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Chapter 1 : Human Physiology in Extreme Environments | R2 Digital Library

Human Physiology in Extreme Environments is the one publication that offers how human biology and physiology is affected by extreme environments while highlighting technological innovations that allow us to adapt and regulate environments.

Received Jul 10; Accepted Nov This article has been cited by other articles in PMC. We propose that, in practice, systems biology rests on three pillars: The number of ethical and physiologically relevant perturbations that can be used in experiments on healthy humans is extremely limited and principally comprises exercise, nutrition, infusions e. Intralipid , some drugs and altered environment. Thus, we argue that systems biology and environmental physiology are natural symbionts for those interested in a system-level understanding of human biology. However, despite excellent progress in high-altitude genetics and several proteomics studies, systems biology research into human adaptation to extreme environments is in its infancy. A brief description and overview of systems biology in its current guise is given, followed by a mini review of computational methods used for modelling biological systems. Special attention is given to high-altitude research, metabolic network reconstruction and constraint-based modelling. One could be forgiven for believing, therefore, that it is something new, yet this would be misleading. The first condition is clear enough. The second can be better expressed mathematically. For von Bertalanffy, violation of either or both of these conditions defined a system [1]. Few with any experience of biological research would argue that these conditions are true of living things. Life is, by its very nature, awesomely complex and chaotic. Yet, what does it mean in practice? That is the focus and purpose of this review. Thus, examples will be drawn from high-altitude research and the use of metabolic network reconstructions. Yet, these perspectives, we hope, will be broadly generalisable, and we aim to provide a basic introduction to systems biology for the non-expert. We also propose that systems biology and environmental and exercise physiology are particularly complementary. We will also briefly discuss some of the challenges that lie ahead. What is and is not systems biology? If then it is nothing new, why is systems biology suddenly so visible? Some have implicitly argued that systems biology is a mirage, no more than a rebranding of the type of holistic thinking that some biologists and integrative physiologists have been using for decades [2]. Yet, systems biology in its current guise is different to these earlier disciplines. It stems from advances in technology, particularly in genome sequencing, computing and in analytical platforms such as mass spectrometry and nuclear magnetic resonance. In order to truly study a large system in its entirety, one requires the ability to model and measure it in its entirety or at least make an effective attempt to do so. Until the advent of whole genome sequencing, this was an insurmountable experimental challenge for biologists. Yet, another common misconception is that systems biology and the so-called omics disciplines are one and the same. This, too, is misleading. An omics discipline is defined by its methods, as an attempt to measure every instance of a species in a specific class. Thus, proteomics is an attempt to measure every protein in a cell or tissue. Systems biology, while leveraging much of the data these experiments generate, transcends the methods. Reconstructions of cell metabolic networks not only undoubtedly leverage data from genomics, proteomics and metabolomics, but also use data from traditional enzyme assays and measures of physiological function. Indeed, a key test of any reconstruction is whether it has the capacity to recapitulate the normal physiological functions of the system of interest [3]. Another feature that distinguishes systems biology from omics disciplines is recursivity. Systems biology as defined herein and elsewhere [4] comprises an iterative cycle of experiment and modelling rather than a single experiment and modelling cycle. In practice, perhaps the single feature that distinguishes systems biology from both the omics disciplines and other relatives such as integrative physiology is the central role of mathematical modelling and computer simulationsâ€”a distinction that has been overlooked by previous commentators [5]. Yet, we are not alone in emphasising the central role of computation in systems biology [6 - 8]. Although there has been substantial variation in how systems biology has been defined previously, we believe that our definition here is consistent with the emerging consensus [4 , 6 , 9]. Given the huge amounts of data generated by the trademark techniques of genomics, transcriptomics, proteomics and metabolomics,

unaided human interpretation is utterly inadequate, and systems biology, as defined here and elsewhere, arises spontaneously. Yet, typical omics experiments in isolation fail this test; most involve the de novo building of multivariate statistical models to the data from each experiment in isolation rather than progressive model refinement statisticians who specialise in multivariate modelling are well aware of the problems associated with this approach; instead, they recommend that such statistical models are confirmed using newly acquired data or bootstrapping procedures [10].

Chapter 2 : Applying systems biology methods to the study of human physiology in extreme environments

Exploration of human physiology under extreme environmental conditions is another facet of this association. Understanding physiology at the limits of human tolerance to environmental conditions is a worthy goal in itself but may in addition lead to developments in both knowledge and treatments in clinical settings.

Mike Grocott Downloaded from pmj. Michael P W Grocott Postgrad. Rapid responses You can respond to this article at: The Fellowship also hosts and on additional clinical background FPM was founded in the United a range of seminars and conferences, important for examination candidates; Kingdom after World War I by the merger supported by national and international to provide flexible educational and prac- of the Fellowship of Medicine and the fellows with expertise in the practice of tical resources for teaching; and to con- Postgraduate Medical Association. The medicine, medical education and transla- tribute to the continuing professional FPM pioneered the development of post- tional and clinical research. Enquiries regarding application to Medical Journal, which was founded in sional development CPD within join the Fellowship are welcome www. Today, the Fellowship continues to medicine and related disciplines. Human physiology in extreme justify the requirement for adaptation or innovation in order to survive. Whilst some definitions incorporate the psycho- environments: Michael P W Grocott There is a long tradition of human experimentation often self-experimenta- tion in environmental extremes. The Progress in medical science is intimately studies of human responses to extreme great Scottish physiologist J S Haldane linked with understanding and advancing environments have used the tools of exposed himself to both hyper- and hypo- the limits of human survival: Exploration processes and detrimental responses. Understanding physiology at contextually dependent on the object or sickness. More recently, the study of the limits of human tolerance to environ- person exposed to the environment and humans exploring increasingly harsh ter- mental conditions is a worthy goal in itself the subject of study. Most definitions restrial, aquatic and extraterrestrial envir- but may in addition lead to developments with respect to the study of human onments has defined new medical in both knowledge and treatments in medicine and biology incorporate the specialties and associated journals and clinical settings. Recently, larger systematic requirement for either physiological adap- taught courses: Dr M Grocott, Centre for Altitude, order to survive. Simple stress does not diving and hyperbaric , aviation, space Space and Extreme Environment Medicine, UCL Institute and thermal physiology and medicine. Amongst the key sure to microgravity are good examples. Over and and as a means of improving treatment for extreme altitude. The relationship between bubble extreme environments and discussing the human space flight to Mars will be critically dependent on managing the formation and susceptibility to illness in potential clinical lessons that can be medical and psychological risks posed by DCS and following cardiopulmonary learnt from the study of humans under this unique environment. The epidemiology of exposure to spe- and pulmonary vascular physiology, and cific extreme environments varies widely. Caudwell Xtreme Everest CXE mountainous, desert and polar regions of Most recently, investigators, including our is a research project coordinated by the Centre for our planet. Membership, roles and techniques of population genetics. For clinical phenomena that are otherwise responsibilities of the CXE Research Group can be found other environments, life can only be difficult to explore and thereby driving at www. The sustained using physical counter-mea- translational studies to improve patient research was funded from a variety of sources, none of sures developed to protect against the care. For example, we have made the case which are public. BOC Medical, now exposure. For some environments, such as exposed to environmental hypoxia at part of Linde Gas Therapeutics, generously supported the space, it is likely that they will remain the altitude as a model for exploring variations research early on and continues to do so. Lilly Critical preserve of a very few individuals many in human adaptation to hypoxia amongst Care, The London Clinic a private hospital , Smiths more people have stood on the summit of critically ill patients. All monies were given as unrestricted grants. However, and importantly for tify the underlying genetic determinants in Specific research grants were awarded by the the practicing clinician, large numbers of order to elucidate mechanisms and thereby Association of Anaesthetists of Great Britain and Ireland, individuals are now exposing themselves develop

therapeutic interventions to bene- and the UK Intensive Care Foundation. The Caudwell Xtreme volunteers who trekked to Everest basecamp also kindly donated to support the research. Many millions are exposed annually approach and sought to explore two areas. Postgrad Med J ; Griffith Pugh, pioneer Everest need to have a reasonable acquaintance lined in the previous sentence. High Alitude Medicine and Biology ;3: The next small step. Several novel clinical syndromes have tolerance to hypoxia by making novel 3. High-altitude been identified occurring solely in response measurements in a small group of climbing physiology and pathophysiology: Critical Care to specific environmental challenges. The investigators high on the mountain.

Chapter 3 : Human physiology in extreme environments: lessons from life at the limits?

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