Mathematical modelling the systemic regulation of blood glucose: 'a top-down' systems biology approach

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Abstract

The objective of this article is to review the mechanisms which the body uses to regulate its function. The author considers, in particular, the nature and structure of the physiological systems with a specific focus upon the systemic regulation of blood glucose and highlights an innovative technology, based upon the top-down cognitive approach, which incorporates a unique mathematical model of the physiological systems and autonomic nervous system.

Most systems biology is a development of the prevailing reductionist biomedical paradigm. It adopts a bottom-up approach seeking systemic justification for biochemical and biophysical research findings. By contrast the 'top-down' approach considers the neural regulation of the physiological systems and the neurological, cognitive and biochemical consequences of systemic dysfunction i.e. the consequences of sensory input upon the neural regulation of the body's systems, organs, and its cellular and molecular biochemistry.

In conclusion, the evidence suggests that the onset and progression of Diabetes Mellitus cannot be accurately assessed by individual biomedical indices but instead that the regulation of blood glucose is one of a number of inter-related physiological systems which act in a coordinated manner in order to maintain the body's physiological stability.

1. INTRODUCTION

There is a level of coordinated function between organs which cannot yet be explained by biochemistry alone. It is increasingly apparent that reductionism in biology has significant limitations (Ewing & Parvez 2010). This has led to the study of biological systems although mainly to justify findings of biochemical research (Beard *et al.* 2005). Nevertheless there are those who recognise the dynamic nature of the body's function i.e. the stability of the physiological systems which determine the body's biochemistry are influenced by biochemistries (Bruggeman & Westerhoff 2007) and by the biological consequences of sensory input (Kandel 2006). The quandary faced by researchers is how to integrate such understanding into current medical research when faced with a

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system which is heavily biased in favour of the prevailing biomedical paradigm. To illustrate the case:

- The diagnosis of medical conditions remains significantly below expectations, perhaps indicating significant limitations with the biomarker approach (Ewing & Parvez 2010).
- Diagnosis by the GP ranges from typically 20–80% depending upon the nature of the condition to be diagnosed, the time available for the diagnosis, the age of the GP, etc.
- The effectiveness of most drugs is considered to be circa 50% (Spear *et al.* 2001). Many medical conditions remain poorly understood or are considered to be of undiagnosable nature.
- The occurence of auto-immune disease(s) continues to rise yet no-one offers a satisfactory explanation for this steadily increasing burden on society. If disease is the consequence of genetic changes, subsequently inhibiting the production of proteins, substrates, and/or their reactivity (Ewing & Ewing 2008), which factors could be responsible for such dysfunction? Known contributors include stress, vaccines and perhaps also GM foods.

Various techniques have been used to determine levels blood glucose although none are considered to be an accurate and reliable indicator of the condition. It has been recommended that the fasting glucose test (FST) and oral glucose tolerance test (OGTT) be replaced and that the measurement of glycated haemoglobin A_{1c} (HbA1C) may be a more suitable measure of the condition however there are significant problems with HbA1C measurement which appear to provoke disagreement: (i) the merits of the various tests and (Kilpatrick *et al.* 2009; Bennett *et al.* 2007) and (ii) limitations of the test (Bando *et al.* 2009; Gray *et al.* 2003; Adams *et al.* 2005) e.g. inconsistencies in diagnosing diabetic patients with chronic liver disease (CLD). This indicates the complex and systemic nature of diabetes mellitus (Ewing & Ewing 2008).

2. REGULATION OF THE AUTONOMIC NERVOUS SYSTEM

The stability of the Autonomic Nervous System is expressed as homeostasis. (i) Biological systems which maintain homeostasis must be stable, yet must be able to reconfigure when challenged by stress-related influences, in order to maintain optimum stability. (ii) The nature, structure and function of such systems must be clearly evident. (iii) Their function must be predictable and must be able to respond rapidly to the body's requirements i.e. responding to stress-inducing sensory input and/or the body's requirement for energy.

For example, the proliferation of chronic disease and especially that of autoimmune disorders is a relatively recent phenomena which has become increasingly apparent since the introduction of vaccines by injection. Such disease is the consequence of the body's best efforts to maintain its stability perhaps when challenged by genetic stressors. Most vaccines are designed to act at the genetic level. Vaccinal RNA, derived mainly from attenuated strains of disease, binds with human RNA and DNA, and suppresses the expression of proteins. They introduce foreign proteins which alter the body's physiological stability and function. By this means they alter the stability of the autonomic nervous system and physiological systems, and create autoimmune disorders (Ewing 2009; Ashwood & Van de Water 2004).

The body's stability is maintained by the sympathetic and parasympathetic nervous system. There are many examples of how this is manifest – one hormone appearing to provide an apparently compensating effect for the other e.g. of adrenaline and cortisol (adrenal), insulin and glucagon (pancreas), leptin (fat cells) and ghrelin (stomach), oxytocin and vasopressin (pituitary), melatonin (pineal) and serotonin (digestive tract), secretin and cholecystokinin (small intestine), etc. The problems facing researchers are due to the complexity of the body's function. Such biochemical relationships are often non-linear and multi-functional i.e.

- The single reaction between a protein and its substrate could produce more than one chemical which has biological significance e.g. the adrenals produce circa 30 corticosteroids, the pituitary produces many hormones, the action of light upon bilirubin influences the range and biological significance of isomers produced, the action of light upon the skin influences the range and biological significance of vitamin D isomers produced, etc.
- The production of specific biochemicals often occurs at different physiological locations e.g. serotonin is produced in the digestive and respiratory tracts; and they are subject to an immense number of influences as the body strives to maintain its stability.

Medical research has to some extent recognised that it is the stability of the body's function which is significant. It has adopted the approach of (i) controlled release of drugs and (ii) supplementing the body's function in the event of detectable biochemical deficits e.g. using thyroxine, insulin, heparin, vitamins, minerals, etc; however there are many instances which illustrate the limitations of this approach. If the body is deficient in such biochemicals there are two explanations for its occurrence: (a) there is a deficit due to dietary or other causes e.g. lack of sunlight influencing the body's ability to produce vitamin D; or (b) it's function no longer encourages the absorption of such chemicals by the digestive system. In the latter case, which issues would prevent their uptake?

A significant function of the brain is the regulation of the body's physiological stability. It regulates the function of the neural networks (organ networks),

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and consequently that of the physiological systems, and ultimately of cellular and molecular biology i.e.

- sensory input influences the stability of the physiological systems (see Figure 1) and ultimately that of the visceral organs.
- colour perception is altered by pathologies e.g. in the diabetic: a blue-yellow colour perception deficit (Bessman 1987) is prevalent.
- the reaction conditions e.g. pH and temperature, influence the rate at which proteins react with their substrates. This releases light, the colours being unique for each protein-substrate reaction and the intensity being a measure of rate of reaction. Regulation of the reaction conditions is the function of the physiological systems.
- many medical conditions regress in the course of time and under the right circumstances (Zahl *et al.* 2008).
- altered behaviour (Figure 1) is the consequence of pathology. In diabetes this results in depression, altered cognition (including colour perception and memory), and influences mood, emotional stability, eating and sleeping patterns, anger, etc.

Disease is not the inevitable and irreversible consequence of physiological dysfunction. It is influenced by the biochemical mechanisms which, under normal circumstances, maintain homeostasis i.e. (i) how sensory input can have a positive, or negative (stress), influence or (ii) by understanding and adapting the mechanisms which stimulate recovery. Drug treatments are based upon the assumption that relief from symptoms will enable the body's physiological stability to be reasserted by the natural processes however this must consider whether the body's natural mechanisms, structures, organs and biochemistries are able to handle the resumption of normal physiology and function. This may not be so. That brain structure, neuroplasticity and function, can be modified by different intensities of physical activity e.g. modifying behaviour and/or 'retraining the brain', indicates the multi-level nature and significance of such processes.

3. PHYSIOLOGICAL SYSTEMS

3.1 The conventional understanding of the physiological systems is as follows: cardiovascular, musculoskeletal, nervous, respiratory, urinary, digestive, endocrine, reproductive, immune, skin and blood

The Endocrine system has been considered to comprise pituitary, thyroid, adrenal and ovaries/testes; the **Cardiovascular system** has been considered to comprise the heart, blood vessels and blood; the **Respiratory system** has been considered to comprise the nose, mouth, pharynx, trachea, diaphragm, abdominal muscles and lungs; the **Digestive system** has been considered to comprise the oral cavity, oesophagus, gall bladder, liver, stomach, duodenum, pancreas, small intestine, large intestine; the **Renal system** has been considered to comprise the kidneys, ureters, urinary bladder and urethra; and the **Reproductive system** has been considered to comprise the ovaries and uterus; or testicles, penis, and prostate. The remainder i.e. **skin, blood, nervous** and **immune;** have been considered to be physiological systems.

Such an explanation excludes several functions e.g. temperature, sleep, osmotic pressure and pH; each of which significantly influence the body's function and longevity. Moreover medical research has noted the existence of other physiologically significant systems e.g. blood volume, blood glucose, blood pressure, blood cell content, osmotic pressure, and sexual function. Accordingly there may be scope for a revised understanding of the systems which regulate the body's function e.g. (i) the skin is an organ, not a system; (ii) the

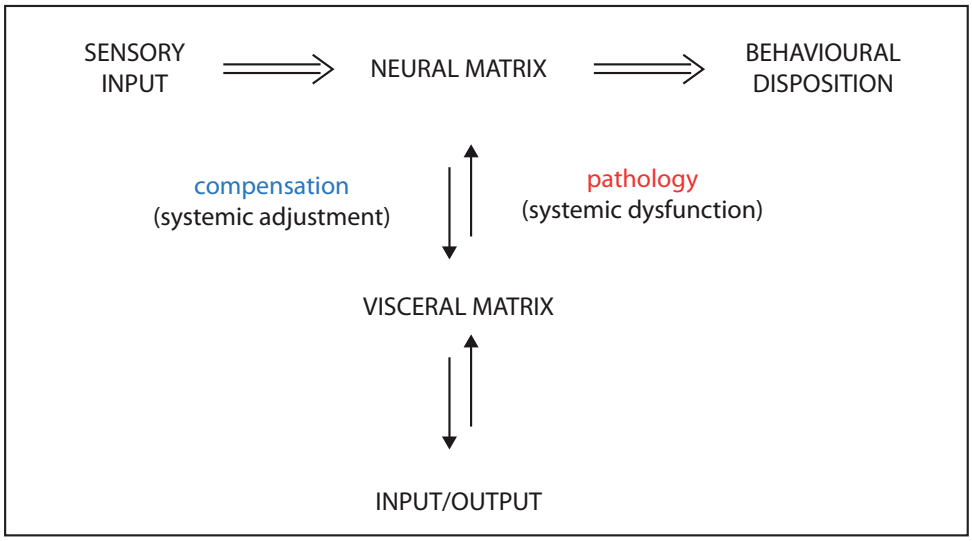

Fig. 1.

nervous system is the biochemical means of conveying information and functions as an organ, rather than a system; (iii) there is little evidence for an immune *system* although there is evidence of immune function i.e. the production of immunochemicals is a significant function of the spleen, endothelium, and bone marrow.

The endocrine organs: in particular the thyroid, pituitary and adrenals; participate in the regulation of all physiological systems (with the possible exception of sleep). It is understandable that this could lead to the conclusion that they are part of an endocrine system. There is however an alternative i.e. that these endocrines may be part of each physiological system. The endocrines produce hormones and immunochemicals, and regulate or influence the production of immunochemicals by other organs (Dardenne & Savino 1996). Accordingly the current explanation for immune and endocrine *systems* may have to be reviewed and revised.

That there are physiological systems and homeostatic limits (St Clair Gibson *et al.* 2005; Ader 2003; Schulkin 2005) is not in doubt however there is not yet agreement on their nature and structure (Shelhamer 2006). The systems involved in the body's function are increasingly researched however this mainly assumes that systems can be used to explain the origins of complex biochemistries and pathologies. It fails to consider that the brain – through its neural structures, and the neural/organ networks – could be acting in a co-ordinated and/or synchronised manner to regulate the body's function and that pathology is the consequence of systemic dysfunction. In fact, both approaches appear to be correct: (i) the brain regulates the physiological systems with biochemical consequences and (ii) biochemical changes at the organ level can induce change at the neural level i.e. the brain is regulating the function of the visceral organs and feedback is being provided by the visceral organs to the brain. This is not new to researchers who have studied the effect of stress upon the body's biochemistry and subsequent behaviour. Sensory input acts at the neural and visceral levels. Accordingly any explanation for the body's function must recognise the influence of cognition (sensory input, sense perception, sense coordination, memory, speed and nature of movement, etc) and the influence of stress – considered to be any effect beyond the body's natural physiological tolerance limits (Marks 2008). This induces biochemical instability in the body; affects the regulation of organ function, cell function or molecular biology; lowers immune function; and generates ROS, oxidative stress and its subsequent manifestation as pathology(s).

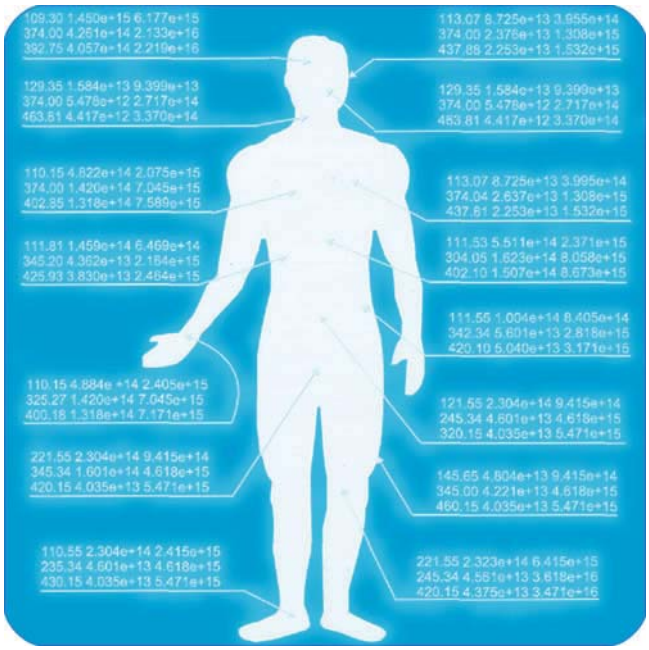

Fig. 2. Biomathematical model.

The study of the physiological systems has been limited by the lack of identifiable and measurable phenomena by contrast with biomedicine. Nevertheless, the lack of evidence for physiological systems does not mean that they do not exist, only that their significance has not yet been fully established i.e. of EEG frequencies (Ewing 2009). There are empirically recognised limits for system stability i.e. that recognised as *hyper* or *hypo* function, within which homeostasis prevails. This indicates that the body's complex structures and biochemistries are regulated and coordinated. The current understanding that the body's biochemistry (i) may be more complex than can be explained by reductionist-style research, and (ii) there are organ networks, (iii) should take into account the complex nature of the interactions governing their function. Paradoxically medical research has applied a systemic understanding to treat multi-systemic medical conditions. For example complex drug formulations are used to treat cardiovascular disease with (i) a drug to lower blood pressure and (ii) a diuretic to reduce blood volume. Consequently, it may be appropriate to redefine the nature and structure of such organ networks and the mechanisms which regulate their function.

- Russian researchers (Anokhin, Sudakov, Bekhtereva, Kryzhanovsky, Vysochin and others) have recognised that the body's nervous structures are linked to all aspects of its function and that such manifestations are linked to EEG brain frequencies.
- IG Grakov has mathematically modelled such relationships with diagnostic and therapeutic consequences (Vysochin *et al.* 2003). Using industry terminology, he appears to have *mathematically modelled the physiological systems*. To be more accurate he has mathematically modelled the consequences of cognition (in particular of visual perception and memory) upon the autonomic nervous system and physiological systems (see Figure 2).

The model takes into account the influence of pathologies upon sensory input and memory, in particular upon colour perception, which are manifest as

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departures from the predicted biomathematical model i.e. the light released from protein-substrate reactions has a colour and intensity which is unique to each reaction and to its rate of reaction (see Figure 3 example report). The stability or progression of each pathology and its influence upon the stability of each system and/or organ are mathematically expressed and reflect the influence of genotype and phenotype.

(Similar reports are available for all organs and glands in the blood glucose system i.e. brain, blood and peripheral blood vessels, adrenal, thyroid, pituitary, liver, kidneys and small intestines).

It is rarely considered that human function is context dependent however there are significant precedents which illustrate that human existence (i) is dependent upon sensory feedback from its environment and specifically from other humans (Kiecolt-Glaser & Glaser 2002; Marks 2008) and (ii) is dependent upon its local environment i.e. latitude, altitude, temperature, water quality, gravity, exposure to natural sunlight, etc. The biological limits or control points which influence mortality and morbidity are context dependent (Rostand 1997). Accordingly any understanding of physiological stability should consider genetic predisposition (genotype), environmental influences (phenotype), and/or the influence of context.

3.2 Physiological systems

The following systems have been identified and included in the mathematical model developed by IG Grakov: optimum levels of cell content of blood; blood volume, pH; osmotic pressure; blood glucose; blood pressure; breathing; digestion; body temperature; extraction; sexual functions; position of body in the environment; sleeping pattern; and locomotion, communication, etc.

Each system includes brain; blood and peripheral blood vessels; thyroid, adrenal and pituitary glands. Only the 'sleep' system differs i.e. it involves only the pituitary gland by comparison with all other systems (which feature thyroid, adrenal and pituitary glands). It is for this reason that sleep is essential for the regulated function of all other systems (i.e. the sleep system comprises brain, pituitary gland, spinal cord, peripheral nervous system, ear and nose).

For a system to be considered a system it must perform a physiological function e.g. (i) The regulation of the amounts of water and minerals in the body i.e. osmoregulation. The conventional explanation is that this takes place in the kidneys. (ii) The removal of metabolic waste for which the reductionist explanation considers that this involves the kidneys and lungs. Such organ-specific explanations appear oversimplistic i.e. it involves excretion, urination and breathing. Consider the example of the Blood Glucose System:

4. REGULATION OF BLOOD GLUCOSE

4.1 This mathematical model of the blood glucose system comprises the following organs:

Brain	Pituitary gland	Thyroid gland
Adrenal glands	Liver	Pancreas
Blood and peripheral blood vessels	Small intestine	Kidneys

(Origin: IG Grakov)

i.e. the brain regulates systemic function through the autonomic nervous system (blood supply), endocrine (pituitary, thyroid, adrenal and pancreas) and gluconeogenic organs (liver, kidney and small intestine).

Diabetes Mellitus (DM) is a disorder of regulation of blood glucose (Ewing & Ewing 2008). The occurrence of DM is statistically linked to the incidence of many forms of cancer and to diabetic complications including coronary heart disease, congestive heart failure, pulmonary embolism, polycystic ovarian syndrome, fatty liver disease, erectile dysfunction, urinary incontinence, renal failure, lymph oedema, cellulitis, stroke, sleep disorders, depression, osteoarthritis, gout, gallbladder disease, dementia, diabetic retinopathy, etc.

Known contributory factors which alter the nature and extent of protein expression include lack of sleep (Spiegel *et al.* 1999), viruses, vaccines (Ewing 2009), the influence of stress (Marks 2008), and dietary causes e.g. too rapid ingestion of high GI foods (Volek & Feinman

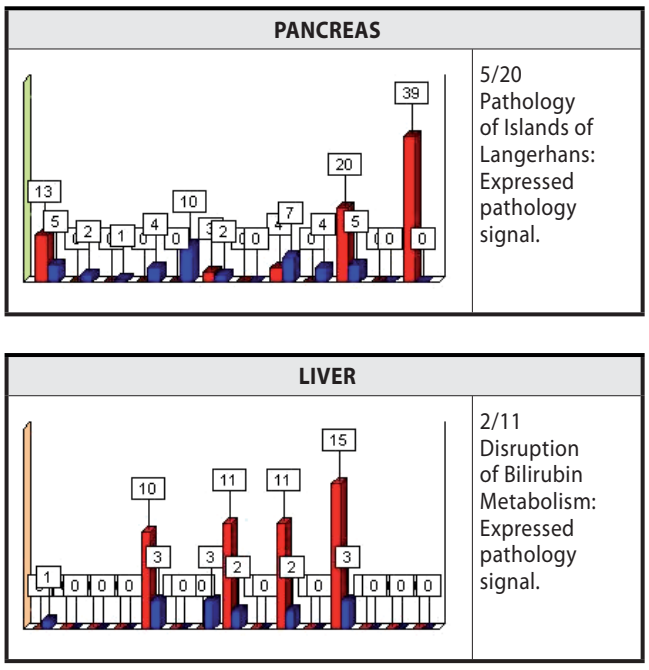

Fig. 3. Example report.

2005), excessive alcoholic consumption (Damodaran *et al.* 2006), GM foods (Séralini *et al.* 2007), and perhaps also low pH drinks (Erlanson-Albertsson 2005; Ostman *et al.* 2005).

DM has multi-systemic consequences: it affects the levels at which most systems function i.e. of blood glucose, blood volume (Laederach-Hofmann *et al.* 1999; Schiel 2002), sleep (Zee & Turek 2006; Spiegel *et al.* 1999) and subsequently the function and/or regulation of blood pressure (and circulation), blood cell content, pH and all other physiological systems. This influences the ability of insulin and other hormones to react and is noted, primarily, as *insulin-sensitivity* or *insulin-resistance*. The greater the extent of disease the more will each system be affected i.e. at the chronic level this will affect sexual performance, frequency of urination, digestion, excretion (stool quality), regulation of temperature, bone metabolism, posture and locomotion, etc.

*4.2 That the **brain** is involved in neural regulation of this system (see Figure 1) is supported by the following observations:*

- the brain is able to initiate the processes leading to increased availability of glucose e.g. to compensate when faced with lack of food supply and/or starvation (Smythe *et al.* 1984).
- insulin-receptors in the brain lower the levels of blood sugar (Gelling *et al.* 2006).
- alterations to blood glucose levels in the brain influence cognition (Evans & Sherwin 2002) and memory (Riby *et al.* 2009).
- the brain processes sensory input in particular that of visual perception. Biochemical change(s) due to the influence of pathologies or drugs influence visual perception of colours and visual contrast.
- aberrant behaviour is associated with glucose levels in diabetic children (Kemp 2008).
- the brain regulates blood pressure in order to maintain the supply of oxygen to the brain (Wade 1983).

*4.3 That the **pancreas** is involved in the regulation of blood glucose is supported by the following observations:*

- the pancreas produces insulin and glucagon which regulate the levels of blood glucose and glycogen.
- the ability of pancreatic beta-cells to produce insulin are influenced by the autonomic nervous system (Campfield & Smith 1980).
- the pancreatic exocrine glands produce a pancreatic fluid; comprising typically digestive enzymes, bicarbonate and salt; which is supplied to the small intestine in response to signals from the small intestine hormones secretin and cholecystokinin.
- too rapid digestion of high GI foods leads, ultimately, to an excess of insulin production by the pancreas (Daly *et al.* 1998).
- pancreatic polypeptide regulates the endocrine and exocrine balance of the pancreas i.e. it regulates the prevailing levels of glycogen in the liver and pancreatic secretions to the small intestines.

*4.4 That the **thyroid, adrenal and pituitary glands** are components in this system is supported by the following observations:*

- The thyroid hormones influences the function of every cell in the body. They are involved in the regulatory metabolism of fats, proteins, carbohydrates and vitamins.
- production of thyroid hormone is regulated by the pituitary. The pituitary releases TSH (thyroid stimulating hormone).
- thyroid problems are age-related and become more significant beyond 50 years i.e. following the menopause.
- thyroid problems are typically autoimmune type disorders which often occur alongside other similar conditions e.g. diabetes, rheumatoid arthritis, etc.
- hypothyroidism increases insulin requirements and hyperthyroidism increases glucose intolerance/regulation.
- adrenal insufficiency influences the production of cortisol and aldosterone (Ten *et al.* 2001).
- the pituitary gland may not be able to sustain production of adrenocorticotrophin (ACTH), oestrogen or testosterone, and/or other pituitary hormones, at the level required for homeostasis.
- light influences the function of the pituitary gland (Kostoglou-Athanassiou *et al.* 1998).
- light (295–297 nm) catalyses the production of Vitamin D3 in the skin (MacLaughlin *et al.* 1982). The relationship between the skin and the endocrines (Littorin *et al.* 2006) manifests as a vitamin D deficiency (Slominski 2005). This influences the metabolism of afrocaribbean immigrants to the UK and their descendants often resulting in DM, obesity, hypertension (Chaturvedi *et al.* 1993) i.e. increased morbidity and mortality.

The common explanation is that the hypothalamus releases hormones to the pituitary gland which responds by secreting hormones which regulate growth, and thyroid and adrenal function, and hormones e.g. estrogen and testosterone. The pituitary secretes ACTH (adrenocorticotropin), which stimulates the adrenal glands to produce cortisol. Cortisol then signals the pituitary to lower secretion of ACTH. This explanation does not consider that the endocrine glands are significantly more complex and involve many other hormones e.g. the pituitary produces HGH, oxytocin, vasopressin, FSH, TSH, LH, PRL; the adrenal produces an estimated 30 different corticosteroids; and the thyroid produces thyroxine and tri-iodothyroxine in a ratio of circa 20:1.

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*4.5 That the **liver, kidneys and small intestines** are essential components of this system is supported by the following observations:*

- the liver and kidneys are recognised as the most significant gluconeogenic organs. The small intestine has been identified as a third insulin-sensitive organ. Inhibiting the function of the small intestines reduces the occurrence of type 2 diabetes (Croset *et al.* 2001; Rubino 2008; Toshikatsu & Yutaka 2002; Aguirre *et al.* 2009).
- the prevalence of chronic liver disease influences the stability of blood glucose and/or the measurement of blood glucose levels (Bando *et al.* 2009).
- the degree of progression of chronic kidney disease, and hence of impaired kidney function, influences the regulation of blood glucose (Kalantar-Zadeh *et al.* 2009) i.e. kidney function influences the onset and progression of diabetes.
- absorption of zinc by the digestive system and small intestines is essential for the production of insulin (Chausmer 1998).
- absorption of magnesium by the digestive system and small intestines influences the occurrence of DM (Nadler *et al.* 1993).

*4.6 That the **blood and peripheral blood vessels** are involved in the regulation of blood glucose levels is supported by the following observations:*

- increased levels of blood glucose raise blood viscosity and blood pressure (Cinar *et al.* 2001).
- the blood conveys hormonal signals from all organs within each physiological system to the various receptors located in the organs, cells and/or blood vessels.
- endothelial dysfunction is associated with dysfunction of the ANS and is a common indicator or side-effect of coronary artery disease, hypertension, atherosclerosis, high levels of cholesterol, diabetes mellitus, etc (De Vries *et al.* 2000).

4.7 Autonomic instability

Such **autonomic instability,** in particular of the regulation of blood glucose, leads to oxidative stress (Baynes 1991; Kaneto *et al.* 1996; Rudich *et al.* 1998), the generation of ROS (Hunt *et al.* 1991), impaired regulation of homeostatic processes associated with regulation of blood glucose and of associated systems (Ewing *et al.* 2008; Ewing & Parvez 2008), increased blood viscosity, endothelial dysfunction (De Vries *et al.* 2000), and their subsequent manifestation as pathologies (Bhor *et al.* 2004). This is supported by noting, for example, the compensating effect of anti-oxidants upon the oxidative stress processes associated with diabetes (Shirpoor *et al.* 2006; Kaneto *et al.* 1999); the destressing effect of summer factors including exercise, sunlight and warmer weather; and that the liver stores essential vitamins and minerals e.g. vitamin A, vitamin D, vitamin B12, iron and copper.

5. DISCUSSION

The regulation of blood glucose may be too complex to be accurately described by the levels of individual biochemical components. There is significant evidence that the body's function is multi-systemic i.e. there is neural regulation of the physiological systems (Ewing & Ewing 2008; Ewing 2009), and that DM is a disorder of *the physiological system* which regulates the levels of blood glucose. Depending upon the extent of progression of a medical condition, the stability in one system may be accompanied by instability in other system(s) as the brain seeks to assert the best-fit homeostasis (Sudakov 1987) i.e. in more severe cases the body's stability will become stable around non-typical parameters (the chronic condition). In the case of DM the normal balance of autonomic nervous system hormones is destabilised and influences the regulated function of organs in this system including (but not limited to) the pancreas, liver, kidneys and small intestines. This results in the development of pathologies influencing the organs in the blood glucose system and subsequently in related systems e.g. blood pressure, blood volume, breathing, blood cell content, etc. The example outlined illustrates how regulation of blood glucose is a systemic phenomena and that systemic dysfunction has stress-related origins and multi-systemic consequences.

The altered reaction conditions, arising from the influence of stressors, influence (i) the absorption of minerals including zinc, the bioavailability of zinc, and the ability of pancreatic beta cells to produce insulin and/or (ii) the ability of insulin to react with its reactive substrates e.g. through lack of availability of essential minerals (Cr, Mg, Zn), altered pH and/or temperature, and (iii) the availability of components which influence the production of insulin and metabolism of blood glucose (i.e. the role of light to stimulate the pituitary gland, and to activate protein reactions, regulate liver function, produce vitamin D, etc).

The top-down systems biology approach outlined in this article has been incorporated into a commercialised cognitive technology (Ewing *et al.* 2007; Hankey & Ewing 2007; Hunter *et al.* 2001) which includes the mathematical modelling of the autonomic nervous system and physiological systems. Grakov IG has determined that the brain and organs work in a manner – analogous to a pair of mathematical matrices – which can be mathematically modelled. This has significant diagnostic and therapeutic significance. It compares with research which has modelled the function of the heart or other organs although perhaps without the apparent limitations associated with such biomedical approaches e.g. (i) inaccuracies associated with measurement of blood components e.g. the significance and accuracy of experientially derived limits of dysfunction,

instability of blood samples, time of sampling, sampling and test errors, etc; (ii) influence of variables upon the function and stability of the autonomic nervous system; (iii) the prevailing understanding of the nature and structure of the physiological systems. (iv) Colour perception can be used as a measure of the rate of reaction from protein-substrate reactions. It can be used to measure the rate of reaction for all key physiological processes and for developing pathologies: a cognitive test, measuring the full spectrum of colour perception, providing the core data to diagnose all medical conditions. This reduces the measurement of all medical conditions to a common biomathematical standard.

COMPETING INTERESTS

Graham Ewing is a Director of Montague Healthcare, a company devoted to the commercialisation of Virtual Scanning technology.

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