# Coupled microbial and human systems: evidence for a relationship between infectious disease and gross national product

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## Abstract

We provide evidence that maternal metabolic energy is diverted to increased birth rates in nations experiencing high infectious disease risk. The "economic stoichiometry" of such situations limits the availability and distribution of metabolic resources available for national production. Lowering disease risk, and thus the metabolic energy required for replacement human biomass production, makes energy available for national production during the demographic transition, and increases the national GDP.

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## Introduction

The biological flux of materials in the environment is a function of metabolism, establishing for all organisms-ranging from microbes to higher forms-their respective fundamental life history strategies. A metabolic theory of ecology views this flux of materials as a continuum that connects energy flow at many levels, from individual organisms to population and whole ecosystem levels of organization [1,2]. However, as we progress from one scale to the other, new characteristics arise that reveal an increasingly complex, selforganized and power law-dependent network [3,4]. Another feature of complex systems, which is our primary interest here, is the coupling of complex systems between microbial and human systems. Our main thesis is that the metabolic costs of infectious disease incurred by populations/nations results in trade-offs between human biomass production and industrial domestic production.

To begin, we recognize that human energy functions are constrained by metabolic rate; our capacity to acquire energy is limited and our ability to redistribute metabolic energy is finite. This constraint operates within the limits of the socalled *energetic-equivalence rule*, which reflects the characteristic connections between individual metabolic rates, rates of energy flux by populations, and the partitioning of available energy among species within a community [1].

The energy status of an individual is under strict cortical and hypothalamic control [5]. A simple way of putting it is 'we can only eat so much!'. Appetite is tightly coupled to the metabolic demands of the body, which depends on the energy needed for reproduction, growth, maintenance, physical activity, etc.

However, not only is the energy status of individuals constrained, but so too is it constrained in the life history of the human species. For instance, relative sizes of the human heart, kidney and liver, all of which have relatively high mass-specific metabolic rates, are the expected proportions for a primate of our body size. However, gut and brain size, which also have relatively high mass-specific metabolic rates, are not what we expect. Aiello and Wheeler [6] have shown that, because of a finite metabolic foundation, evolution of the human brain, which is much larger than expected for our body size, was energetically possible because of the evolutionary reduction of the gut. Energy once required to support gut metabolism was given over to support the metabolism of the larger brain. This became possible with the evolution of a higher-quality diet, making less work for the gut to provide the metabolic requirements of our larger brain.

A metabolic growth law for female mammals states that the amount of energy needed for the young female mammal to develop and grow is also that metabolic fraction of energy available to her for reproduction when growth is complete in adult life [7]. The importance of this for human life history in the presence of infectious disease leads to specific expectations concerning the allocations of energy (Fig. 1).

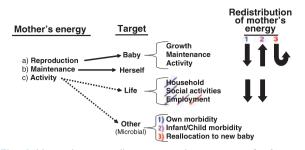


Fig. 1. Maternal energy allocations in the presence of infectious disease. See text for explanation of numbering.

Fig. I shows that a mother's energy allocations are divided among: (a) that amount of energy she herself took to grow, which, as an adult, she now targets to her baby during reproduction; (b) her basal metabolic rate, or maintenance, which is targeted only to herself; and (c) her daily activities, which are targeted to life, and which are mainly household, social, and employment activities. However, in the presence of infectious disease, most women in the world will expend energy on microbial-related targets, and the redistribution of energy will be expected to ramp away from normal life activities as follows. (1) If she herself is morbidly ill, all household, social and employment activities will be expected to suffer at a level corresponding to the severity of the disease. In this case, energy that she has available for baby and for life will be redistributed downwards; (2) If her child is ill, employment activity is most likely to suffer, this energy now being redistributed to her baby, thus increasing its prospects of recovery and survival; that is, reproductive effort is salvaged if, by increasing parental care, her baby will survive [8], (3) However, Quinlan [8] has shown that when pathogen stress reaches a high and critical threshold, parental care and age at weaning are reduced proportionally to the level of stress. This transfers her energy allocations away from a perceived high-risk endeavour-that is, concentrating energy on a baby increasingly less likely to survive-so that metabolic energy may be re-allocated to those resources needed to produce a new baby. By reducing energy flow to a severely ill child, she increases the probability of regaining positive energy balance, achieving an appropriate pre-pregnancy weight gain, and resuming competent ovarian function [9].

Although human fertility is clearly constrained by individual metabolic flux, it has also been shown that birth rates scale negatively with per capita energy consumption, which includes energy allocations beyond individual biological metabolic requirements, such as the national share of end-consumer use and production [10]. The demographic transition, characterized by increasing energy consumption/production and lowered fertility, is explained by these authors as a function of the cost of raising children, this cost being relatively

low in impoverished nations, resulting in high fertility, and relatively high in wealthy nations, resulting in low fertility. The observed -1/3 power scaling of birth rate is suggested to result from the increased costs of infrastructure and resource distribution to children in industrialized nations.

Because birth rate is directly connected to both infectious diseases and per capita consumption/production, we hypothesize a connection between the metabolic costs incurred by levels of infectious diseases on individuals within nations and their respective per capita share of national production. With confirmation of Moses and Brown's [10] quantitative relationship between birth rate and per capita energy consumption, we provide here the first qualitative evaluation of the role of infectious diseases in causal association with the gross domestic products (GDPs) and demographic profiles of nations.

## **Methods**

The Central Intelligence Agency World Factbook was consulted for data on crude birth rate (births per 1000 of population per year) and the gross domestic product (GDP) per capita (GDP at purchasing power exchange rates divided by the population) (see https://www.cia.gov/library/publications/ the-world-factbook/index.html). Data concerning 47 nations are presented in Fig. 2. Superimposed on these data are US government assessments of the degree of risk of major infectious disease risk to government personnel spending less than 3 years in the host country; HIV/AIDS is not included. Every country assessed in the World Factbook for the degree of risk as 'very high', 'high' or 'intermediate' was

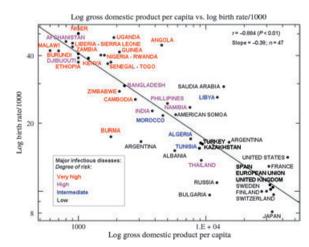


Fig. 2. Ordinary least-squares regression of log-transformed data on log scales, examining the association between birth rate/1000 and gross domestic product per capita.

included in the analysis, and a random assortment of nations not evaluated for risk were given a rank of 'low' (Fig. 2). It must be noted that these measures of risk probably underestimate the infectious disease load on the local population.

# Results

The results remain true to Moses and Brown's [10] quantitative relationship between national birth rates and per capita energy consumption for 98–166 nations in six periods between 1971 and 1997, whose slopes ranged from -0.33 to -0.37. The slope observed in our analysis, -0.38, is slightly higher, which is probably because Moses and Brown [10] subtracted infant mortality from fertility in order to more accurately reflect the number of children raised by parents. However, our interest here lay in the metabolic cost of infectious disease on total fertility, which should include child losses.

As can be qualitatively observed in Fig. 2, nations in which the risk of major infectious disease is very high dominate where relatively high birth rates linearly regress with low GDP per capita. High risk is scattered, although concentrated at relatively lower birth rate and higher GDP per capita than in very high-risk nations. Intermediate-risk nations are located centrally on the regression, and nations in the low-risk disease category dominate where low birth rates linearly regress with high GDP per capita.

# Discussion

We suspect that it is the disease burden on local populations that leads to metabolic costs being diverted to birth rates, these costs and rates increasing together and consequently reducing the net metabolic energy that would otherwise be available for industrial production and national consumption. We believe that this is one factor that limits access of developing nations to the less connected periphery of the network linking global production and export commodities (cf. [11], establishing a connection between the availability and distribution of metabolic resources for nations and a concept that we dub 'economic stoichiometry'. We further suspect that the classical demographic transition is a result of increased access to healthcare and reductions in the risk of infectious disease. Lowering risks allows women to allocate reproductive metabolic energy to fewer surviving children and a larger share of metabolic energy to various activities, particularly employment.

We have shown that if a nation's risk of infectious disease is low, the cumulative metabolic energy otherwise required for replacement human biomass production is probably converted into national production, effectively driving the demographic transition and increasing the national GDP.

#### **Transparency Declaration**

The author declares no conflicts of interest.

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