‘Positive biology’ as a new paradigm for the medical sciences

Focusing on people who live long, happy, healthy lives might hold the key to improving human well-being

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On 27 April 2009, during a speech at the National Academy of Sciences, US President Barack Obama pledged to invest more than 3% of US GDP in scientific research and development—the amount represented the largest ever investment in research and innovation. However, even a financial investment of such magnitude does not ensure that science is ‘well-ordered’ [1], in the sense that the scientific research that is prioritized aspires to address the most significant challenges and problems for humanity.

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Among the many issues facing society that research must address, improving human health and tackling disease rank high, if not first, on the agenda. Accordingly, a huge fraction of research funding is spent on basic and applied research to further our understanding of the causes of disease and to find new cures and therapies. But is this focus on pathology the most efficient way to conduct research with the aim to improve human health and well-being?

Most of today’s medical research could be called ‘negative biology’. It is conducted in an intellectual framework that presumes that the most important question to answer is: what causes pathology? Disease is its central focus and this explains why medical research and research funding is mainly concerned with trying to understand, prevent and treat specific diseases. The design of the US National Institutes of Health, which is largely composed of individual institutes dedicated

to specific diseases such as cancer, mental illness or infectious diseases, reflects this prevalence of pathology-oriented negative biology.

Positive biology, by contrast, focuses on a different set of questions and priorities. Rather than making pathology and disease the central focus of intellectual efforts and financial investments, positive biology seeks to understand positive phenotypes: why do some individuals live more than a century without ever suffering from the chronic diseases that afflict most humans much earlier in their lives? Why are some individuals more happy, optimistic, talented, or have a better memory than most people? The paradigm of positive biology is based on the insight that the process of evolution by natural selection does not create a perfect organism in terms of life expectancy, resistance to disease or other abilities. Observations of exceptional longevity or superior cognition therefore present fascinating puzzles for positive biology: which biological mechanisms would explain these exemplars of health and well-being? The goal of understanding positive phenotypes is that such knowledge might lead to new interventions that generally improve human well-being. This might be achieved by modulating the rate of ageing or by increasing opportunities for play and joy at all stages of the human lifespan, or by developing pharmaceuticals that safely enhance cognition or positive emotions, and so on.

This is distinct from negative biology, which focuses on the proximate causes of specific diseases, rather than on the evolutionary causes of positive phenotypes. It presumes that health, survival and happiness are the default states and aims to explain the deviations: why do we develop cancer? Why

do we suffer from depression? Why do we develop hypertension? Negative biology therefore faces the laudable but insurmountable task of trying to prevent or cure all disease. This is a costly and ultimately futile endeavour. Eliminating all types of cancer would increase life expectancy in the USA by approximately only three years [2]. Even eliminating cancer as a cause of death would not prevent any of the other chronic diseases of ageing—cardiovascular disease, Alzheimer and Parkinson disease, diabetes and so on—from afflicting the elderly. Moreover, the more than 40 years of ‘war against cancer’ has not defeated a single type of cancer: we still have a long way to go before we can realistically expect to reap the three-year increase in life expectancy that eliminating all cancers could yield.

In fact, negative biology has not yet developed a single cure for any one of the hundreds of chronic diseases that afflict millions of people living today. Of course, it has made significant advances to help prevent and treat chronic disease, but the fixation on pathology has meant that other potential avenues for research have been neglected.

Indeed, a better understanding of exemplars of health and happiness—the goal of positive biology—could create more benefits for humans more quickly and more easily. A drug that would safely mimic the effects of caloric restriction, for instance, might delay, simultaneously, most diseases and afflictions of ageing. It would generate a much greater health dividend for ageing populations than defeating any one specific disease of ageing because slowing down the rate of ageing by seven years would reduce the age-specific risk of death, frailty and disability by about half at every age [3].

Scientists are already making good progress on the project of positive biology, even if the intellectual framework is not yet clearly defined and their topics are rather piecemeal. Richard Miller, for example, a professor of pathology at Michigan University, USA, studies the genetics of ageing in mice and participates in the National Institute of Aging's multi-institutional programme that evaluates the effects of drugs and nutraceuticals on the ageing process in mice. David Sinclair from Harvard University, USA, and others found that the plant compound resveratrol, which is found in the skin of grapes, can modulate the ageing process. Nir Barzilai and colleagues at the Albert Einstein School of Medicine in New York, USA, have conducted genetic research on more than 500 healthy elderly people between the ages of 95 and 112 years. Michael Rose from the University of California, Irvine, USA, has quadrupled the lifespan of fruit flies by delaying the age of reproduction. Finally, the biologist Cynthia Kenyon demonstrated that in *Caenorhabditis elegans*, a single gene can control the ageing process. Any of these research projects could eventually lead to the development of a new drug that retards the ageing process and diminishes the onslaught of chronic diseases that typically afflict humans after their sixth decade of life.

Similarly, a lot of pioneering work is being undertaken in the burgeoning field of 'positive psychology'. Rather than studying why people suffer from mental illnesses such as depression, schizophrenia or ADHD (attention deficit hyperactivity disorder), positive psychology is primarily interested in how to improve the happiness of the 'average' person. Martin Seligman, a psychologist at the University of Pennsylvania, USA, and a pioneer in the field of positive psychology, distinguishes different kinds and levels of happiness [4]. Hedonists who pursue immediate rewards such as the pleasure of buying something or receiving a compliment seek momentary happiness or what Seligman calls 'the pleasant life'. But these pleasures fade quickly and do not leave a lasting impact on subjective well-being. Enduring happiness, by contrast, is realized when we lead a meaningful life. After years spent studying what makes people happy, Seligman contends that it is rooted in attachment to something larger, and the larger the entity to which you attach yourself, the more meaning your life has [4].

This is clearly illustrated by the role of wealth. People often assume that being

richer will mean being happier, yet surveys in many countries indicate that global levels of life satisfaction or happiness have not changed much during the past four decades despite large increases in real income per capita [5]. Most disposable income is spent on consumer goods that do little to actually enhance our well-being.

In a recent study of the daily behaviour of happy people, researchers used an electronically activated recorder to record, and then later classify, participants' daily conversations with others as either 'small talk', that is banal conversations, and 'substantive talk', where meaningful information was exchanged. They found that higher well-being was associated with less small talk and more substantive conversations [6]. While such a study does not establish the truth of Socrates' famous claim that "the unexamined life is not worth living", it does suggest that our need to feel attached to something larger is important to our happiness and well-being. This hypothesis is supported by recent studies on how people spend their money. Researchers from the University of British Columbia and Harvard Business School found that when individuals spend more money on prosocial goals, such as charity, they actually experience greater happiness than when they spend money on consumer products for themselves [7]. Similarly, the psychologist Barbara Fredrickson's research on positive emotions—joy, serenity and gratitude—suggests that these expand cognition and behavioural tendencies [8].

Finally, research on exemplars of resilience, that is, the ability of some people to cope and manage with tragic and traumatic events, could lead to the development of drugs that would increase people's resilience. Avshalom Caspi and colleagues found that individuals with one or two copies of the short allele of the promoter of the 5-HTT serotonin receptor experience more depressive symptoms, diagnosable depression and suicidal thoughts in response to stressful events compared with individuals who are homozygous for the long allele [9].

Cognitive functioning is another central topic of positive biology. What are the genetic and environmental determinants of high IQ, exceptional memory or social intelligence? Barbara Sahakian and colleagues found that the analeptic drug modafinil significantly enhanced performance tests of digit span, visual pattern recognition memory, spatial planning and stop-signal reaction time in healthy volunteers [10]. These

findings of positive biology will eventually give us a better understanding of our human nature than the very limited focus on disease and pathology of negative biology and might then lead to new interventions, environments and attitudes that improve human well-being and happiness.

Negative biology dominates medical research, from the questions researchers tackle to the education of physicians and government regulation of health interventions. The dominance of this approach to the medical sciences presumes that the most important questions concern the causes of pathology rather than the causes of exemplar health and happiness. Positive biology takes a different approach: it does not limit the moral duty to apply knowledge and technology to improve human welfare to only treating specific diseases or impairments. Rather, it works under the assumption that if knowledge and research can improve people's lives, there is a moral duty to advance that knowledge and promote well-being. Nor is positive biology predicated on a sharp distinction between therapy and enhancement. Instead, as the bioethicist John Harris has argued, "the overwhelming moral imperative for both therapy and enhancement is to prevent harm and confer benefit. Bathed in that moral light, it is unimportant whether the protection or benefit conferred is classified as enhancement or improvement, protection or therapy" [11].

Generally, the medical system as a whole could be much more efficient if it concentrated its efforts on making people healthier and happier in the first place instead of its current focus on understanding and treating disease. Advancing the paradigm of positive biology should therefore help the medical sciences transcend the limited perspectives and aspirations of negative biology. Such a paradigm could help the world's population to reap the benefits that new knowledge and technologies can offer in terms of making people healthier and happier. Societies and individuals already seek to achieve these goals: we educate our children to eat healthily and exercise and to develop their social goals to find fulfilment in life. The paradigm of positive biology simply encourages us to make use of the full range of options to realize these goals.

In conclusion, positive biology is not contrary to the goals and aspirations of negative biology. Indeed the two paradigms are often complementary. For example, understanding

why some high-risk individuals, such as sex workers, seem to have an intrinsic resistance to HIV-1 might spur the development of an HIV vaccine [12]. Similarly, understanding human brains with exceptional cognitive functioning might lead to new avenues for developing drugs and therapies against severe cognitive impairment. Understanding exemplars of health could create real benefits for those who are more vulnerable to disease and disability.

CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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