in healthcare mirror pre-existing disparities in the population or in medical practices, penalizing vulnerable groups such as women or ethnic minorities. A striking example is represented by the algorithms used to estimate cardiovascular risks. In fact, in the past these algorithms underestimated the risks for women because they were primarily based on data collected predominantly from male samples. This dynamic reproduces and amplifies the inequalities that already exist, making it necessary to intervene in order to ensure that the data used to train the models are representative of demographic and clinic diversity. However, the balance between bias correction and statistical integrity is a technical and bioethical challenge that is not easily solved.

Privacy and data protection represent an additional and particularly delicate area in the discussion of its real applicability. AI systems in medicine require the processing of large amounts of sensitive data, such as healthcare, genetic and clinical information. However, the use of such data must be in compliance with strict standards that protect patient rights, ensuring that their consent is informed and authentic. This requires greater transparency in the use of data and the adoption of innovative technological solutions, such as federated learning. It allows training algorithms directly where the

data were generated, without transferring them to a central server. This approach minimizes risks of privacy violation and ensures an ethical use of medical information. One of the most relevant criticisms that can be mentioned to continue, and which explains most of the suspicion towards the application of AI on a large scale in medicine is the doctor-patient relationship. The automation of many functions traditionally developed by doctors, such as diagnosis or monitoring, could erode the human aspect of medicine based on empathy, listening and mutual trust. A chatbot, no matter how sophisticated, will never be able to grasp the emotional nuances of a patient or to comprehend the cultural and personal context in which a disease is developed. Therefore, AI should be seen as a complimentary tool, not a substitute for the role of the doctor, ensuring that the human relationship remains the focal point of a medical experience. In this perspective, AI should strengthen the doctor's ability to offer personalized treatments and improve communication with the patient, rather than transforming medicine in a mechanical process.

Medical-legal aspects are yet an additional issue that will need to be addressed and regulated: who should be considered responsible if an AI system makes a mistake: the doctor who used the system, the hospital that adopted it, or the company that developed it? The answer is not simple and requires a new conception of shared responsibility, in which the different actors involved have clear and well-defined obligations. It is necessary to develop a regulatory framework that protects patients' rights without discouraging innovation, while ensuring that doctors can exercise critical control on the decisions taken by intelligent systems.

Finally, human autonomy issue deserves a thorough reflection. Excessive trust in AI systems may lead to a progressive flattening of clinical competencies of doctors, that is to the reduction of their ability to exercise critical thinking and make autonomous decisions. Therefore, it is essential to ensure that AI is designed in a way that supports and does not replace human decision-making autonomy. In this perspective, research in the field of Explainable AI, which aims to make algorithms more interpretable and understandable, represents a crucial step in balancing automation with the critical ability of healthcare professionals.

Ethical and bio-ethical dialogue on AI in medicine cannot be limited to a mere technical analysis of its applications, but must embrace a broader vision, placing the human being, their rights and their dignity at the center. Only through a balanced approach that combines innovation and responsibility will it be possible to build a future in which artificial intelligence truly contributes to the common good.

I strongly believe that introducing AI in medicine is helping doctors and healthcare professionals improve the health care system and that it has the potential to further improve it in the near future. Just as the microscope has allowed doctors to see the invisible, AI can transform medicine, making visible those connections and solutions that today are not caught even to the most experienced eye.

We will probably learn to collaborate with these technologies as they develop and, in a way, we will learn alongside them. AI will not replace a doctor, but it will help us perform our work more effectively, leaving more time for that unique property that makes the healthcare profession so fulfilling and valuable: human interaction.

It is not about fearing that AI will transform our profession into an "artificial medicine", but rather hoping that it will transform it into "intelligent medicine". In order to do so, it is necessary to train a new generation of doctors and researchers who are capable of leading this transformation, towards an integrated multidisciplinary approach that includes all the specialists involved in the diagnostic and therapeutic process, with the goal of optimizing the personalization of the care pathway. The task is complex, but it will be possible to carry it forward provided that our young doctors have been trained to use, recognize and master a language with which they will communicate with the world.