Introduction: Trends, Puzzles, and Hopes for the Future of Healthcare

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Abstract

This book is being published at a time when the collective attention of the world has been focused, for more than 2 years, on the coronavirus pandemic. The interrelatedness of various facets of biomedicine (whether scientific, societal, political, legal, or cultural) has been vividly illustrated to health practitioners, researchers, and the public at large—often on a very personal level. It is now manifestly obvious to many that planning for the future of clinical and experimental medicine is a must. Although the task of predicting the exact trajectory of any profession might be in vain, it is essential that one at least looks at past and current trends in order to envision future scenarios and plan for them.

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We can thus shape our *expectations* about how the various threads of biomedicine could develop; these could then inform our preparedness.

The chapters in this volume each cover one or more of four general themes. First, there is the rapid pace and ubiquity of technological advances in areas such as artificial intelligence (AI), machine learning, additive manufacturing, and wearable electronics. Second, there is the theme of healthy aging, longevity, and the management of chronic diseases. Third, there are the ethical dimensions of medical decisions. And fourth, there is the notion of uncertainty in various domains of medical knowledge and its mitigation and translation into clinical practice. This introductory chapter is meant to provide a broader context for the book, providing an up-to-date analysis of current trends and areas that deserve our attention over the next several years.

1 The Essentials

A commentary on the future of healthcare cannot begin without stating the obvious: the essentials of life must first be in place. These essentials include access to safe drinking water and nutrition of suitable quantity and quality. The essentials also include the broader topics of climate change, air pollution, and environmental damage (Bernstein et al., 2022; Chase et al., 2022; Lin et al., 2021a). On this topic, *Thomas Spittler* and *Helana Lutfi* write about "Innovations for Sustainable Healthcare" in Chap. "Innovations for Sustainable Healthcare".

Other layers of healthcare essentials pertain to improving child health and ending preventable deaths in the very young (Perin et al., 2021), addressing inequities in birth registrations around the globe (Bhatia et al., 2019), and providing widespread, inclusive, and affordable access to healthcare and medicine, such as ready access to insulin (Sharma & Kaplan, 2021). This is why an underlying theme of discussions about future trajectories in biomedicine should always be health equity, understood as the "absence of unfair, avoidable and remediable differences in health status among groups of people" (WHO, 2021, p. 2).[1]

Medically, perhaps one of the most (if not the most) pressing dangers over the coming years is the threat from antimicrobial resistance or AMR (Kirchhelle, 2018; Kwon & Powderly, 2021). The most recent comprehensive analysis based on data from 2019 paints an alarming picture: "there were an estimated 4.95 million (3.62–6.57) deaths associated with bacterial AMR in 2019, including 1.27 million (95% [uncertainty interval] 0.911–1.71) deaths attributable to bacterial AMR" (Antimicrobial Resistance Collaborators, 2022). Although various novel solutions are being explored (Ardell & Kryazhimskiy, 2021; Atanasov et al., 2021; Brives & Pourraz, 2020; Deghelt & Collet, 2022; Durand-Reville et al., 2021; Huynh &

[1] For the topic of universal health coverage, see The Lancet (2021).

Wood, 2021; Kaplan et al., 2021; Larsen et al., 2022; Leimer et al., 2021; Miethke et al., 2021; Mitcheltree et al., 2021; Vandenbroucke-Grauls & Kluytmans, 2022; Tibbits et al., 2022; Wang et al., 2022), much more urgent and widespread attention needs to be directed at the global problem of AMR. Parallel to AMR, antifungal drug resistance also poses a global challenge in need of serious research and policy investment (MacAlpine et al., 2021; Revie et al., 2018; Rocheleau, 2022).

2 Longevity and Aging

Notwithstanding variations in local patterns and projections (Finkelstein et al., 2021; Janssen et al., 2021; Livingston et al., 2020), humans now generally live longer than in the past. This could be due to many factors, such as public health campaigns, increased hygiene, antibiotics, and so on. As Steven Johnson (2021) points out, "during the century since the end of the Great Influenza outbreak [1918–1920], the average human life span has doubled." Increased longevity has brought about changes in the leading causes of mortality around the world. For example, the ten leading causes of death in 2020 in the United States comprised the following proportions of the total number of deaths attributed to those ten causes (2,506,540): heart disease (28%), cancer (24%), COVID-19 (14%), accidents (unintentional injuries) (8%), stroke (cerebrovascular diseases) (6%), chronic lower respiratory diseases (6%), Alzheimer's disease (5%), diabetes (4%), influenza and pneumonia (2%), and nephritis, nephrotic syndrome, and nephrosis (2%) (CDC National Center for Health Statistics, 2020). A decade earlier, the ten leading causes and their proportions (out of a total of 1,852,349 cases) were as follows: heart disease (32%); cancer (31%); chronic lower respiratory diseases (7%); stroke (cerebrovascular diseases) (7%); accidents (unintentional injuries) (7%); Alzheimer's disease (5%); diabetes (4%); nephritis, nephrotic syndrome, and nephrosis (3%); influenza and pneumonia (3%); and intentional self-harm (suicide) (2%) (Heron, 2013, p. 9).

Each one of these categories has seen impressive research advances in the past few years. For instance, one could point to cancer immunotherapy (Ochoa de Olza, 2021; Ravaud, 2021; Sriram et al., 2021) and the strides toward understanding the mechanisms of tumor immune evasion (Baldwin & Gattinoni, 2022; Kaufman, 2021; Saha et al., 2022; Zhang et al., 2021). There have also been substantial reductions in cervical cancer rates due to human papillomavirus vaccinations (Falcaro et al., 2021). For type 1 diabetes (100 years after the discovery of insulin), stem cell-based islet replacement therapy is progressing (de Koning & Carlotti, 2021; Ramzy et al., 2021), and there have been successful gene therapies for monogenic conditions, such as sickle cell disease and β-thalassemia (Esrick et al., 2021; Frangoul et al., 2021) or rare liver disease (Kaiser, 2021a). However, this success has been checkered in the case of conditions such as Huntington's disease (Kwon, 2021a). Highly targeted gene delivery techniques are also advancing rapidly (Tabebordbar et al., 2021). *Maryam Parhizkar* and *Dimitrios Tsaoulidis* describe these and other approaches in depth in "The Outlook for Novel Pharmaceutics" (Chap. "The Outlook for Novel Pharmaceutics").

The topic of aging and longevity is itself a very active area. Researchers are learning about the biology of lifespan by studying bats, whales, naked mole rats, elephants, and albatrosses, among other species (Austad & Finch, 2022; Belzile et al., 2022; da Silva et al., 2022; Eisenstein, 2022; Holmes, 2021; Kaya et al., 2021; Kolora et al., 2021; Lu et al., 2021a; Reinke et al., 2022). A Seychelles giant tortoise (called "Jonathan," hatched c. 1832) is currently the oldest known living land animal. The microscopic multicellular animals, bdelloid rotifers, have been reported to survive for extremely long periods in an Arctic permafrost environment (Shmakova et al., 2021). There are also studies of the ability of tardigrades to withstand conditions that are otherwise too extreme for other living things (Hashimoto et al., 2016; Neves et al., 2020) and the extreme longevity of the plant species *Welwitschia mirabilis* (Wan et al., 2021).

There are now different biotech start-ups focused on antiaging therapies (Dolgin, 2021; Regalado, 2021). In the laboratory and beyond, the underlying biology of aging in humans and other species is under intense scrutiny (Augustin & Kipnis, 2021; Fan et al., 2017; Garcia et al., 2021b; Gorbunova et al., 2021; Grunewald et al., 2021; Hägg & Jylhävä, 2021; Lengefeld et al., 2021; Lin et al., 2021b; Lu et al., 2021c; Martinez-Miguel et al., 2021; Sato et al., 2022; Stein et al., 2022; Vidal-Pineiro et al., 2021; Wang & Blau, 2021; Wiley & Campisi, 2021). These projects pursue many different exciting threads, including the so-called "senotherapeutics" (Robbins et al., 2021); the relationship between aging and the microbiome (Rimal & Patterson, 2021; Sato et al., 2021; Shukla et al., 2021); biological constraints on the rate of human aging (Colchero et al., 2021); the effects of physical activity on aging (Horowitz et al., 2020; Lieberman et al., 2021); the effect of dietary polyamines (Schroeder et al., 2021), fasting (Helfand & de Cabo, 2021; Ulgherait et al., 2021), and the efficacy of supposed "antiaging diets" in general (Lee et al., 2021; Longo & Anderson, 2022); the role of the immune system (Yousefzadeh et al., 2021); the social aspects of healthy aging (Charles et al., 2021; Hanc, 2021; Savage, 2022); and the economics of treatments that target aging (Scott et al., 2021).

Within the context of longevity and aging research, there is also intense focus on understanding conditions that are all grouped on the spectrum of dementias and Alzheimer's-like presentations (Mesulam et al., 2021). *Sepehr Ehsani* delves into the theoretical aspects of Alzheimer's disease research in "New Horizons in Studying the Cellular Mechanisms of Alzheimer's Disease" (Chap. "New Horizons in Studying the Cellular Mechanisms of Alzheimer's Disease").

The leading causes of death vary widely across both local and global regions. As an important case in point, it is estimated that neglected tropical diseases "affect more than one billion people globally" (Ackley et al., 2021). Tuberculosis continues to pose a significant burden, particularly in low- and middle-income countries (Jesus et al., 2022; Wang et al., 2021). Dengue fever, a neglected tropical disease, has recently seen advances on the therapeutic front (Biering & Harris, 2021; Kaptein et al., 2021). But in the case of malaria, we may be facing the prospect of artemisinin-resistant *Plasmodium falciparum* (Balikagala et al., 2021; White, 2021).

3 The Technological Turn

There is a dizzying pace to the addition of new technological tools in both the laboratory and the clinic. Various AI and related approaches are being used in medicinal chemistry and for drug repurposing (Carvalho et al., 2022; Fang et al., 2021), in structural biology to help with predicting protein and RNA folds (Baek et al., 2021; Berg, 2021; Nature Editors, 2021a; Weeks, 2021), in analysis of electronic health records (Ehsani et al., 2008; Murray et al., 2021), in the field of pathology (Lu et al., 2021b), and in the diagnosis of Alzheimer's disease (Sohn, 2022). In this volume, *Amir Feizi* and *Jahir M. Gutierrez* write on "Harnessing AI and Genomics to Accelerate Drug Discovery" (Chap. "Harnessing AI and Genomics to Accelerate Drug Discovery"), *Tim-Rasmus Kiehl* discusses "Digital and Computational Pathology: A Specialty Reimagined" (Chap. "Digital and Computational Pathology: A Specialty Reimagined"), and *Kevin Lano*, *Sobhan Y. Tehrani*, *Mohammad Umar,* and *Lyan Alwakeel* expound on "Using Artificial Intelligence for the Specification of m-Health and e-Health Systems" (Chap. "Using Artificial Intelligence for the Specification").

What exactly is AI? And what can the various tools categorized under the "AI" label (e.g., machine learning, deep learning, and artificial neural networks) actually do? This is an important issue. For instance, the machine learning pioneer Michael I. Jordan cautions that "while the science-fiction discussions about AI and super intelligence are fun, they are a distraction", and that "there's not been enough focus on the real problem, which is building planetary-scale machine learning–based systems that actually work, deliver value to humans, and do not amplify inequities" (quoted in Pretz, 2021b). In "An Assessment of the AI Regulation Proposed by the European Commission" (Chap. "An Assessment of the AI Regulation Proposed by the European Commission"), *Patrick Glauner* discusses the usual conflation that occurs between AI and software that performs statistical tasks.

AI approaches, such as deep learning, face some basic obstacles. For instance, "it has been claimed that deep learning is untrustworthy because it is not explainable—and unsuitable for some applications because it can experience catastrophic forgetting," and hence it might be "risky to use deep learning on any life-or-death application, such as a medical one" (Pretz, 2021a). Commentators have also noted the questionable utility of many AI tools built to deal with the COVID-19 pandemic (Heaven, 2021; Roberts et al., 2021). For these and other reasons, a subfield within AI research has emerged that tries to move toward "explainable AI" (see, for example, Lauritsen et al., 2020 and Lundberg et al., 2020). At the same time, concerns remain about how explainable "black box" algorithms can ultimately be (Babic et al., 2021).

Moving beyond the realm of AI, the expanded technological toolbox that has been in the spotlight in recent years includes additive manufacturing (Gu et al., 2021), robotic surgery (Metz, 2021), robotic manufacturing platforms for cell therapies (Winn, 2021), exoskeletons that can remove "kinetic energy during the swing period of the gait cycle [and reduce] the metabolic cost of walking" (Shepertycky et al., 2021, p. 957), the application of optogenetics in vision restoration (Sahel et al., 2021), artificial kidneys and miniaturized dialysis (Gura et al., 2016; Huff, 2020), artificial pancreas systems (Ware et al., 2022), functional human organoids (Eicher et al., 2022), modern microscopy techniques such as cryo-electron tomography (D. Kwon, 2021b), organ-on-chip systems for novel compound screenings (Roth & MPS-WS Berlin 2019, 2021), ultrasound-on-chip platforms for medical imaging (Rothberg et al., 2021), inertial microfluidic platforms for sepsis monitoring (Jeon et al., 2021), wearable optically pumped magnetometers (Tierney et al., 2019), wearable sensors for physiological monitoring (Dunn et al., 2021), and DNA-hydrogel-based wound infection sensors (Xiong et al., 2021).

In relation to these novel technological areas, *Jens Eckstein* writes about “Mobile Sensors in Healthcare: Technical, Ethical, and Medical Aspects” (Chap. “Mobile Sensors in Healthcare: Technical, Ethical, and Medical Aspects”); *Anna Kasparbauer*, *Veronika Reisner*, *Cosima Schenk*, *Anna Glas*, *Helana Lutfi*, *Oscar Blanco*, and *Thomas Spittler* on “Sensor Devices, the Source of Innovative Therapy and Prevention” (Chap. “Sensor Devices, the Source of Innovative Therapy and Prevention”); *Estefanía Lang*, *Alice Martin,* and *Elien Wallaeys* on “Teledermatology: Current Indications and Future Perspectives” (Chap. “Teledermatology: Current Indications and Future Perspectives”); *Florian M. Thieringer*, *Philipp Honigmann* and *Neha Sharma* on “Medical Additive Manufacturing in Surgery – Translating Innovation to the Point-of-Care” (Chap. “Medical Additive Manufacturing in Surgery: Translating Innovation to the Point-of-Care”); and *Andy W. K. Yeung* and *Michael M. Bornstein* on “Personalized Dental Medicine with Specific Focus on the Use of Data from Diagnostic Dental Imaging” (Chap. “Personalized Dental Medicine with Specific Focus on the Use of Data fromDiagnostic Dental Imaging”).

It is essential that we carefully consider the responsibilities and ethical questions that arise when specific technologies are put into actual practice (Chiang et al., 2021). *Hannah Howland*, *Vadim Keyser,* and *Farzad Mahootian* meticulously analyze the web of such responsibilities and considerations in “Redesigning Relations: Coordinating Machine Learning Variables and Sociobuilt Contexts in COVID-19 and Beyond” (Chap. “Redesigning Relations: Coordinating Machine Learning Variables and Sociobuilt Contexts in COVID-19 and Beyond”). *Masoud Ghalambor* explains the context of “Ethical Challenges in Applying New Technologies in Orthopedic Surgery” (Chap. “Ethical Challenges in Applying New Technologies in Orthopedic Surgery”). In doing so, he reminds us to ask the following questions: Does a new technology solve a problem that cannot be solved with our available tools? And are we solving a problem more effectively?

The technological turn and the involvement of myriad corporations, companies, and start-ups in biomedicine is so significant that commentators now talk of the “commercial determinants of health” (Kickbusch et al., 2016). The pitfalls associated with the long-term consequences of monetized user-generated personal (health) data require discussions among all stakeholders (see, for example, Sharon & Lucivero, 2019). So, too, does the question of the ethics of patents and their effects on creativity in different areas of biomedicine (Moser, 2016; Nature Editors, 2021b, c). *Anna Katharina Heide* provides a detailed outline of “Patents on Inventions

Involving AI in the Life Sciences and Healthcare” in Chap. “Patents on Inventions Involving AI in the Life Sciences and Healthcare”. Furthermore, as healthcare technologies evolve, the concomitant adaptation of robust, timely, and efficient regulations that protect patients’ health and privacy is vital (Avin et al., 2021; Marks, 2021; McGraw & Mandl, 2021).

4 Uncertainty Everywhere

“Progress” in biomedicine and healthcare can be defined using several components. Two of these components could be the *augmentation of our understanding* of the underlying biology of medical diagnoses and phenomena and the *implementation* of this augmented understanding. Bearing these two prongs of “progress” in mind, we can see how progress ebbs and flows. For example, understanding a new facet of cancer metastasis can lead to both new questions and new unappreciated unknowns. Similarly, implementing a new treatment program can lead to unexpected consequences. As such, the twin tasks of dealing with uncertainty and mitigating its effects are crucial in biomedicine and healthcare.

Uncertainty can come in different shapes and forms. For example, there are “different types of uncertainty involved in diagnostic and prognostic judgments” (Chiffi & Zanotti, 2017, p. 928). There is also the uncertainty that results when implementing the outcomes of clinical trials, such as in the case of cancer screening programs (Menon et al., 2021) (see also Couzin-Frankel, 2021). Crucially, uncertainty also lies in the nature of the evidence, confirmation, reproducibility, and robustness of laboratory and clinical results (Bird, 2021; Errington et al., 2021a, b; Guttinger & Love, 2019; Kaiser, 2021b; Nature Editors, 2021d; Schupbach, 2018). At a more theoretical level, researchers often encounter uncertainty when making claims of causality and have to navigate between differing conceptions of correlation, association, causation, and so on (e.g., for recent studies on the association of the Epstein–Barr virus with multiple sclerosis, see Bjornevik et al., 2022; for causal claims concerning obesity, energy balance and fat storage, see Ludwig et al., 2021). Finally, more general types of uncertainty can arise at a system level, such as in relation to how hospital systems are funded under different governance models for healthcare (Colmers & Glied, 2021).

In the present volume, *Erman Sozudogru* provides a philosophical analysis of these issues in “Uncertainty in Medicine: An Active Definition” (Chap. “Uncertainty in Medicine: An Active Definition”). *Aaron James Goldman* writes on the “Post-Truth Implications for COVID-Era Healthcare: Verification, Trust, and Vaccine Skepticism” (Chap. “Post-Truth Implications for COVID-Era Healthcare: Verification, Trust, and Vaccine Skepticism”). Given the importance of medical education systems in introducing students to conceptualizations of uncertainty (Steele & Stefánsson, 2021) and heuristics under conditions of limited information and time (Chopra et al., 2021; Li & Colby, 2021; Singh, 2021), *Mark H. Wan* and *Qiu Ning Lee* delve into “The Future of Medical Education” in Chap. “The Future of Medical Education”.

5 Puzzles and Paradoxes

Related to the topic of uncertainty is the fact that future healthcare professionals and researchers will have to deal with the various puzzles, paradoxes, and unresolved projects that are handed down to them. These range from issues at the subcellular level all the way up to the anatomical and population-wide levels. Examples of such issues are provided below:

1. Deciphering the nuances of the array of non-protein-coding segments in the genome (Leypold & Speicher, 2021), mapping the spectrum of sequence variations relative to reference human genomes (Aganezov et al., 2022; Pennisi, 2022; Vollger et al., 2022), and completing the full sequence of the Y chromosome (Nurk et al., 2022; Reardon, 2021).
2. Studying the “nongenetic” functions of the genome (Bustin & Misteli, 2016).
3. Better understanding the basics of protein biochemistry (including its interactions with water molecules) and protein–protein interaction at the amino-acid level (Fass & Semenov, 2021; Hosseinizadeh et al., 2021; Ourmazd, 2019; Pullanchery et al., 2021; Wensien et al., 2021).
4. Better understanding the intricate interactions of genes and the environment (e.g., see Garcia et al., 2021a).
5. Better understanding the nature of transcriptional noise in gene expression (Ham et al., 2021).
6. Studying extant puzzles in evolutionary biology (Lucas et al., 2020).
7. Studying species-wide mechanisms of organ and tissue repair and regeneration (Griffin et al., 2021; Murugan et al., 2022).
8. Shedding light on “idiopathic” conditions (see Richeldi et al., 2017) and conditions such as sporadic Creutzfeldt-Jakob disease (Mead, 2021).
9. Augmenting efforts at systematizing correct diagnoses and disease classifications (Liu et al., 2021; Nassiri et al., 2021) and better understanding the spectrum of rare diseases (Genomes Project Pilot Investigators et al., 2021). Indeed, many “rarer” conditions may often get diagnosed as a more common disease, which means the patient never receives the right kind of care and treatment. The “Undiagnosed Diseases Program” at the US National Institutes of Health (Macnamara et al., 2020) is an example of a creative approach to systematically tackling this issue.
10. Better understanding the cellular mechanisms of metastasis (Dai et al., 2022; Diamantopoulou et al., 2022; Fares et al., 2020; Pascual et al., 2021), the spontaneous regression of cancer (Brodeur, 2018; Colom et al., 2021; Diede, 2014; Riedmeier et al., 2021), natural cancer resistance (Vincze et al., 2022), and seasonal patterns of presentation of cancers and other diseases (Ehsani et al., 2009).
11. Akin to AMR, deciphering resistance mechanisms toward novel cancer treatments (Awad et al., 2021) and further exploring creative treatment modalities such as oncolytic virotherapy (Melcher et al., 2021).

12. Finding the means to analytically determine drug–drug interactions and what one might call the "polymechanisms" of action of novel compounds (Abolhassani et al., 2021; Wolff et al., 2021; Zhang et al., 2016). In this context, consider that 50 new drugs were approved by the FDA in 2021; indeed, the "5-year average sits at 51 drugs per year [and] a decade ago, it was 24 drugs per year" (Mullard, 2022).
13. Better understanding placebo and nocebo effects (Crawford et al., 2021; Haas et al., 2022; Resnick, 2021).
14. In the context of neurotrauma (traumatic spinal cord injury), studying what is called the neuroanatomical–functional paradox (Fouad et al., 2021).
15. Deeply exploring the fields of neuroscience, cognitive science, and perception, which are rife with puzzles (Ekroll et al., 2016; Gallistel, 2021; Hulse et al., 2021; Langille & Gallistel, 2020; Potrich et al., 2022; Robinson & Brandon, 2021). Let us take one example: when writing on motor planning, Emilio Bizzi and Robert Ajemian pose the following question: "how is an evanescent wish to move translated into a concrete action? This simple question and puzzling miracle remains a focal point of motor systems neuroscience" (Bizzi & Ajemian, 2020, p. 1815). They further note that "nature needed millions of years to achieve the sublime level of performance of a tennis player or a gymnast, a level of adroitness that far surpasses state-of-the-art robotics capabilities. Somehow, nature has generated a system that, with variations (a cerebral cortex is not present in all vertebrates), works for the entire universe of species" (Bizzi & Ajemian, 2020, p. 1821).
16. Finally, bridging "alternative" approaches to healthcare with what may be considered "mainstream" disciplines. These approaches could include the effects of different nutritional components and regimens (Guasch-Ferre et al., 2022; Neal et al., 2021), neurofeedback methods for psychiatric conditions (Dudek & Dodell-Feder, 2021), and studying the modes of action of traditional medicines (Lin et al., 2021c; Molimau-Samasoni et al., 2021; Shi et al., 2021).

While tackling puzzles such as these and finding innovative solutions, it may help to remember that, in the words of Chuck Hull, "when you're trying to do something new, very few people see the wisdom of it" (quoted in Brooks, 2016, p. 41). Taking this reality in stride, innovation also requires risk-taking and persistence. Francis Collins, the former director of the US National Institutes of Health (NIH), noted that "hypothesis-driven research is the bedrock of NIH's success. Thus, one should prioritize support of risk-taking research and pay less attention to preliminary data and more to the potential importance of a premise" (Collins, 2022, p. 123).

6 Hopes

More than a century ago, before the advent of the new relativistic physics, a prevailing thought in the physical sciences was that most fundamental issues in the field had been resolved. For example, the physicist Albert A. Michelson remarked the following:

> While it is never safe to affirm that the future of Physical Science has no marvels in store even more astonishing than those of the past, it seems probable that most of the grand underlying principles have been firmly established and that further advances are to be sought chiefly in the rigorous application of these principles to all the phenomena which come under our notice. It is here that the science of measurement shows its importance—where quantitative work is more to be desired than qualitative work. An eminent physicist remarked that the future truths of physical science are to be looked for in the sixth place of decimals. (Michelson, 1896, p. 159)

We should not make the same mistake in the realm of biomedicine, thinking that all the fundamental cellular and molecular "principles" have been discovered. Moreover, qualitative and quantitative work in biomedicine should go hand in hand. This is why much effort should now be devoted to theoretical and philosophical biology and to the re-amalgamation of theory and experiment in the life sciences (Ehsani, 2020; Gershman et al., 2021). Different areas of philosophy could have widespread and/or specific applications to biomedical research. There are too many cases to enumerate, but examples range from studies around the idea of a "universal genome" in evolutionary biology (Sherman, 2007) and "genomically minimal" cells (Pelletier et al., 2021) to generating diagnostic hypotheses at the clinical level (Stanley & Nyrup, 2020), applying Kant's "non-pathological definition of mental illness" to mental health research (Thomason, 2021, p. 189), and determining what the so-called "ends of medicine" could and/or should be (MacDougall, 2020).

Realizing the above path is a major hope. Another hope—one of no lesser significance—is that areas traditionally relegated somewhat to the periphery of attention in both the laboratory and the clinic are integrated more fully into future research paradigms. The first such area could be that of palliative care (Mathews & Zimmermann, 2020). The second is the management of chronic pain (Donnelly et al., 2020). For the third, we need a greater focus in medical schools on the "medical philosophy" of physician-/surgeon-trainees (akin to how teachers and lecturers are asked to provide a "teaching philosophy" statement when applying for a job). This is of importance because a physician's personal philosophy toward their job manifests itself in all domains of their profession. Finally, we need to pay equal attention to what patients expect from the healthcare system along with their own roles in the diagnoses and treatments they receive and the medical research in which they participate (Feinsinger et al., 2022; Servick, 2022).

A further hope to mention here is greater emphasis on the question of "medicalization." "Is old age, for example, a medical condition? Should it be?," asks Julian Sheather (2019, p. 88). Moreover, for various mental health conditions, what should be the first line of treatment in each case, and why (Callesen et al., 2020; Nakao et al., 2021)?

In relation to some of these areas, *Julia Plugmann* and *Philipp Plugmann* write about "The Future Open Innovation Approach in Health Care Needs Patients' Support" (Chap. "The Future Open Innovation Approach in Health Care Needs Patients' Support"), *Horst Kunhardt* on "Modern Home Care: A Glimpse into the

Future of Patient-Centered Healthcare Systems" (Chap. "Modern Home Care: A Glimpse into the Future of Patient-Cen-tered Healthcare Systems"), and *Kristin Beizai*, *Ashley Stone,* and *Yash Joshi* on "Innovations in Psychiatric Care Models: Lessons from the Past to inform the Future" (Chap. "Innovations in Psychiatric Care Models: Lessons from the Past to Inform the Future").

In closing, we should note that the road to progress in biomedicine does not have to be convoluted and challenging. Practicable solutions often require the initial step of a simple and theoretically sound enunciation of the problem at hand, followed by rational inquiry. It is helpful to always remain cognizant of puzzles posed by seemingly mundane and at-first unrelated observations. Take, for example, the intriguing question of whether understanding the physiology behind the very high blood pressure of giraffes could aid our understanding of hypertension and cardiovascular problems in people (Aalkjær & Wang, 2021).[2] In all, the adage about the "optimism of the will and pessimism of the intellect" may be the right framework for hoping to build on past successes and to confront the challenges facing biomedicine and healthcare over the next decade.

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[2] See also Gil et al. (2022) for an analogous and intriguing area of investigation with the potential of impacting our understanding of human physiology.

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