

## A complex systems approach to cancer prevention

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### ABSTRACT

Cancer incidence continues to be a major health problem possibly because cancer is a complex system comprising many agents that interact in a non-linear manner resulting in many possible outcomes. The degree of complexity of a cancer system could be vast involving multiple endogenous and exogenous agents interacting with the over 10 trillion cells comprising the body. It is hypothesized that the practical management of this complexity may be a key to cancer prevention and possibly treatment. But the management and resolution of such an immensely complex system is difficult and may require a multidisciplinary approach including physics, biology, biochemistry and medical science. Research such as in systems biology involving large data sets may offer resolution in time, but the scale of the task is daunting. In evaluating the hypothesis, this paper proposes a method of resolution of the complex cancer system through a proxy in the form of the vital body system, energy balance, involved in several cancer processes. Although I suggest that the energy balance system is itself complex, it may permit access to factors that may be used in limiting cancer initiation. Meta-analysis related to factors of blood sugar, inflammation, stress and immune response reveal that they could be likely candidates for management. Analysis also reveals certain devices that may give practical effect to these management options. Due to the inherent complexity of a cancer system, multiple devices may need to be applied in a combination. The analysis suggests that the low-risk and low-cost devices metformin, vitamin D and vitamin C, may prove to be suitable for use as a practical cancer prevention strategy. If the presented hypothesis is correct, a practical method for prevention or management of cancer may be possible. A trial to test the hypothesis is proposed.

### Introduction

Cancer is a significant health problem as shown by the National Cancer Institute in the United States projecting new cancer cases worldwide to double from 2012 to 2030 [1]. The numbers involved, projected to reach 21 million, suggests that there is a need for additional methods of cancer prevention. Cancer's management is made difficult because it appears that cancer may form a complex system in the human body in terms of complexity theory. As such, cancer can be defined as a collection of multiple agents that interact in a non-linear and unpredictable manner [2]. Heylighen describes an important characteristic of complex systems as their ability to 'self-organize' and form emergent, new, properties, from interactions. In complexity terms, a tumour then could be viewed as an emergent property of a complex system within the body. The description of cancer as neoplastic disease supports this view. A description of the full range of views of the causes of cancer is beyond the scope of this paper but it is significant that cancer as an emergent property of a complex system may have many possible causes.

### AIM/objective

An example of a complex system or network is the human cell that exhibits large numbers of interacting chemical reactions [3]. Albert et al. describe a complex network or system as comprised of nodes and edges that are connections between the nodes. They suggest that order in this complexity can be seen through statistical analysis. The difficulty in carrying out such analysis is evident in the significant complexity of any cancer system in the human body with trillions of cells, multiple organs and systems interacting with many endogenous and exogenous factors including the environment. It is this complexity that may make cancer unpredictable and difficult to manage. The resolution of this complexity therefore may be fundamental to cancer prevention or treatment. The aim of this paper is to develop a hypothesis concerning the resolution of complexity to offer a cancer prevention strategy.

### Method

It is hypothesized that the complexity of a cancer system can be resolved by employing a system in the body, energy balance, and

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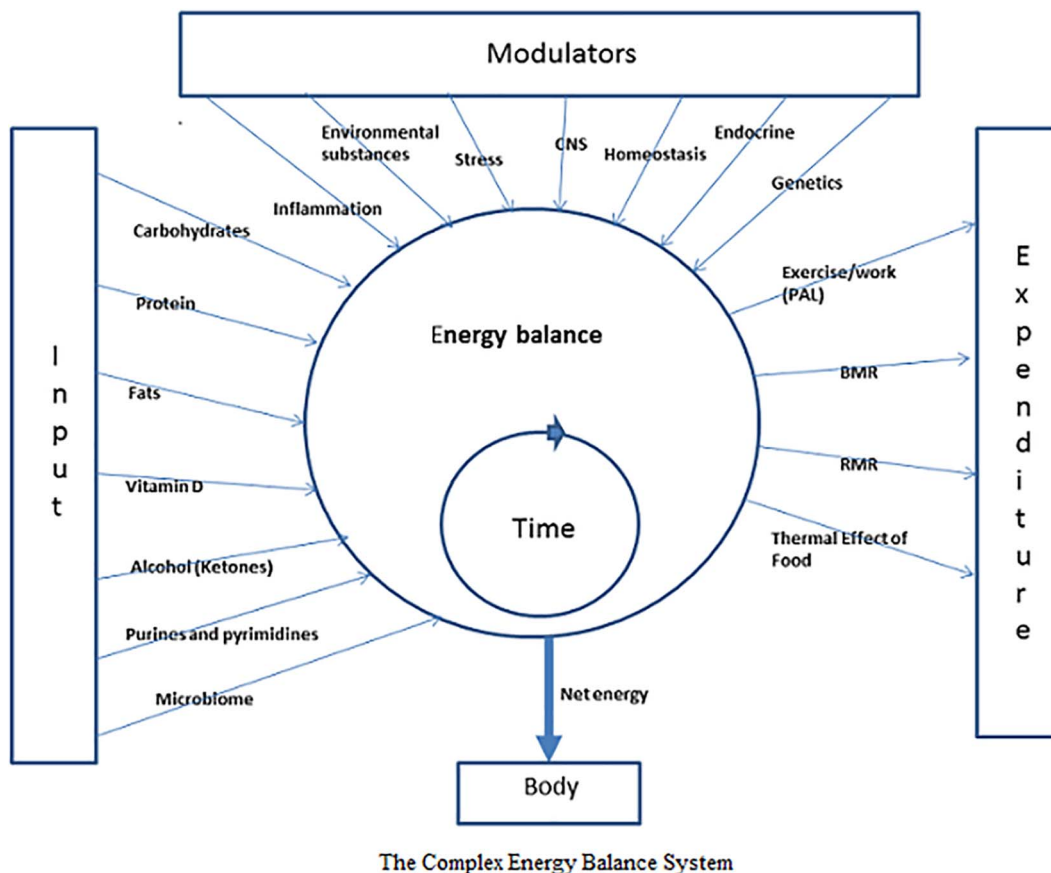


Fig. 1. The complex energy balance system – The diagram shows energy inputs, energy expenditures, energy modulators and stores of energy in the body. Time is shown in the diagram because flows of energy are time related. The abbreviations used in this diagram are CNS (central nervous system), PAL (physical exertion level), BRM (basal metabolic rate) and RMR (resting metabolic rate).

thereby to define a method to help prevent cancer incidence. This hypothesis is important because it could point to a practical approach for cancer prevention, possibly affecting many people.

Energy balance is an important system in the body that is involved in cancer [4,5] and that I suggest is itself complex. I propose that links between a cancer system in the body and the complex energy balance system can be used to identify factors that significantly impact cancer.

In defining complex energy balance, its key components are energy input, energy expenditure and energy modulators. These are shown in Fig. 1. By identifying and employing appropriate variables in the complex energy balance system, a practical cancer prevention protocol may be defined. Such a protocol should be easy to employ over time. This protocol could be appropriate for people at risk of cancer including those with diabetes type 2, those with a family history of cancer and for cancer survivors wishing to avoid recurrence.

To evaluate the hypothesis, it is possible to:

- carefully consider the complex energy balance system using systems analysis to identify key factors that influence cancer
- employ meta-analysis of the literature to validate these factors that influence cancer and to identify and evaluate devices, drugs or behavioural, that could give actual effect to cancer prevention
- develop a decision matrix to determine a suitable combination of devices that could produce a practical cancer prevention protocol.

Possible feedback loops between the complex cancer system and the complex energy balance system variables reveal dynamic contributors to health outcomes. These variables include glucose homeostasis, inflammation, stress, and environment that affects immune response. These represent candidate cancer management factors that can be

tested through meta-analysis to show cancer effect and that they may be candidates for management. This analysis is carried out by a search of PubMed with the following search terms:

- “blood sugar cancer adverse” with PubMed search terms (“blood glucose”[MeSH Terms] OR (“blood”[All Fields] AND “glucose”[All Fields]) OR “blood glucose”[All Fields] OR (“blood”[All Fields] AND “sugar”[All Fields]) OR “blood sugar”[All Fields]) AND (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “cancer”[All Fields]) AND adverse[All Fields]
- “chronic inflammation cancer adverse” with PubMed search terms (Chronic[All Fields] AND (“inflammation”[MeSH Terms] OR “inflammation”[All Fields]) AND (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “cancer”[All Fields]) AND adverse[All Fields])
- “all stress cancer adverse” with PubMed search terms (“Stress”[Journal] OR “stress”[All Fields]) AND (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “cancer”[All Fields]) AND adverse[All Fields]
- “immune system cancer benefits” with PubMed search terms (“immune system”[MeSH Terms] OR (“immune”[All Fields] AND “system”[All Fields]) OR “immune system”[All Fields]) AND (“neoplasms”[MeSH Terms] OR “neoplasms”[All Fields] OR “cancer”[All Fields]) AND benefits[All Fields].

**Results and discussion**

The meta-analysis reveals the following:

- Blood sugar: 1291 papers

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