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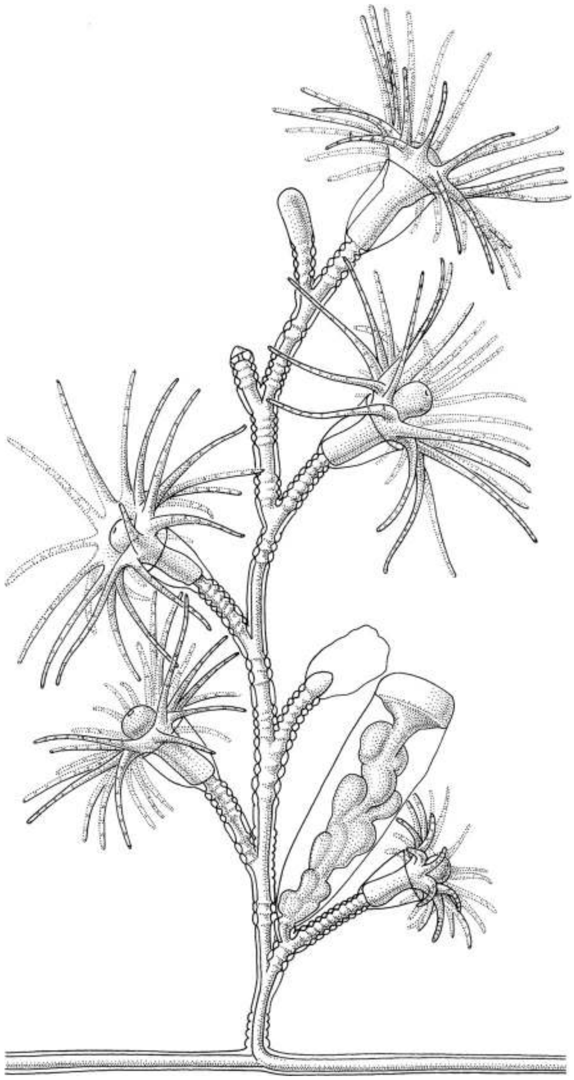
A Cybernetic View of Biological Growth: The Maia Hypothesis

Maia is the story of an idea, and its development into a working hypothesis, that provides a cybernetic interpretation of how growth is controlled. Growth at the lowest level is controlled by regulating the rate of growth. Access to the output of control mechanisms is provided by perturbing the growing organism, and then filtering out the consequences to growth rate. The output of the growth control mechanism is then accessible for interpretation and modelling. Perturbation experiments have been used to provide interpretations of hormesis, the neutralization of inhibitory load and acquired tolerance to toxic inhibition, and catch-up growth. The account begins with an introduction to cybernetics, covering the regulation of growth and population increase in animals and man, and describes this new approach to access the control of growth processes. This book is suitable for postgraduate students of biological cybernetics and researchers of biological growth, endocrinology, population ecology and toxicology.

TONY STEBBING has been at the Plymouth Marine Laboratory (PML) since its inception in 1971. He worked initially to develop bioassay techniques for pollution studies. His later discovery of the stimulatory effect of low concentrations of toxic substances ('hormesis') led him to develop a novel method of accessing the output of growth control mechanisms. The coordination of scientific programmes occupied the later years of his career. He was awarded an Honorary Fellowship from PML, which has given him the opportunity to write this account of his research and its implications.



The marine colonial hydroid *Laomedea flexuosa*, used as a clone in the early experiments described in this book. I thank Peter Stebbing for the drawing; permission to use the image was given by The Royal Society.

A Cybernetic View of Biological Growth

The Maia Hypothesis

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Foreword

Compared with the high-profile discoveries of molecular genetics concerning individual genes and their specific expression at the tissue and organ level, studies of general patterns of growth in living organisms often receive less public attention in the media. Yet an understanding of the processes of biological growth at the level of the individual and in populations of organisms is key to human survival. Uncontrolled growth is a feature of human cancer cells which prejudices survival at the level of the individual, while unchecked growth of global human population density has to be considered against a background of finite limitations of planetary living space and natural resources. Indeed, this book begins with the premise that the basis of all biological growth is exponential, with an inherent tendency for constant doubling with time. A priori, therefore, it is argued that there would be evolutionary adaptive advantage to be gained by the acquisition of mechanisms which induce self-limitation of growth processes and therefore enhance the chances of survival of individuals and populations of organisms, including humans.

The author's interest in these phenomena started when he was studying the biological effects of toxic chemicals discharged into the sea. In laboratory experiments, the growth of simple marine organisms such as hydroid coelenterates was tested in response to the application of various toxins. As expected, growth of the test organisms was inhibited following exposure to high concentrations of chemical toxins such as copper. However, at low concentrations of some normally toxic agents it was found that growth rate was in fact enhanced. This phenomenon, called 'hormesis', was presumed to occur when a naturally occurring growth inhibitory mechanism, which normally modulates a growth promoter, was partially disinhibited. In a practical sense the phenomenon of hormesis demonstrates that the test organisms, and therefore naturally occurring species, may acquire some tolerance to toxic agents. However, in a theoretical sense it permits the development of ideas throughout this book concerning a wide range of biological growth processes which can be analysed from a cybernetic point of view and which are shown to be self-regulatory. Experimental evidence for self-limiting growth, generated by interacting promoter and inhibitory processes, is provided for unicellular and multicellular organisms, leading to the notion of the 'Maia hypothesis', deriving analogously from James Lovelock's grand-scale Gaia hypothesis but named after the Roman goddess of growth, who gave her name to the month of May.

The basic hypothesis is then extended from the physiological level in individual organisms to animal populations which, by analogy, show reduced rates of reproduction induced by negative feedback mechanisms when an animal population threatens to overburden the carrying capacity of its habitat. Finally, developing the concept of population-density control achieved by animal populations in nature, the book turns to the implications for humankind on Earth. It is argued that human overpopulation has been recognised for over a hundred years and is set to continue to increase, notwithstanding a fall in the rate of increase in recent decades. In a naturally occurring situation it is inferred that self-regulatory population density mechanisms would have come into play by now, but it is argued that the extent to which humans have manipulated their environment in recent centuries has overridden the onset of inhibitory population control. Political recognition of the Earth's carrying capacity for the human race is not possible at the present time, but scientific estimates suggest that sustainable population density had already been exceeded by the end of the twentieth century, as evidenced by the critical manifestation of anthropogenic global climate change. On this basis the book raises the challenge for humanity to move towards a stable global population and a steady-state world economy. The challenge is immense and provocative. However, it is argued that on a planet with a seemingly continuously increasing human population and finite global resources, the challenge for human ingenuity is to devise feedback mechanisms which would bring the world population into something like a steady state, or to live with the consequences of uncontrolled growth.

The book has much to offer as a rational exposition in current debates concerning human population density on Earth and the 'belief' that anthropogenic global climate change is a myth.

Emeritus Professor Ernest Naylor
School of Ocean Sciences
Bangor University
Wales

*Preface: 'A fragment of a possible world'**

Anyone who is practically acquainted with scientific work is aware that those who refuse to go beyond the facts, rarely get as far.

Thomas H. Huxley

To give priority to invisible process, rather than tangible structure.

Douglas Hofstadter

This book is the narrative of an idea about the control of biological growth that has developed over the course of my career. At an early stage it was given the name Maia, after the Roman goddess of spring, growth and fertility. The origin of the idea goes back to attempts to explain how it could be that toxic agents at low concentrations have the improbable consequence of stimulating growth. Later, perturbation experiments revealed the output of a control mechanism responsible for regulating growth. This breviary of the Maia hypothesis explains the central idea of the book. All that follows derives from the key finding of how to access the output of growth control mechanisms, as ultimately growth must be controlled and constrained. It is one of many homeodynamic processes, all controlled by cybernetic mechanisms. This account is pitched to make the biology accessible to cyberneticists, and the cybernetics accessible to biologists. These preliminary remarks therefore give the crux of the idea, summarising its development, in a few paragraphs, from growth experiments with simple organisms to the point where Maia bears on the two engines of growth on Earth.

During early sensitivity tests of a seawater bioassay with a clonal hydroid (see Frontispiece), it was discovered that low concentrations of toxic agents stimulate biological growth ('hormesis'). It was suspected

* Quoted by P.B. Medawar (1969) from the German philosopher and psychologist Oswald Kulpe (1895).

that such paradoxical stimulation was not an effect of the agent itself, but was due to an adaptive and generalised response to toxic inhibition. This led to the finding that the specific growth rate is maintained at a constant velocity optimal for the physiological processes involved in biosynthesis. There emerged a method that could be used to access the output of growth control mechanisms, thus revealing the alluring oscillatory behaviour of feedback mechanisms. An understanding of acquired resistance to toxicity followed, with hormesis as a byproduct. Data from perturbation experiments made it possible to establish the limits of the counter-response, and its capacity to neutralise toxic inhibition. The capacity to neutralise toxic inhibition led to a re-interpretation of the toxicologists' 'dose–response' relationship. Growth is considered here in its broadest sense, from physiological growth of tissues to the growth of populations of organisms. Although these fields belong to different branches of biology, they are related mathematically and by descent.

A key part of this story is that early in evolution there must have been a significant advance in the evolution of growth control from plants to animals. Autotrophs (plants) make their own organic constituents from inorganic materials, typically by photosynthesis, and gave rise to organotrophs (animals) that consume organic carbon created by plants and other animals. A necessary corollary was a change in the way that growth and reproduction were controlled.

In the ocean, the autotrophs responsible for photosynthesis are algae, which generate half of all the oxygen created on Earth. Within the space of a few weeks, offshore microalgae grow to form vast blooms, before they die back as nutrients are used up. Their life strategy is to grow rapidly and strip all the available nutrients from the seawater; as the nutrients are used up, the microalgae form spores capable of remaining dormant for many months until the nutrients have been recycled and favourable conditions for growth return. Autotrophs control their internal processes of biosynthesis and replication, kept constant by means of a specific rate-sensitive feedback mechanism, which has the consequence of generating exponential population growth. Such growth may be adaptive at first, but becomes unsustainable later. Survival of this 'boom and bust' lifestyle is made possible by spore formation and dormancy, providing an opportunity to literally 'drop out' of the photic zone. A discontinuous life inevitably limits the scope of such organisms, but a continuous life can only become sustainable with the self-limitation of exponential growth.

Organotrophs evolved from autotrophs and depend on consuming organic compounds, typically as microscopic algae, planktonic invertebrates and their products. If organotrophs were to behave as autotrophs do, they would rapidly extinguish the plants and animals on which they depend, and ultimately bring about their own demise. So to ensure survival, organotrophs must avoid extinguishing food species, and exploit them at a level that allows the food species a sustainable existence, and thus ensure their own survival. The evolutionary solution to this problem was the superimposition of a population self-limitation loop on the rate-control mechanism inherited from autotrophs. This has the advantage of allowing first the maximum growth rate made possible by positive feedback, leading later to self-limitation by negative feedback. For the organotroph, it is considered probable that these requirements are met in the logistic equation as a nested, dual loop control mechanism, in which the inner loop controls the specific rate of biosynthesis, while the cumulative products of growth are monitored by the outer loop, which imposes a limit on population size.

The logistic control mechanism allows positive feedback, when a 'virtuous' circle and exponential growth has survival value, but prevents a 'vicious' circle when growth threatens 'runaway' and instability. So when exponential growth becomes maladaptive, self-limitation by the outer loop cuts in and arrests further growth. In organotrophs therefore, it is proposed that rate control is coupled to the self-limitation of population growth. A key property of population self-limitation is that the maximum sustainable carrying capacity becomes the goal setting for the growth control mechanism, such that numbers can be maintained within the limits of the habitat to support them. So with exponential increase constrained, there is advantage both for the consumer and the consumed, and so organotrophs evolved to lead a continuous and sustainable life, when conditions for growth allow. The logistic equation viewed as a control mechanism provides a means of maintaining sustainable populations. Such control mechanisms are conjectural, yet provide a minimal mechanism that can reproduce the population growth behaviour of such organisms.

Multiplication is not reserved for individual organisms, as there are modular replicators in all organisms. By a process termed 'endosymbiosis', some micro-organisms became internal modules of higher organisms. J.B.S. Haldane (1892–1964) suggested that inhibitory exocrines, which limit population numbers, may have become the endocrines that constrain the multiplication of self-replicating modules within metazoa, anticipating the development of the idea of endosymbiosis. The limits to the number of cells within a tissue are genetically prescribed, and are imposed by such specific inhibitors as endocrines, apparently descended from specific inhibitors known as population limiters in many aquatic species from protozoa to amphibians. So it seems likely that a mechanism that evolved in free-living unicells and their populations later became internalised by more complex life forms, providing control and limitation to those replicating modules that make up the bodies of metazoa. Here the logistic control mechanism is adopted once more as a minimal control mechanism for replicators, as their requirements for growth control are similar. The control mechanism is used as a conceptual model to interpret failure of control in neoplastic growth. Cancer is understood as a failure by some cells to respond to specific inhibitors that, within tissues, limit cell numbers. Not only does limitation cease, but regulation reverts to the inner loop, which continues to maintain growth at a constant specific rate, resulting in a positive feedback. Consequently, unlimited exponential increase ensues, and the growth of cell numbers proceeds without limit.

It can then be asked, if self-control and self-limitation are such important attributes of all biological systems, what of human populations? Early man was a hunter-gatherer, and so sparsely distributed that density-dependent limitation was ineffective, because space was not limiting. We can therefore not expect any intrinsic mechanism to provide human population regulation of the kind found in animals. In the absence of the ability to limit population growth, it reverts to control by the inner loop alone, and unlimited population growth. Self-limitation characterises biological populations from unicells to mammals, yet ironically, it appears that our species lost the innate capacity to limit population numbers. As a result, our numbers have already exceeded the carrying capacity of the Earth for humanity, which has been estimated at 5 billion using ecological footprint analysis.

In 1992, D.H. Meadows, D.L. Meadows and J. Randers in *Beyond the Limits* expressed the fear that positive socio-economic feedback loops induce the exponential growth of the human population and economic capital. Biological growth and the growth of economic capital have the same structure and systems, in that they both create growth by positive feedback due to birth or investment, and slow down due to negative feedback by death or the depreciation of capital assets. Not unlike biological growth, the investment of capital earns interest, leading to more capital and so more interest. Both biological and economic increase is exponential, which without constraint ultimately becomes destabilising 'runaway'. Self-limitation of the kind found in animal populations is apparently due to the limitation of population size in relation to the maximum sustainable carrying capacity of its habitat. If we take biological systems as exemplary of sustainability, this tells us that the size of the human population, and of the economy, both need to be limited in relation to the ecological capacity of the Earth to assimilate the consequences of human activity. Presently this is not happening.

Power is required to drive the economy, which continues to be provided primarily by fossil fuels, resulting in carbon dioxide emissions that are increasing beyond the capacity of natural processes to return them to the earth. The result is global warming and the destabilisation of the global climate system, which will itself ultimately impose its own limit on growth. The point is that the Earth is finite, and that human populations and economic growth must ultimately be constrained by the capacity of the Earth to assimilate the polluting byproducts of man and his economic activity. Climate change shows us that population and economic growth have already exceeded the capacity of the Earth to draw down atmospheric carbon dioxide. This is not only due to the release of carbon dioxide, but also to the clearing of the forests that provide the natural means of drawing down carbon dioxide. In the absence of humanity choosing to limit the growth of the economy at a sustainable level, the effect of carbon dioxide as the principal metabolite of economic growth will impose its own constraints. Such effects can already be recognised in the various facets of man-made global change.

I read James Lovelock's book *Gaia* in 1979, when it was first published, and realised that I was grappling with a similar problem. Like Lovelock, I had strong evidence of a cybernetic mechanism at work, but there was, it seemed, no known control mechanism on which the evidence could be hung. Maia is a much younger, fraternal hypothesis that still needs to establish itself as a factor in the way in which the biosphere regulates growth processes. This book provides evidence that for growth at all levels, from cells within organisms to populations of free-living populations of organisms, growth rate is controlled and numbers are limited in relation to the capacity of their interior or exterior environment to sustain them. I dedicate this volume to James Lovelock, in appreciation of his achievement in demonstrating Gaian control, and in gratitude for his inspiration to a young scientist over 30 years ago when this hypothesis was in its formative stages.

Acknowledgements

A list of sources is given for further reading, and scientific papers are cited for those readers who wish to explore more deeply the ground I cover. At the end of each chapter there is a short summary, which may be read either as an introduction, or in retrospect. In some cases, findings that are only now coming to fruition had their origin in research carried out 50 years ago or more, and some have been traced from their origins to the present time.

I am indebted and thankful to Professor Ernest Naylor, my tutor at university, and mentor since, for writing the Foreword to this book. I have held an Honorary Fellowship at Plymouth Marine Laboratory for the 12 years since my retirement in 1998. All of the Directors – Fauzi Mantoura, Nick Owens and Steve de Mora – have supported and encouraged the writing of this book.

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Any errors, lapses in citation, or oversights in seeking permissions are my own responsibility.