BioSystems xxx (xxxx) 105018

Contents lists available at ScienceDirect

BioSystems

journal homepage: www.elsevier.com/locate/biosystems

Short Communication

Laws of taxation for multicellular organisms: The economics of sleep

Arturo Tozzi

Center for Nonlinear Science, Department of Physics, University of North Texas, 1155 Union Circle, #311427, Denton, TX, 76203-5017, USA

ARTICLE INFO

Keywords:
Syncope
Electroencephalography
Spike frequency
Volterra equations
Inelastic commodity

ABSTRACT

In macro-public finance, the Ramsey rule (RR) concerns variable taxation to maximize social welfare and economic efficiency in a purely competitive monopolistic system. To extract tax revenue with the least loss of utility to the representative individual, RR dictates that optimal, proportionate taxes should be such as to diminish in the same proportion the production of each commodity taxed. The sources of supply that are inelastic, i.e., necessities/utilities, must be taxed more. We hypothesize that the Ramsey's economical approach might provide a general mechanism to investigate far-flung biological issues, such as preys/predators dynamics, food restriction in ecological niches, local changes in blood flow in rival or complementary organs of multicellular organisms. In particular, RR suggests a quantifiable relationship between the physiological decrease in cortical spike frequency occurring during sleep and energy consumption. Since small decreases in spike frequency during sleep are correlated with large decreases in the amount of consumed ATP, the brain could be considered an inelastic commodity which can be “taxed” more than other organs, allowing the whole organism to spare energy. Shedding light on the energy budget of the central nervous system, RR improves our knowledge of cerebral perfusion during sensory-evoked responses and tissue hypoxia caused by decreased blood flow, suggesting that energy from outside can be provided to counteract brain ischemia. In sum, the economical approach provided by Ramsey stands for a useful methodological tool that could be used in biological contexts to investigate the dynamical correlations among different organs in multicellular organisms.

1. Introduction

The Ramsey rule concerns the introduction of taxes in a public monopoly with no foreign trade, in which commodities' price regulation is adjusted to maximize both social welfare and statal earning (Ramsey, 1927; Boiteux 1956). Contrary to the stable equilibrium provided by absence of taxes, the Ramsey's approach paves the way for progressive income taxes and indirect taxation (a: KEEP this REFERENCE). Ramsey's premises sound as follows: if individuals were the same, the best policy option for a public monopoly is to lump sum taxes. Yet individuals are not the same in the real world, therefore a second-best policy solution is needed, consisting of an array of different taxes inside a system of taxation that is not uniform (Misak 2020).

In this paper, we aim to “borrow” the Ramsey rule from the economic field of macro-public finance to assess biological issues. In particular, we focus on the energy budget of the mammalian central nervous system, assessing.

1) Physiological conditions, such as sleep and task-evoked brain activity.
2) Pathological conditions, such as acute decrease of blood supply leading to brain tissue ischemia.

We discuss how the relationships between the Ramsey's economic framework and the energy requirements/constraints of the central nervous system make it possible to predict the frequency of the electric spikes and the amount of ATP spent in different settings, including sleep and task-related cerebral activation. We show that the Ramsey's framework can be also used to shed light on other biological issues, such as the blood supply of different organs in multicellular living organisms, the response of prey's population to changes in hunter's population and the case of food restriction in ecological niches. We conclude that the potential application of the Ramsey rule to biological affairs might stand for a useful methodological tool to shed light on unnoticed biological correlations. Further, the Ramsey rule suggests novel therapeutical approaches to counteract injuries in multicellular organisms and restore the proper functioning of impaired organs.

E-mail address: tozziarturo@libero.it.

https://doi.org/10.1016/j.biosystems.2023.105018
Received 5 July 2023; Received in revised form 30 August 2023; Accepted 30 August 2023
0303-2647/© 20XX

2. The Ramsey rule in macro-public finance

The dictates of the Ramsey rule are illustrated in Fig. 1A. The plot displays the quantity demand on the axis x and the price on the axis y. Ramsey assumes that the utility is a non-homogeneous quadratic function, so that the supply curves can be illustrated in terms of straight lines (red lines I and II). When the tax is kept constant (red lines I and II), changes in quantity demanded are linearly correlated with increases in price: the more the quantity, the more the price, and vice versa. The demand (the blue line) is expressed in terms of a Hicksian demand function, indicating how an economic agent would react to changes in the price of a good, if the agent is guaranteed the same previous utility. Ramsey suggests that the net utility is maximum when tax income is infinitesimal (Ramsey, 1927). Sufficiently small taxes can be described as a Taylor approximation, making the blue demand curves linear in the relevant range. The current price is given by the intersection between the red and the blue lines (green dot I). When tax is raised (red line II), the intersection between the red line II and the blue line (green dot II) reveals decreases in quantity demanded and increases in price.

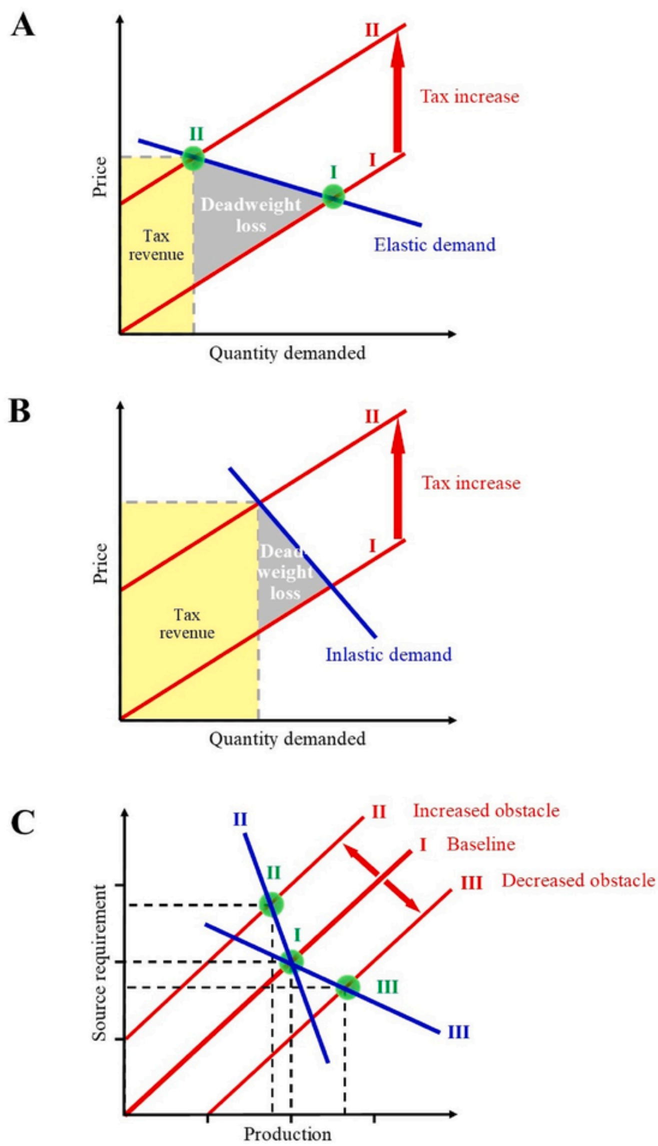

Fig. 1. Ramsey rule in economics and biophysics. Fig. 1A–B. Geometric analysis of the Ramsey rule after and before tax increase, in the two cases of elastic (Fig. 1A) and inelastic (Fig. 1B) demands. Fig. 1C. Putative use of the Ramsey rule to assess physical and biological issues. The Figure provides a rather general sketch that will be used in the next paragraphs to tackle manifold biological issues. See the main text for details.

Ramsey asks: when a tax revenue needs to be raised, how can the public monopoly minimize the unavoidable losses? In other terms, how much taxes on specific commodities must be increased or decreased by the public monopoly in order to optimize individual utility? He concludes that, in case of rivals (e.g., wine and beer) or complementary (e.g., tea and sugar) goods, optimal taxes should reduce in the same proportion the production of each taxed commodity to leave unchanged the proportions in which they are consumed (Gruber 2015). After raising the tax on a commodity, the state gets some revenue, corresponding to the shaded yellow area under the demand curve. Since raising taxes decreases production, some quantity demanded disappears (the grey area) and cannot be taxed anymore. Therefore, the state suffers losses too, corresponding to the shaded grey area under the demand curve, namely, the excess burden of deadweight losses, which stands for the difference in production and consumption of a given product or service. By the consumer's standpoint., the entire shaded grey and yellow area is what the consumer is willing to pay to avoid the tax.

Fig. 1A depicts the blue line of elastic demand, but there is also the case of inelastic demand (Fig. 1B). Price elasticity of demand is the change in quantity demand of a commodity in response to price change. It is the ratio between percentage changes in quantity and price, so that the demand is elastic when the quotient is greater than one and inelastic when smaller than one. Concerning elastic commodities, the change in quantity demanded is greater than the change in its price. In elasticity of demand, little change in the price of goods results in substantial change in quantity demanded, and vice versa. Decreases in price lead to significant increases in demand, resulting in increases in total spending and revenues of the seller. Elastic goods include luxury items that are subjected to infrequent change purchases. Elastic good also include brand-name food and beverages, such as spirits, Coca-Cola, cereals or candy bars. In this case, increases in price due to taxes will affect the demand, leading consumers to stop purchasing the commodity and shift to available substitute.

Demand is considered inelastic if the quantity demand for a good or service remains almost constant despite changes in price within a specific period. The percentage change in quantity demanded is less than in price. Large change in the price of goods results in little change in quantity demanded, and vice versa. The demand is insensitive such that consumers buy nearly the same amount as the price increases, leading to decreases in the seller's total revenue. When demand is more inelastic than supply, consumers bear a greater proportion of the tax burden than producers do. Inelastic commodities are usually necessities without acceptable substitutes, such as utilities, telecommunications, bus travel, oil, petrol, car fuel in short run, medical insurance, salt, rice, eggs, livestock. Inelastic goods include also the commodities for which consumers are addicted such as cigarettes, beer, etc.

The blue line is shallow in elastic demand (Fig. 1A) and steep in inelastic demand (Fig. 1A). In a perfectly elastic demand, the blue line must be parallel to the x axis. In the case of elastic demand, the total revenue and price move in opposite direction, whereas in the case of inelastic demand move both in the same direction. When taxes are increased, the excess burden of deadweight losses, i.e., the grey area, is higher in case of elastic than inelastic goods (Fig. 1B). In turn, the tax revenue, i.e., the yellow area, is higher for inelastic than elastic goods. In technical terms, in case of independent commodities, the optimal tax on each good should be inversely proportional to price elasticities. In colloquial terms, the taxation of inelastic goods provides economic advantages to the state, compared with the taxation of elastic goods. By taxing elastic goods, the government earns less and loses more. Therefore, the Ramsey rule suggests that, to lower deadweight loss and maximize social welfare, commodities which are inelastic must be taxed more in order to provide higher earnings to the state.

Summarizing, the Ramsey rule concerns goods pricing in a public monopoly with the purpose of maximizing social welfare and covering the fixed costs. The following conclusions can be drawn.

1) When taxes are fixed, increases in price lead to decreases in quantity demanded, while decreases in quantity demanded lead to increases in price.
2) Production must be depressed to raise a revenue.
3) Every increase in taxes corresponds to both an increase in price and a decrease in quantity demand, while every decrease in taxes corresponds to both a decrease in price and an increase in quantity demand.
4) Differences in price and demand occur between the lines of elastic or inelastic demand, leading to areas of deadweight loss of value and of tax revenue that are bigger for inelastic demand than for elastic demand.
5) The more the commodity is inelastic, the more it must be taxed.

In the sequel, we will see that the economical sketch provided by the Ramsey's approach can be used to tackle biological issues such as, e.g., various brain activities including sleep and task-related increase in electric spikes frequency.

Towards the Ramsey rule in biophysical affairs: the general framework. Could the dictates of the Ramsey rule be used to investigate the general features of physical and biological affairs? A viable solution is suggested in Fig. 1C. The plot illustrates a general scheme where the produced quantity is displayed on the axis x and the amount of the resources that can be spent on the axis y. Together with Ramsey, we assume that, at least for small adjustments, the produced quantity is always linearly correlated with the resource requirement such that the red lines I, II and III are straight. This means that the more the produced quantity, the more the resource requirement, and vice versa. Every value on the red line I (e.g., the green dot I) defines a parallelepipedal surface (dotted figure).

Every organism is characterized by a physiological baseline, corresponding to a default state (red line I). Departures from the default state can be caused by increased (red line II) and decreased (line III) obstacles to the baseline activity. To achieve the best advantage, the organism would react to deviations from the baseline. Novel equilibria would be achieved, exemplified by different parallelepipedal surfaces (demarcated by the green dots II and III) that can be quantitatively compared.

Summarizing, three parameters can be estimated when assessing biophysical issues through the Ramsey rule.

1) the parameter on the axis x, standing for the produced quantity.
2) the parameter on the axis y, standing for the required energy.
3) The parameters on the red lines. They correspond to the default state of the organism (**red line I**), to the state of the organism after an obstacle has been posed (**red line II**), to the state of the organism after an obstacle has been removed (**red line III**).

According to the Ramsey rule, the knowledge of two parameters leads automatically to the knowledge of the unknown third. For instance, when a quantifiable obstacle occurs (red line II) and the produced quantity can be experimentally computed on the axis x, the unknown amount of the required energetic resource on the axis y can be easily calculated (green dot II). In turn, if the values on the axes x and y are known (e.g., the green dot III), the unknown red line III can be drawn. Once identified the percent deviation of the obstacle from the baseline, we can quantify how far from the red line I we should draw the parallel red line III. Note that the blue lines could have different slopes, configurating the economical situations of elastic or inelastic demand. The steeper the blue line, the more the biological phenomenon will be inelastic, such that small decreases in quantity production will lead to great changes in energetic requirement.

In the sequel, we will give practical examples illustrating the dynamical responses provided by physical and/or biological organisms to optimize systemic utility.

3. The Ramsey rule and the central nervous system

We hypothesize that the Ramsey's rule concerning monopoly in macro-public finance could be used to investigate the energy budget of the central nervous system, improving our knowledge of neuroscientific issues such as sleep energetics, brain tissue hypoxia, and so on.

The brain requires a large amount of energy, mostly derived from glucose metabolism (Cuenoud et al., 2020). The brain corresponds to 2% of the human body mass yet it accounts for ~20% of the energy consumed (Fox and Raichle, , 2007; Fox,M.D.,Raichle,M.E.,2007.Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat.Rev.Neurosci.8,700e711 Raichle, 2010) (Raichle, M.E.,2010Apr. Two views of brain function. Trends Cogn.Sci.14(4), 180e190. http://dx.doi.org/10.1016/j.tics.2010.01.008). Almost 20–60% of the energy allocated for the brain supports the cortical grey matter's metabolic rate, including brain “housekeeping” under the isoelectric state, action potentials and transmembrane potentials restoration (Sengupta et al., 2013). The required energy is mainly generated from ATP hydrolysis, tightly correlated to changes in energy demand under various brain activities (Du et al., 2008). For example, the energy required for memory formation in fruit flies corresponds to ~10mJ/bit (Girard et al., 2023). During resting, a single human cortical neuron consumes 4.7 billion ATPs per second and the brain 5.7 kg ATP per day (Zhu et al., 2012).

The production of electric spikes requires energetic costs that can be quantified. ATP consumption at the “baseline” mean rate of 4 Hz is 3.29×10^9 molecules of ATP/neuron/sec, while each additional spike requires 6.5 μmol/ATP/gr/min (; Attwell and Laughlin, 2001) Attwell D, Laughlin SB. 2001. An energy budget for signaling in the grey matter of the brain. J Cereb Blood Flow Metab Off J Int Soc Cereb Blood Flow Metab21(10):1133–1145.doi:10.1097/ 00004647-200110000-00001Attwell et al., 2001). A spike's oscillation combines amplitude and frequency. For the Ohm's law, the electric spikes' energy consumption due to the *amplitude* is negligible as compared with energy consumption due to the *frequency* (Tozzi et al., 2016). Therefore, the higher the spike frequency, the higher the energetic cost, quantifiable through the amount of ATP consumption. This means that evoked activities of the brain such as perceptual and motor tasks require local increases in spike frequency, compared with the spontaneous activity. Beta and gamma waves generated during task performance require additional energy consumption of ~5% (Attwell et al., 2001; Sengupta et al., 2013). It is noteworthy that recent technologies such as cerebral tissue perfusion's real-time monitoring have made biochemical energetic analysis widely available and accessible (Smolders et al., 2003; Schmidt et al., 2021; Si et al., 2023).

The cerebral blood flow is another factor that must be considered when assessing the brain energy budget via the Ramsey rule. Being not capable of glucose storage, the brain can be considered a monopoly that requires a continuous supply of energy sources provided by the cerebral blood flow (Takahashi 2022). The latter can be regulated in response to neuronal activity so as to ensure adequate supply of glucose to meet the neuronal metabolic demands of the grey matter (Takahashi 2022).

The alleged dictates of the Ramsey rule in the biological context of the central nervous system can be illustrated by a plot displaying the spike frequency on the axis x and the amount of ATP consumption on the axis y (Fig. 2A). It can be assumed that spike frequency and ATP consumption are linearly correlated (**red line I**), such that the energetic steps from low-frequency spontaneous activity to high-frequency task activity can be quantified. When the blood flow is kept constant throughout the brain (**red line I**), changes in spike frequencies are linearly correlated with increases in ATP consumption: the more the spike

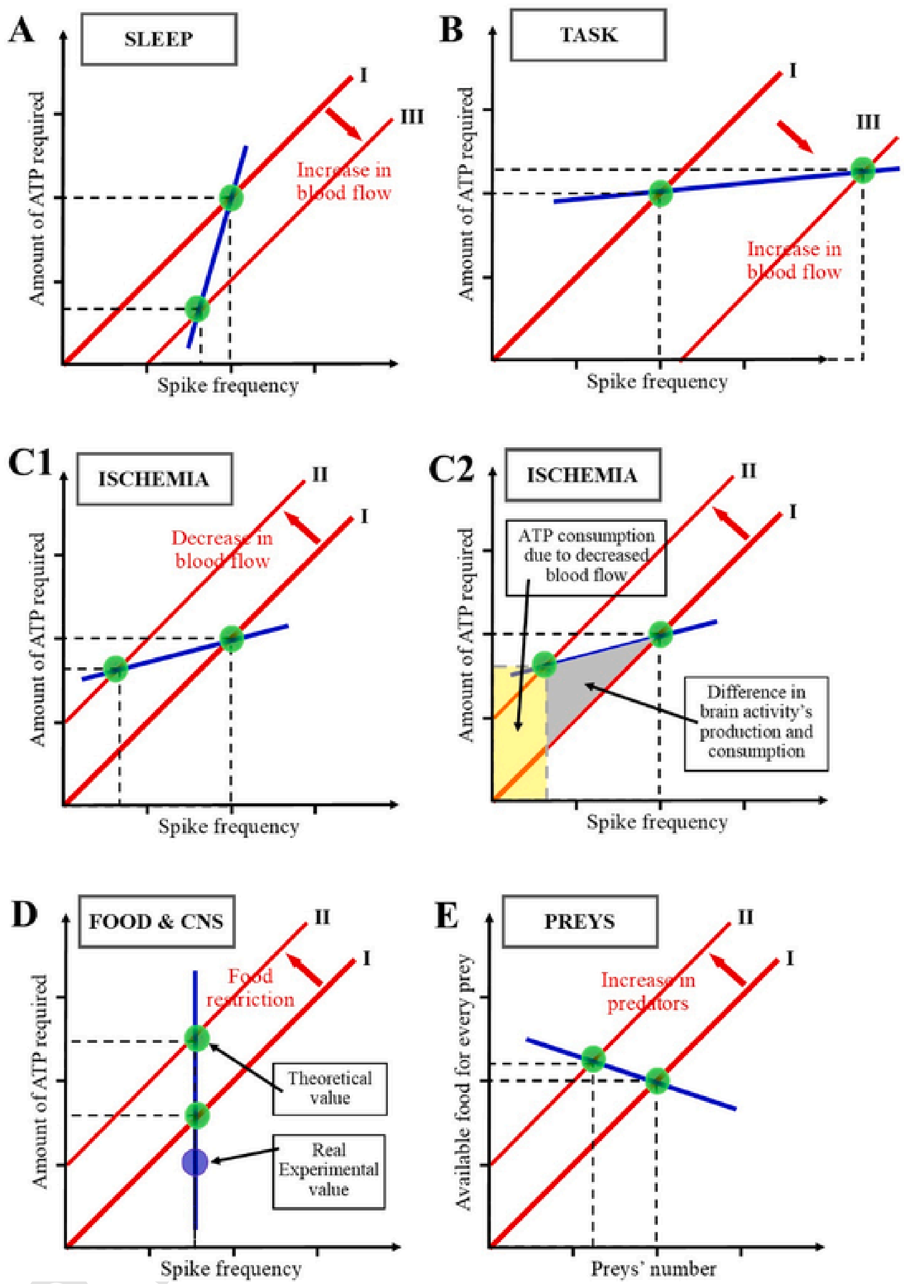

Fig. 2. Putative geometric analysis of the Ramsey rule in different biological settings. Fig. 2A–C cope with the brain's energy budget before and after changes in cerebral lood flow caused by different factors, i.e., sleep (Fig. 2A), task-related activities (Fig. 2B), cerebral ischemia (Fig. 2C1–2C2) and the relationship between food availability and spike frequency (Fig. 2D). Fig. 2E illustrates a biological example concerning the relationships between changes in number of preys/predators and food availability. See the main text for further details.

frequency, the more the ATP consumed, and vice versa. Small decreases in blood flow can be described by the **red line II**, while small increases by the **red line III**. When the blood flow locally decreases (**red line II**), increases in ATP consumption and decreases in spike frequency simultaneously occur (**green dot II**).

If we want to investigate the putative nervous counterparts of the Ramsey's rule, we are required to establish a few equivalences.

a) Ramsey's equilibrium without taxation stands for the default mode network at the system's baseline.
b) The cost stands for the ATP quantity required to go from lower to higher Hz in a given brain area.
c) The profit stands for the physiological activity gained by increase in Hz to perform the job.
d) The produced quantity stands for the spike frequency.
e) The quantity demanded stands for the ATP required to produce every type of spikes,
f) The tax baseline stands for the blood intake required to produce the brain activity at rest.
g) During task, an increase in quantity demand is achieved.

In the sequel, we will provide a few examples that illustrate how the Ramsey rule could (and could not) be used to investigate nervous issues.

Sleep. The above-described methodological approach leads to our first neuroscientific application of the Ramsey rule, i.e., the case of sleep. Thanks to the connections among CBF, BOLD, CMRO2 and CMRGlu, changes in blood flow have been detected both during awake states and sleep (Davis et al., 1998; Elvsåshagen et al., 2019; Park et al., 2021). The metabolic relationship between CBF and CMRO2 is still being investigated, with recent models adopting the action of glymphatic system as an additional player (DiNuzzo et al., 2023; Holstein-Rønsbo et al., 2023). It has been established that the brain blood flow increases of ~4–26% during slow-wave sleep and of about 80% during REM sleep (Douglas 2011). In mammal models, the arteriole diameter and the cerebral blood volume increase 2–5 times more during sleep than the increases evoked by sensory stimulation (Turner et al., 2020). Marked increases in amplitude and decreases in frequency of bilateral low-frequency oscillations have been found during sleep, with neural activity being substantially larger than the neural activity elicited by sensory-evoked responses (Stevner et al., 2019; Schreiner et al., 2021). Therefore, matching the Ramsey rule's previsions, experimental findings suggest that increases in blood flow during sleep are correlated with decreases in both spike frequency and energy consumption (Fig. 2A).

In touch with the Ramsey's previsions, increase in blood flow, decrease in spike frequency and decrease in energy consumption take place during sleep. If the Ramsey rule holds true, the experimental knowledge of two factors leads automatically to the calculation of the unknown third. For example, the known values of blood flow and spike frequency leads to extrapolate the unknown value of energy consumption. Note that the Ramsey rule does not hold for very low frequencies, where the amount of ATP consumption reaches the zero on the axis x. Therefore, it can be predicted that sparing energy during sleep holds only for a certain range of spike frequency.

The Figure suggests that the demand is rather inelastic (steep blue line), leading to the prediction that small decreases in spike frequency during sleep are correlated with large decreases in energy consumption. This means that the brain can be "taxed" more than other organs during sleep, since the deadweight loss is lower than in other organs. Therefore, the Ramsey framework suggests that sleep is a very convenient and affordable activity for the whole living organism, allowing to spare large amounts of energy at the expenses of higher cognitive activities.

Task-related brain hyperperfusion. During sensory-evoked responses, increase in cerebral blood flow leads to simultaneous increases in number of spikes and ATP consumption (Lin et al., 2010). It would be tempting to believe that task-induced neuronal activation, characterized by higher spike frequencies with higher energy demands, would require very large increases of both ATP production and cerebral blood flow. However, contrary to this claim, the energy demand of task-induced brain activation is small relative to the hyperemic response. Indeed, increases in cerebral blood flow are large (about 58%), compared with relatively small increases in ATP (about 15%) (Lin et al., 2010). This scenario is outlined in Fig. 2B. The Ramsey rule holds true also in this case, where a paradoxical increase of spike frequency occurs despite a small increase of required energy. It is noteworthy that the blue line is shallow as in case of elastic demands. This issue will be deepened further in the conclusions.

Syncope, EEG & brain perfusion. Cerebral perfusion represents a single parameter encompassing various phenomena such as arterial pressure, vascular anatomy, viscosity, regional variations of vascular tone, etc (Pranevicius and Pranevicius, 2009). Cerebral ischemia can be caused by several factors, such as hypoperfusion during normothermia or incomplete hypothermia, vaso-vagal depression, syncope (Levy and Parcella, 1987). Cerebral ischemia in animal models brings down cortical blood flow to <2 ml/100 g/min, depleting levels of ATP throughout the whole brain (Marcy and Welsh, 1984) and generating long-term metabolic changes (Tukacs et al., 2023). During spontaneous and induced vasovagal reaction, the total blood volume and the tissue oxygenation strongly decrease in the central nervous system, compensated by a slight blood volume pooling in the lower body part (van Dijk et al., 2014). Following vasodepressor syncope, a slowdown in EEG activity occurs, characterized by generalized high-amplitude waves followed by frequency reduction at 1.5–3 Hz (Ammirati et al., 1998; Aebi et al., 2019). Slow-flat-slow patterns are correlated with more severe cerebral hypoperfusion (Solbiati and Sheldon. 2014). Also, brain electrical activity during acute ischemic stroke and subsequent hyper-acute cerebral tissue hypoperfusion leads to increases in delta and theta EEG power (Ajčević et al., 2021). Increases in slower EEG frequency bands also occur as early as ~10–15 s during cerebral hypoperfusion following cardiac arrest (Razavi and Meador, 2016).

In touch with the Ramsey's framework, the effective outflow pressure could be taken as uniform throughout the brain. As dictated by the Ramsey rule, decreases in cerebral blood flow during ischemia lead to decreases in spike frequency corresponding to specific values of ATP consumption (Fig. 2C1). If the Ramey rule holds true, the knowledge of the flow perfusion and of the EEG spike frequency permits to quantify the unknown amount of ATP required by the brain to compensate the injury. This would mean that the amount of external energy to administer during ischemia to avoid long-term brain damage could be quantified. Yet, if the values of EEG spike frequency and energy consumption are known during a brain ischemic attack, the percentage of cerebral flow reduction might be calculated. Fig. 2C2 suggests that, after the occurrence of an obstacle interfering with the baseline state, there is a leftover amount of energy (corresponding to the grey area) that gets lost and cannot be used anymore, while there is a beneficial part (corresponding to the yellow area) that can be fruitfully used by the organism.

Food restriction and the central nervous system. The effects of food restriction on the central nervous system suggest that metabolic states are able to dynamically regulate the neocortical energy budget. Nevertheless, the Ramsey rule does not hold in case of food restriction. The Ramsey rule would predict that spike frequency preservation during food restriction might give rise to increase in ATP consumption (see the theoretical value illustrated in Fig. 1D). However, it has been experimentally demonstrated that food restriction does not increase, rather reduces by 29% the utilization of synaptic ATP in the visual cortex (Padamsey et al., 2022). Neuronal excitability is nonetheless preserved by compensatory increases in input resistance and depolarized resting potentials. This means that neurons under food restriction spike at similar rates as controls but spend less ATP (see the experimental value illustrated in Fig. 1D).

Therefore, the Ramsey rule doesn't always apply to biological issues and researchers needed to be careful with its use.

Summarizing, the Ramsey rule is a useful methodological tool to elucidate some issues concerning the central nervous system's dynamics. In the next chapter, we will tackle other biological potential applications of the Ramsey rule.

4. The Ramsey rule and multiorgan living systems

Modifications in energy budgets are an ecologically relevant parameter for livings systems embedded in their biological niches (Smolders et al., 2003). Biophysical constraints related to animal body mass, energy expenditure for maintenance, growth, reproduction and heat-dissipation, represent an a priori cost deeply impacting metabolic resources (Dyer et al., 2023). The Ramsey's framework suggests that living beings' energetic requirements can be used to test physiological responses under the same exposure regime and link cellular effects to other endpoints within the same population (Smolders et al., 2003). Note that the requirements of a living organism can be compared with Ramsey's demand of a monopoly. The use the Ramsey's rule in biology underlies a general framework: *when an obstacle occurs to the physiological dynamics of multiorgan living systems, organ production is lowered and more resources are spent*. An available amount of energy is left for the organism, while another part is irreparably lost for the organism. In the next paragraphs we will describe feasible and unfeasible applications of the Ramsey rule to biological issues.

Nutrients and organ efficiency. The Ramsey rule might be used to analyze the introduction of variable intake of nutrients in an energetically self-sufficient multicellular system, in order to maximize both the well-being of each organ and the total energetic efficiency of the whole organism (Aytaç 2018). In Ramsey's jargon: the extraction from the organism of revenue (with the least loss of utility to the single organ) requires that the optimal amount of nutrients (expressed in terms of increases or decreases in flow to single organs) should be such as to diminish in the same proportion the production of each involved organ. Increases or decreases in blood flow may occur in different organs due to either physiological conditions like the activation of the adrenergic system during running to avoid predators, or to pathological conditions such as stroke. The Ramsey rule might answer to the questions.

a) When the energetic requirements need to be raised, how can the whole organism minimize the unavoidable losses?
b) How much the whole organ might increase or decrease the local blood flow to optimize the well-functioning of every one of its single organs?

In case of rival organs (e.g., skin and hearth while running) or complementary organs (e.g., gut and kidney after eating), local changes in blood flow should reduce in the same proportion the specific activity of each involved organ in order to leave unchanged the proportions in which they are used. Here is how Ramsey's framework could work. After decreases in blood flow inside a given organ, the whole organism gets some revenue, corresponding to the shaded yellow area under the demand curve in Fig. 1A. In turn, the whole organism suffers losses too, corresponding to the shaded grey area under the demand curve in Fig. 1A, standing for the difference in production and consumption of a given organ. Since local decreases in blood flow lead to reductions in organ's production, some quantity demanded disappears (the grey area in Fig. 1A) and cannot be used anymore. By the single organ's standpoint., the entire shaded grey and yellow area in Fig. 1A is what the organ is willing to pay to compensate the locally decreased blood flow.

Food restriction in ecological niches. Ramsey's rule could also be used to tackle population dynamics in relatively closed ecological niches, the latter corresponding to a monopolistic competition. Take, for example, the dynamics between prey and predator illustrated in Fig. 2E. The number of preys is displayed on the x axis and the available food for every prey on the axis y. The perturbing factor acting as an obstacle for preys is the increase in number of predators (red line II). When predators increase in number, a decrease in number of preys occur. Still, a decrease in preys' number means an increase in available food for the surviving preys. From a real-world perspective, if the number of predators is known, the Ramsey's rule permits to calculate the amount of required food when the remnant preys decrease in number, and, vice versa, the number of preys when the amount of consumed food is known. If the number of preys and the amount of consumed food are both known, the Ramsey rule allows to quantify the number of predators.

The Ramsey rule could be used to complement the Lotka–Volterra equations, i.e., the nonlinear differential equations that illustrate the oscillating dynamics of two interacting species (Lotka, 1910; Zhu et al., 2023). The Lotka–Volterra equations and the Ramsey rule have some features in common and differ on some things. In both, the fluctuating numbers of predators and prey observed in natural populations can be described by a single variable. However, the Lotka–Volterra model assumes that the preys, unless subject to predation, have unlimited food supply and exponential growth, while the Ramsey's framework assumes that the growth is always linear. Yet, the Ramsey rule, being more sensitive to small changes than the Lotka–Volterra equations, might better describe the micro-dynamics occurring between preys and predators. Further, the Ramsey rule might be better equipped in detecting the interactions between species and populations that are not fixed but change over time (Park et al., 2023).

Hormone homeostasis. It would be tempting to use the Ramsey rule to investigate the role of the hormones, i.e., the biological molecules sent to distant organs in multicellular organisms. To provide an example, the thyroid hormones in the human body could be evaluated. In Ramsey's terms.

a) The cost could stand for the ATP required to produce fT3.
b) The earning would be the achievement of the baseline stability guaranteed by the fT3 homeostasis.
c) The tax baseline would be the ATP required to produce fT3.
d) The tax increase would be the decrease in ATP reservoirs required to produce fT3.

However, the Ramsey rule cannot be used in this case. Indeed, the whole organism tends towards a state of homeostasis, so that the earning cannot be quantifiable in biological terms, but just in terms of rather qualitative concepts such as well-being, baseline stability and body preservation.

5. Conclusions

We showed that the economical sketch drawn by the Ramsey rule could be used to assess the brain function, shedding new light on nervous energetic mechanisms that underlie phenomena like sleep and tissue hypoxia. Also, we described how the Ramsey rule's economic dictates can be used to tackle other biological issues such as preys/predators relationships and food shortage in ecological niches. Summarizing, the Ramsey rule applied to biology concerns the occurrence of obstacles in a living systems or group of living systems that try to maximize their welfare and cover their fixed energetic costs. The following inferences can be drawn.

1) Increases in obstacles lead organisms to produce less and spend more.
2) Increase or decreases in obstacles to the system's stable functioning represent departures from the baseline that are able modify the energetic requirement and the production of the quantity demanded.
3) When the obstacles are removed, increases in energetic requirement linearly lead to decreases in production of the quantity demanded, while decreases in production of quantity demanded linearly lead to augmented energetic requirement.
4) Changes in the values of three different biological parameters can be quantified through a powerful mathematical apparatus borrowed from economic disciplines.

Differences in produced quantity and energetic requirement generate different biological settings that resemble the economic concept of elastic or inelastic demand. The Ramsey's framework suggests that some biological situations can be described in terms of elastic demand, while others in term of inelastic demand. For instance, being the blue curve very steep, sleep falls within the case of inelastic demand (Fig. 2A). This means that small decreases in spike frequency during sleep ends up saving large quantities of ATP. In turn, the demand is insensitive such that the brain generates nearly the same spike frequency as the ATP consumption increases. Living organisms must optimize systemic utility at the expenses of their singular components: when demand is more inelastic than supply, the single components will bear a greater proportion of the tax burden than the whole living system will. Therefore, the Ramsey rule suggests that, to both maximize the well-being of the whole organism and spare energy, organs with inelastic behavior such as the brain during sleep must be “taxed” heavily. These findings confirm that sleep is a vital function of the brain which stands for a necessary “good” without acceptable substitutes.

When the blue line is shallow, biological phenomena fall within the case of elastic demand. This is the case for task-evoked brain activity (Fig. 2B), central nervous system ischemia ((Fig. 2C), prey/predator relationships (Fig. 2E). Little changes in energetic expense result in substantial change in quantity produced, and vice versa. By “taxing” elastic commodities, the whole organism earns less and loses more. Indeed, decreases in energetic requirement lead to significant increases in demand, resulting in organism's increases in total spending and revenues. Increases in price due to taxes for elastic commodities will lead consumers to stop using the commodity, shifting to available substitute. This suggests that cerebral perfusion during sensory-evoked responses might be blocked after a certain amount of energy is consumed, not being the highly expensive cerebral activity any more advantageous for the organism.

Apart from being a resourceful tool ensuring public goods/entitlements to be financed by efficient taxation, the Ramsey rule displays another invaluable advantage, i.e., it is quantitatively expressed as a quantitative differential equation that, working like a Euler–Lagrange equation, can be applied to other disciplines (Mulligan et al. 1998) ; Mulligan, Casey B. and Sala-i-Martin, Francesc Xavier, The Optimum Quantity of Money: Theory and Evidence (March 1997). NBER Working Paper No. w5954, Available at SSRN: https://ssrn.com/abstract = 225734). However, there are limitations to the use of the Ramsey rule. For exempting savings from income-tax, we must suppose the taxes imposed only for a very short time. Further, Ramsey suggests that savings as future consumption should be taxed too. Besides, we might be justified to raise revenue by placing bounties or subsides on some commodities and taxes on others. The greatest criticism to the Ramsey rule of optimal taxation is that the indispensable commodities have low price elasticity of demand, while luxury goods have not (Aytaç 2018). This calls for high tax rates on necessities and low tax rates on luxury commodities, introducing conflict between efficiency and social justice (Nahata et al., 2007). As illustrated above, there are also cases, such as food restriction in the brain and hormone homeostasis, in which the Ramsey rule fails to describe biological issues. Ramsey assumes that the quantities on the axis x and y are linearly correlated: for example, spike frequency and ATP consumption in Fig. 2A are on a straight line. This assumption of linearity cannot be taken for granted in biological systems and needs experimental confirmation or rejection. Still, the potential occurrence of nonlinear correlation between the quantities on the axis x and y does not invalidate the Ramsey's approach. Indeed, with the proper calculations, the baseline straight curve could be rather easily replaced by a curved one.

It could be speculated that the legitimacy of the Ramsey rule in contexts different from economics could be endorsed by testing it on other physical and biological phenomena. For instance, it could be conjectured that the relationship between ageing and bodily energy consumption might obey the Ramsey dictates, as well as earthquakes’ seismic waves amplitude and ground energy. To stay in the field of human biology, a theoretical relationship obeying the Ramsey rule could be explored between the volume of intestinal gases and the contraction/dilation of the gut walls. Other issues worth investigating are the relationships between muscle contraction and ATP expenditure, or between changes in colonic pH and intestinal motility. Do these phenomena obey elastic or inelastic dictates? For instance, being the muscles more essential for mammals than large brains, could the muscular apparatus be compared with inelastic commodities?

In conclusion, we argue that the Ramsey rule borrowed from macroeconomics seems a promising candidate to investigate the dynamics of (at least) some physical and biological phenomena.

Ethics approval and consent to participate

This research does not contain any studies with human participants or animals performed by the Author.

Consent for publication

This research does not contain any studies with human participants or animals performed by the Author.

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Availability of data and materials

All data and materials generated or analyzed during this study are included in the manuscript. The Author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

The Author performed: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, obtained funding, administrative, technical, and material support, study supervision.

Uncited references

INSERTED IN THE MAIN TEXT; Barro and Sala-i-Martin, 2004; Fox and Raichle, 2007; Raichle, 2010.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

References

Aebi, Mathias R., Bourdillon, Nicolas, Meziane, Hadj B., Nicol, Edward, Jérôme Barral, et al., 2019. Cardiovascular and cerebral responses during a vasovagal reaction without syncope. Front. Neurosci. 13, 2019. https://doi.org/10.3389/fnins.2019.01315. . 10 December 2019.

Ajčević, M., Furlanis, G., Miladinović, A., et al., 2021. Early EEG alterations correlate with ctp hypoperfused volumes and neurological deficit: a wireless EEG study in hyper-acute ischemic stroke. Ann. Biomed. Eng. 49, 2150–2158. https://doi.org/10.1007/s10439-021-02735-w. . 2021. .

Ammirati, Fabrizio, Colivicchi, Furio, Di Battista, Giancarlo, Garelli, Fausto Fiume, Santini, Massimo, 1998. Electroencephalographic correlates of vasovagal syncope induced by head-up tilt testing. Stroke 29 (11), 2347–2351. https://doi.org/10.1161/01.STR.29.11.2347Stroke. . 1998;29.

Attwell, D., Laughlin, S.B., 2001. An energy budget for signaling in the grey matter of the brain. J. Cerebr. Blood Flow Metabol. 21 (10), 1133–1145.

Aytaç, Deniz, 2018. Optimal taxation of consumption in the scope of changing. Taxes and taxation trends. In: Jolanta Iwin-Garzy?ska. https://doi.org/10.5772/intechopen.74378.

Barro, Robert J., Sala-i-Martin, Xavier, 2004. Growth Models with Consumer Optimization. Economic Growth, second ed. McGraw-Hill, New York, p. 91, ISBN 978-0-262-02553-9.

Boiteux, M., 1956. Sur la gestion des Monopoles Publics astreints a l’equilibre budgetaire.

Econometrica 24 (No. 1), 22–40. https://doi.org/10.2307/1905256. . Jan., 1956.
Cuenoud, Bernard, Özlem Ipek, Shevlyakova, Maya, Beaumont, Maurice, Cunnane, Stephen C., et al., 2020. Brain NAD is associated with ATP energy production and membrane phospholipid turnover in humans. Front. Aging Neurosci. 12, 2020. https://doi.org/10.3389/fnagi.2020.609517.
Davis, Timothy L., Kwong, Kenneth K., Weisskoff, Robert M., Rosen, Bruce R., 1998. Calibrated functional MRI: mapping the dynamics of oxidative metabolism. Proc. Natl. Acad. Sci. USA 95 (4), 1834–1839. https://doi.org/10.1073/pnas.95.4.1834.
DiNuzzo, Mauro, Dienel, Gerald A., Behar, Kevin L., Petroff, Ognen A., Helene Benveniste, et al., 2023. Neurovascular coupling is optimized to compensate for the increase in proton production from nonoxidative glycolysis and glycogenolysis during brain activation and maintain homeostasis of pH, pCO2 , and pO2. 2023 May 7. J. Neurochem. https://doi.org/10.1111/jnc.15839. . Online ahead of print.
Douglas, Neil J., 2011. Respiratory physiology. In: Kryger, Meir, Roth, Thomas, William, C. (Eds.), Principles and Practice of Sleep Medicine. 2017.
Du, Fei, Zhu, Xiao-Hong, Zhang, +3, Yi, Chen, Wei, 2008. Tightly coupled brain activity and cerebral ATP metabolic rate. Proc. Natl. Acad. Sci. USA 105 (17), 6409–6414. https://doi.org/10.1073/pnas.0710766105.
Dyer, Alexander, Brose, Ulrich, Berti, Emilio, Rosenbaum, Benjamin, Myriam, R., Hirt, 2023. The travel speeds of large animals are limited by their heat-dissipation capacities. PLoS Biol. https://doi.org/10.1371/journal.pbio.3001820.
Elvsåshagen, Torbjørn, Mutsaerts, Henri JMM., Zak, Nathalia, Norbom, Linn B., Quraishi, Sophia H., et al., 2019. Cerebral blood flow changes after a day of wake, sleep, and sleep deprivation. NeuroImage Volume 186 (1), 497–509. https://doi.org/10.1016/j.neuroimage.2018.11.032. . February 2019.
Fox, M.D., Raichle, M.E., 2007. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat. Rev. Neurosci. 8, 700–711.
Girard, Maxime, Jiang, Jiamu, van Rossum, Mark CW., 2023. Estimating the Energy Requirements for Long Term Memory Formation. arXiv:2301.09565.
Gruber, Jonathan, 2015. Public Finance and Public Policy. fifth ed. Worth Publishers. -13 : 978-1464143335.
Holstein-Rønsbo, Stephanie, Gan, Yiming, Giannetto, Michael J., Rasmussen, Martin Kaag, Sigurdsson, Björn, et al., 2023. Glymphatic influx and clearance are accelerated by neurovascular coupling. Nat. Neurosci. 26 (6), 1042–1053. https://doi.org/10.1038/s41593-023-01327-2. . Epub 2023 Jun 1.
Levy, W.J., Parcella, P.A., 1987. Electroencephalographic evidence of cerebral ischemia during acute extracorporeal hypoperfusion. J. Cardiothorac. Anesth. 1 (4), 300–304. https://doi.org/10.1016/s0888-6296(87)80041-8. . 1987 Aug.
Lin, Ai-Ling, Fox, Peter T., Jean Hardies, +1, Gao, Jia-Hong, 2010. Nonlinear coupling between cerebral blood flow, oxygen consumption, and ATP production in human visual cortex. Proc. Natl. Acad. Sci. USA 107 (18), 8446–8451. https://doi.org/10.1073/pnas.0909711107.
Lotka, A.J., 1910. Contribution to the theory of periodic reaction. J. Phys. Chem. 14 (3), 271–274. https://doi.org/10.1021/j150111a004.
Marcy, V.R., Welsh, F.A., 1984. Correlation between cerebral blood flow and ATP content following tourniquet-induced ischemia in cat brain. J. Cerebr. Blood Flow Metabol. 4 (3), 362–367. https://doi.org/10.1038/jcbfm.1984.53. . 1984 Sep.
Misak, C., 2020. Frank Ramsey: A Sheer Excess of Powers. OUP, Oxford. -13 : 978-0198755357.
Mulligan, Casey B. and Sala-i-Martin, Francesc Xavier, The Optimum Quantity of Money: Theory and Evidence (March 1997). NBER Working Paper No. w5954, Available at SSRN: https://ssrn.com/abstract=225734
Nahata, Babu, Izyumov, Alexei, Busygin, Vladimir, Anna, Mishura, 2007. Application of Ramsey model in transition economy: a Russian case study. Energy Econ. 29 (1), 105–125. https://doi.org/10.1016/j.eneco.2005.09.011. . January 2007.
Padamsey, Zahid, Katsanevaki, Danai, Dupuy, Nathalie, Nathalie, L., Rochefort, 2022. Neocortex saves energy by reducing coding precision during food scarcity. Neuron 110 (Issue 2), P280–P296. . E10, January 19, 2022.
Park, S., Hong, H., Kim, R.Y., Ma, J., Lee, S., Ha, E., Yoon, S., Kim, J., 2021. Firefighters have cerebral blood flow reductions in the orbitofrontal and insular cortices that are associated with poor sleep quality. Nat. Sci. Sleep 13, 1507–1517. https://doi.org/10.2147/NSS.S312671.
Park, Youngjai, Shimada, Takashi, Son, Seung-Woo, Park, Hye Jin, 2023. Invasion and interaction determine population composition in an open evolving ecological system. Chaos 33 (6), 063151. https://doi.org/10.1063/5.0142978. . 2023 Jun 1.
Pranevicius, Mindaugas, Pranevicius, Osvaldas, 2009. Can processed EEG monitoring detect postural cerebral ischemia or cerebral hypoperfusion? Circulation 84 (24), 122. . No. 1.
Raichle, M.E., 2010. Two views of brain function. Trends Cognit. Sci. 14 (4), 180–190. https://doi.org/10.1016/j.tics.2010.01.008. . Epub 2010 Mar 4.
Ramsey, F.P., 1927. A contribution to the theory of taxation. Econ. J. 37 (145). . Mar., 1927.
Razavi, Babak, Meador, Kimford, 2016. Dynamics of quantitative EEG changes during cerebral hypoperfusion (I11.002). Neurology (16 Suppl. ment), 86. . April 05, 2016.
Schmidt, Cameron A., Fisher-Wellman 2, Kelsey H., Neufer, P Darrell, 2021. From OCR and ECAR to energy: perspectives on the design and interpretation of bioenergetics studies. J. Biol. Chem. 297 (4), 101140. https://doi.org/10.1016/j.jbc.2021.101140. . 2021 Oct.
Schreiner, T., Petzka, M., Staudigl, T., et al., 2021. Endogenous memory reactivation during sleep in humans is clocked by slow oscillation-spindle complexes. Nat. Commun. 12, 3112. https://doi.org/10.1038/s41467-021-23520-2.
Sengupta, B., Stemmler, M.B., Friston, K.J., 2013. Information and efficiency in the nervous system--a synthesis. PLoS Comput. Biol. 9 (7), e1003157. https://doi.org/10.1371/journal.pcbi.1003157.
Si, J., Li, M., Zhang, X., et al., 2023. Cerebral tissue oximeter suitable for real-time regional oxygen saturation monitoring in multiple clinical settings. Cogn Neurodyn 17, 563–574. https://doi.org/10.1007/s11571-022-09847-6.
Smolders, Roel, De Boeck, Gudrun, Blust, Ronny, 2003. Changes in cellular energy budget as a measure of whole effluent toxicity in zebrafish (Danio rerio). Environ. Toxicol. Chem. 22 (4), 890–899. . 2003 Apr.
Solbiati, Monica, Sheldon, Robert, 2014. Syncope: how the EEG helps in understanding clinical findings. Brain 137 (Issue 2), 309–311. https://doi.org/10.1093/brain/awt363. . February 2014.
Stevner, A.B.A., Vidaurre, D., Cabral, J., et al., 2019. Discovery of key whole-brain transitions and dynamics during human wakefulness and non-REM sleep. Nat. Commun. 10, 1035. https://doi.org/10.1038/s41467-019-08934-3. . 2019. .
Takahashi, Shinichi, 2022. Metabolic contribution and cerebral blood flow regulation by astrocytes in the neurovascular unit. Cells 11 (5), 813. https://doi.org/10.3390/cells11050813. . 2022. .
Tozzi, A., Zare, M., Benasich, A.A., 2016. New perspectives on spontaneous brain activity: dynamic networks and energy matter. Front. Hum. Neurosci. 10, 247. https://doi.org/10.3389/fnhum.2016.00247.
Tukacs, V., Mittli, D., Hunyadi-Gulyás, É., et al., 2023. Chronic cerebral hypoperfusion-induced disturbed proteostasis of mitochondria and MAM is reflected in the CSF of rats by proteomic analysis. Mol. Neurobiol. 60, 3158–3174. https://doi.org/10.1007/s12035-023-03215-z. . 2023. .
Turner, Kevin L., Gheres, Kyle W., Proctor, Elizabeth A., J Drew, Patrick, 2020. Neurovascular coupling and bilateral connectivity during NREM and REM sleep. Elife. https://doi.org/10.7554/eLife.62071.
van Dijk, J.G., Thijs, R.D., van Zwet, E., Tannemaat, M.R., van Niekerk, J., Benditt, D.G., et al., 2014. The semiology of tilt-induced reflex syncope in relation to electroencephalography changes. Brain 137, 576–585.
Zhu, Xiao-Hong, Qiao, Hongyan, Du, Fei, Xiong, Qiang, Liu, Xiao, et al., 2012. Quantitative imaging of energy expenditure in human brain. Neuroimage 60 (4), 2107–2117. https://doi.org/10.1016/j.neuroimage.2012.02.013. . 2012 May 1.
Zhu, Zhenliang, Chen, Yuming, Chen, Fengde, Zhong, Li, 2023. Complex dynamics of a predator-prey model with opportunistic predator and weak Allee effect in prey. J. Biol. Dynam. 17 (1), 2225545. https://doi.org/10.1080/17513758.2023.2225545. . 2023 Dec.