Article

# A Bridge of Light: Toward Chinese and Western Medicine Perspectives Through Ultraweak Photon Emissions

Global Advances in Health and Medicine Volume 8: 1–7 © The Author(s) 2019 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/2164956119855930 journals.sagepub.com/home/gam



Meina Yang, PhD<sup>1</sup>, Eduard Van Wijk, PhD<sup>2,3</sup>, Jingxiang Pang, PhD<sup>1</sup>, Yu Yan, PhD<sup>2,3</sup>, Jan van der Greef, PhD<sup>2,4</sup>, Roeland Van Wijk, PhD<sup>2,3</sup>, and Jinxiang Han, PhD<sup>1</sup>

## Abstract

The gap between Western medicine and traditional Chinese medicine (CM) is closely related to the diversity in culture, philosophy, and scientific developments. Although numerous studies have evaluated the efficacy of acupuncture, the gap in explanatory disease models has not been bridged so far. Developments in research of ultraweak photon emission (UPE) and organized dynamics of metabolism and its relationship with technological advances in metabolomics have created the conditions to bring the basics of the medicines of the West and East together which might open the avenue for a scientific dialogue. The paper discusses (1) the UPE in relation to Qi energy, meridians and acupuncture points in CM, (2) the biochemical explanation of photon emission of living systems in Western biomedicine, and (3) the progress in research on the large-scale organization and dynamics of the metabolic network including photon metabolism.

## **Keywords**

systems biology, ultraweak photon emission, Chinese medicine, metabolic network, reactive oxygen species, mitochondrial network

Received November 21, 2018; Revised received April 18, 2019. Accepted for publication May 16, 2019

# Introduction

The purpose of this article is to stimulate the dialogue between traditional Chinese medicine (CM) and Western medicine (WM) by discussing some recent developments in the field of ultraweak photon emission (UPE), and to suggest that this field of science may offer a perspective to bridge the divergent scientific explanatory models underlying these two medicines. In Western countries, CM serves as an optional complement to WM, driven by patient preference. CM, such as acupuncture, is seen as a gentler, "low-tech," and nonchemical complement to improve the quality of life, in particular in the areas of chronic, noncommunicable diseases, and aging. Such is officially recognized in the WHO Traditional Medicine Strategy (2014–2023).<sup>1</sup> Many clinical studies have evaluated the efficacy of acupuncture, while numerous research papers have been published on their physiological mechanisms. However, the gap in explanatory and diagnostic models is not bridged so far. WM generally prescribes treatment for specific diseases, often on the basis of typical perceived physiological and molecular causes of metabolic derailments. CM, on the other hand, focuses on symptoms as typical disruptions in the body's dynamic energy balance. Acupuncture meridians are thought to represent "channels" through which flows "meridian qi." Measuring the distribution of Qi energy, and hence the interruption in this flow, provides

<sup>4</sup>Division of Analytical Biosciences, Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands

**Corresponding Authors:** 

Jinxiang Han, Shandong Medicinal Biotechnology Centre, Shandong Academy of Medical Sciences, Jinan, Shandong, China. Email: samshjx@sina.com Roeland Van Wijk, Meluna Research, Koppelsedijk IA, 4191 LC Geldermalsen, The Netherlands.

Email: roeland\_van\_wijk@meluna.nl

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (http://www.creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us. sagepub.com/en-us/nam/open-access-at-sage).

<sup>&</sup>lt;sup>1</sup>Shandong Medicinal Biotechnology Centre, Shandong Academy of Medical Sciences, Jinan, China

<sup>&</sup>lt;sup>2</sup>Sino-Dutch Centre for Preventive and Personalized Medicine, Tiel, The Netherlands

<sup>&</sup>lt;sup>3</sup>Meluna Research, Geldermalsen, The Netherlands

important diagnostic information.<sup>2,3</sup> Needling of acupuncture points is used to access and influence the interrupted flow and help the ailing body to reestablish its dynamic homeostasis.

Despite considerable efforts to understand the anatomy and physiology of the acupuncture points and meridians, the characterization of these structures has remained elusive in a Western biomedical model. But how sure can we be about the perfectness of the Western scientific model, in particular with respect to its absence of critical appraisal of life's capacity to direct energy to sustain and repair itself? It has often been considered as remiss of those practicing the Western analytical approach by dissecting the living body into its component parts; based on the conviction that wholes are no more than the additive sums of their parts. This has contributed to a polarization between "traditionalists" and "biomedicalists." However, both credulous acceptance and uninformed rejection of the CM tradition represent flawed positions, and only through rational investigation of the fundamental ideas of CM may it claim validity in the future practice of global medicine.

The present article examines this problem, focusing particularly on research that has explored CM theory using biophysical (in particular biophotonics) and biochemical methods. The article first discusses the UPE of humans in relation to Qi energy, meridians, and acupuncture points. In the 1950s, photomultipliers became available worldwide, and by the 1970s, the technical advances in sensitivity of these phototubes had reached the state where they were able to record from living organisms in the visible range of the electromagnetic spectrum. Researchers in China were the first to study a possible relationship between the UPE from acupuncture points and the Qi (energy) balance as established by CM diagnostics. The article continues with a summary of Western biochemistry studies on the biochemical origin of UPE, its relationship with reactive oxygen species (ROS), and the relationship between UPE and stress, chronic disease, and aging. Finally, the article discusses the progress in research on large-scale organization and dynamics of the metabolic network which has revealed novel energy properties that may bridge CM and WM. We conclude by identifying future ways that these medicines may work together toward a common explanatory model.

# UPE in Relation to Qi energy in CM

CM includes both acupuncture and herbal remedies. Acupuncture is based on meridian theory, which incorporates a system of channels through which vital energy, or Qi, flows. According to CM theory, one's health depends on a dynamic balance between one's internal physiological state and the surrounding environment. CM incorporates both yin-yang and the 5 elements theory, called Wu Xing. Yin-yang are mutually opposing forces, such as hot and cold, light and dark, that are normally in balance with each other, that is, homeostasis is present. Disease occurs when there is an excess or a deficiency of either yin or yang. CM theory holds that our universe is composed of the 5 elements, comprising wood, fire, earth, metal, and water, and they help to express the interaction between our body and the surrounding environment.

In addition to the concept of vin and yang, Qi is crucial to CM. Acupuncture meridians are traditionally thought to represent "channels" through which flows "meridian qi."<sup>2,3</sup> Qi represents the idea that the body is impacted by subtle material and dynamic influences which initiate most physiological functions that maintain the health and vitality of the individual. It is often used synonymously with the term "life" energy, but this conceals its material attributes. Energy is defined as the capacity of a system to do work, while the concept of Qi embraces much more. There are many different types of Qi in the body. In general, the features that characterize each type of Qi derive from its source, location, and function. When the flow of Qi is unimpeded, the body is in a state of health and the flow depends on a dynamic balance between one's internal physiological state and the surrounding environment (e.g., season) as well as on age and gender. All illness (as defined by CM) is an imbalance of Qi within the body, and signs and symptoms reflect the anatomical location of the disturbance or obstruction of Qi. As a therapeutic tool, acupuncture is utilized to assist in the regulation of Qi by providing a specific stimulus to body points that lie along meridian channel pathways and to remove an obstruction.

Yan Zhiqiang and colleagues of the Shandong College of Traditional Chinese Medicine and Zheng Rongrong and colleagues of the Shanghai Institute of Traditional Chinese Medicine were the first to make descriptive studies of UPE from the acupuncture points at the meridian ends, preferentially the fingertips and toes, utilizing photomultiplier tubes with approximately 1 cm opening which were placed in a dark chamber in close proximity to the acupuncture point of interest. Their descriptive and comparative studies included group sizes ranging between 10 and 100 subjects, controlled for sex and age and statistically evaluated. More than 30 studies were published between 1979 and 1998, mostly in Chinese scientific journals. These studies have been evaluated recently by the Sino-Dutch Centre for Preventive and Personalized Medicine of Leiden University, the Netherlands.<sup>4</sup> This evaluation focused on UPE studies of humans that are important for independent repetition. To summarize the results of these studies, the overall fingertip emissions of men and

women in different age groups demonstrated that emissions were not statistically different till the age of 30 years, but then UPE began to increase; UPE of aging men increased more than the UPE of aging women in the same age-group. A seasonal pattern in UPE was observed: emissions in summer were significantly higher than in winter. In all these studies with healthy subjects, the corresponding right and left fingertips behaved similarly, that is, emission was symmetric.<sup>5,6</sup> In contrast, unhealthy subjects-patients-often demonstrated a broken left-right symmetry and increased emission strengths.<sup>7,8</sup> The a-symmetry in UPE was not only observed for Chinese syndromes but also for typical "Western" diseases, including hypertension, facial nerve paralysis, constipation, and cancer.<sup>7-10</sup> A final topic to be mentioned was the effect of acupuncture treatment on the UPE of all patients participating in all studies, independent of type of pathology, as compared to all control subjects. Before treatment, the overall patient group (N = 279) had increased UPE of 70%compared the to the control group (N=315). After treatment with acupuncture, the UPE of the patient group was reduced to 11% higher than the control group.<sup>11,12</sup>

The photon emission of the different finger points was more recently confirmed using UPE imaging techniques.<sup>13,14</sup> These images demonstrated that intensity of the emissions decreased from the finger tips along the fingers to the central area of the hand with a high degree of left-right symmetry.<sup>15</sup> The dynamics of this pattern was studied by repeated measurements showing that the pattern remains stable, but the intensity in UPE could change. The images also illustrated that the detailed heterogeneity of the hand emission (as shown by the fingertips) was reflected in the "average" intensities of the dorsal and palm sides of the hands. The latter procedure was utilized for the evaluation of the intensity and left-right symmetry of photon emission in both patients and healthy subjects.<sup>16-22</sup> This was applied to study the relationship between UPE and the Qi balance by other research teams.<sup>19,21,22</sup> UPE dynamics measured from hands was related to diurnal and annual rhythms.<sup>16-19</sup> In other UPE studies, the left-right symmetry measured from the hands of diseased subjects was shown to be broken<sup>17,18,21,22</sup> and reestablished after acupuncture treatment.<sup>21,22</sup> The influence of age and gender regarding UPE measured from dorsal and palm sides of the hands showed an increase in UPE during aging. The UPE of aging men increased more than the UPE of aging women of the same age.<sup>23</sup> The main results arising from these studies is that human photon emission increases with age as well as with disease. It depends on gender and it is reduced by acupuncture.

# Western Science Perspectives on UPE

Western scientific research on UPE from living organisms has a longer history, beginning shortly after the arrival of the photomultiplier tube for industrial purposes.<sup>24</sup> In the 1960s, Russian scientists estimated UPE from all types of biological organisms and tissues. They also produced emission data in relation to physiology and biochemistry, demonstrating that photon emission is dependent on the presence of oxygen.<sup>25,26</sup> In the 1970s, research centers worldwide began research to address UPE as a sensitive assay for oxidative radical reactions. Around 1980, it was concluded that all organisms emit photons and that the intensity was related to stress and was derived from oxygen radicals. UPE covers a broad spectrum from ultraviolet/visible/near infrared part of the electromagnetic spectrum as a result of biochemical reactions in biological systems. The types of chemical reactions fulfilling the requirements for photon emission and the role of high-energy excited states in the generation of UPE were reviewed from the 1980s.<sup>27–29</sup> In cells, mitochondria are the main source of photon emission; the luminescence was associated with the respiratory chain when the reduction of O2 is incomplete, and superoxide anion and other ROS are formed. Photons are emitted from ROS and related peroxidations of mitochondrial membrane lipids resulting in specific spectral bands, such as 780 nm, 703 nm, 634 nm, photons in the 350-500 nm range and even in the 230 to 300 nm range. Broad spectral bands in mitochondria are caused, when mitochondrial proteins and DNA are excited by UV photons of 230 to 300 nm which results in fluorescence with emissions in the longer regions.<sup>30,31</sup>

The relationship between emission and stress and disease via ROS was another important Western contribution.<sup>32,33</sup> When metabolism is perturbed, excessive amounts of ROS are formed which not only increase UPE but also cause damage to lipids, nucleic acids, and proteins, and even loss of mitochondrial and cellular functions, ultimately leading to cell death.<sup>34</sup> The feasibility of recording UPE as a tool for measuring changes in human health has been reviewed.<sup>35,36</sup>

An important increase in knowledge took place in the 1990s, the decade of the mitochondrial genome, when different deletions and duplications of mitochondrial DNA (mtDNA) were found to be associated with disease.<sup>37–40</sup> While most human cells contain 2 copies of nuclear DNA, these cells contain many more copies of mtDNA (from 1000 to 100 000, depending on the cell type). They are all identical in a healthy individual at birth. By contrast, patients harboring pathogenic mtDNA defects often have a mixture of mutated and wild-type mtDNA.<sup>41</sup> Notably, mitochondria are the major producers of ROS and since mtDNA is not protected by histone and nonhistone chromosomal proteins

like the nuclear DNA, the mtDNA is highly vulnerable to damage by ROS.

Another newly emerging property of mitochondria is that they do not sit idle within the cell cytoplasm, as suggested by the traditional static bean-like picture in textbooks. Although long believed to behave as independent organelles, new evidence is changing this solitary view of mitochondria. Visualizing live cells under the microscope reveals that mitochondria form dynamic networks whose structure is molded by the opposing processes of mitochondrial fission and fusion leading to shape changes and molecular exchange within seconds to minutes.<sup>42</sup> Various cellular environmental stimuli, such as nutrient stress or vital attack, dramatically change the shape of the mitochondrial network.<sup>43,44</sup> It has commonly been reported that mitochondrial morphology is closely associated with the ability of mitochondria to produce energy.45

Bioenergetic adaptation is not the only mitochondrial task that involves changes to mitochondrial architecture. A vital task that engages the fusion and fission machinery is the mitochondrial life cycle. The brief transitions between connected and separated mitochondria enable the reorganization of mitochondrial components and hence, the elimination of damaged material, thereby maintaining a healthy mitochondrial population. One can appreciate that the life cycle of mitochondria would be compromised if mitochondrial fusion or fission was disabled. Mitochondrial dynamics are dependent on interactions with the cellular cytoskeleton-both microtubules and actin filaments. Mitochondrial-cytoskeletal interactions have a well-established role in mitochondrial motility. Recent progress indicates that these interactions also regulate the balance of mitochondrial fission/ fusion as well as mitochondria turnover.46-48

The most recent breakthroughs in mitochondrial research on ROS and its associated UPE include the development of novel mitochondrial targeted fluorescent indicators to probe ROS. Instead of the spontaneous inefficient formation of photons from ROS, these fluorescent substances efficiently utilize the ROS (in particular, superoxide) energy to produce a specific fluorescence signal. Such a tool or indicator in intact cells and live animals led to the observation of a "mitochondrial flash" within individual mitochondria.<sup>49,50</sup> The universal existence from plants to mammals of "flash-like" events detected by mitochondrial ROS indicators represents a major breakthrough. A number of different fluorescent indicators for multiple processes (e.g., superoxide, pH, and membrane potential) can detect flash activity involving multiple transient concurrent changes within the mitochondrion. The similar unitary features "flash-like" events have suggested that many mitochondrial processes/functions are integrated or interconnected, and changes in 1 component directly or indirectly affect the others.<sup>51,52</sup>

Compatible with the significantly increased flash frequency under pathological conditions as outlined earlier is the "ROS-induced ROS release" model. This model was developed based on the findings that laser-induced local ROS production triggers mitochondrial inner membrane permeability to release ROS.<sup>53,54</sup> The released extramitochondrial ROS subsequently triggers neighboring mitochondria to undergo a similar process that leads to whole-cell bursting of ROS oscillations. Since synchronized flash activity is observed in a group of interconnected mitochondria, individual mitochondrial flashes and whole-cell ROS oscillations could be mechanistically linked and reflect the dynamic ROS regulation (and integrated mitochondrial functions) under physiological or pathological conditions, respectively.55,56

The mitochondrial dynamics is part of a larger field of research of pulsating and oscillating cellular processes, which began early in the 1970s, when the glycolytic pathways of yeast cells revealed the existence of metabolic oscillations with a rather constant frequency with a period of 19.6 seconds. In the late 1990s, research regarding cellular and subcellular oscillations of super-oxide production was carried out in leukocytes.<sup>57,58</sup>

The dynamics in metabolism are even extended to pulsing in genetic circuits. Single-cell experiments have revealed a novel and very different picture of genetic regulation. The new insights have emerged from quantitative time lapse video microscopy and fluorescent reporter genes, allowing researchers to accurately track the dynamic behavior of specific proteins over time in individual living cells. A recurring theme from these studies is that many regulatory key transcription factors undergo continual, repetitive pulses of activation even when cells are maintained in constant conditions.<sup>59,60</sup> The main conclusion from the studies presented in this section is that metabolism of cells is regulated by the pulsations of metabolic networks including the photon metabolism. Although some intercellular synchronization has already been established, the next challenge in this research is the scale of this intercellular organization within the body and its organ systems.

# **UPE in Systems Biology**

The arrival of systems biology signifies an improvement in the understanding of the organization of metabolism in health and disease. Systems-based thinking has developed through systems biology in life sciences and is used to study organizations in a wider context. An important feature of systems-based thinking is its focus on relationships rather than individual variables. Systems-based thinking regarding metabolism focuses not on the levels of metabolites but instead on their relative quantities, ratios, and patterns that can be detected within the ocean of thousands of metabolites. The UPE signal might reveal different aspects of system organization and has been studied during changes of this organization. $^{61,62}$ 

One type of approach includes the recent developments in systems biology that evaluate the correlation between the complex metabolic network organization and the dynamic UPE profile.<sup>61,63,64</sup> A targeted metabolomics approach with capillary electrophoresis—mass spectrometry was used to profile intracellular metabolites in HL-60 cells and to compare metabolic patterns with UPE after inducing respiratory burst. The results demonstrate the potential of UPE to monitor overall metabolic changes in oxidative stress without being correlated with single regulators in the reduction/oxidation balance.<sup>64</sup>

We hope to illustrate by this discussion that, in our opinion, there is a way to converge the medicine of the East and West and bring them together through the currently developing biochemical (dynamic connected metabolic network) and biophysical (subtler photon energy mitochondrial network) perspectives.

# **Bridging Medical Disciplines**

The theoretical foundation for integrative medicine practices largely derives from traditional Eastern philosophy where biological processes are conceptualized not in molecular terms but in terms of "vital energy," "biofield," and the flow of "Qi" between organ systems. In this framework, "dissonance" in energetic states is assumed to underlie or drive pathophysiological states or disease. Research on whether conditions such as "excess heat" or "deficient lung Qi" from traditional CM have measurable bioenergetic (UPE) correlates has begun with evaluating the molecular and UPE aspects of "energetically" defined disease states. This kind of systematic comparison could possibly promote dialogue among researchers and practitioners with a common interest to assess usefulness of integrative medicine therapies.

The advent of the noninvasive ultraweak photon counting technology has provided evidence for the existence of ubiquitous photon energy that may be related with Qi energy in CM. The technological progress should additionally facilitate the integration between Western anatomical/molecular and Eastern bioenergetics perspectives by applying the photon counting technology in research in the field of mitochondrial dysfunction.

However, we are not there yet: the real challenge is an intercultural dialogue aimed, according to Eberhard Scheiffele, at "Questioning One's 'Own' from the Perspective of the Foreign."<sup>65</sup> Through such a constructive kind of alienation, it is possible that core concepts of our scientific tradition come to life in a renewed way.

## **Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interests with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This paper is funded by Grants from the International Science and Technology Cooperation Program of China (2014DFA30380) and National Natural Science Foundation of China (No. 81273997).

## **ORCID** iD

Meina Yang D https://orcid.org/0000-0002-5149-2194 Eduard Van Wijk D https://orcid.org/0000-0002-4432-3042

#### References

- World Health Organization. WHO Traditional Medicine Strategy 2014–2023. Geneva, Switzerland: World Health Organization, 2013: 15–56.
- Kaptchuk T. Acupuncture: theory, efficacy, and practice. Ann Intern Med. 2002;136:374–383.
- Qiu J. Traditional medicine: a culture in the balance. Nature. 2007;448(7150):126–128.
- He M, Sun M, van Wijk E, et al. A Chinese literature overview on ultra-weak photon emission as promising technology for studying system-based diagnostics. *Complement Ther Med.* 2016;25:20–26.
- 5. Zheng RR. Experimental study related with several physiological and pathological states based on ultraweak luminescence of human body surface. *Faguang Xuebao*. 1986;7:20–26.
- 6. Yang WY, Zhou WX, Song W, Lv Y. Ultra-weak photon emission experimental study on the four limbs meridian of 130 healthy people. *Shanghai Zhenjiu Zazhi*. 1996;15:34–35.
- Yan ZQ, Yu SZ, Zhang XL. The meridian pathological luminous information of hypertensive patients. *Shanxi Zhongyi*. 1980;2:40–42.
- Yan ZQ, Yu SZ, Li JH. A study on the pathological illuminating signal point investigation of 300 subjects. *J Tradit Chin Med.* 1981;8:50–53.
- Yang WY, Zhou WX, Sun KX. Research on ultra-weak photon emission of acupuncture points on human body in pathologic states. *Shanghai Zhenjiu Zazhi*. 1998;6:4–5.
- Yang WY, Ni XD, Zhang HM, Sun KX, Su Ll. Spectrum observation of ultra-weak photon emission on meridian of spontaneous hypertension patients. *Zhongguo Zhongyi Jichu Yixue Zazhi*. 1998;8:50–52.
- 11. Yan ZQ, Sun SJ, Shu Q, Lin WL, Li JH. Study on the channels passing acupuncture point and the quantitative

determination of needling sensation during acupuncture. *Zhenci Yanjiu*. 1983;3:235–238.

- Yan ZQ, Yu SZ. Relationship between transmission of sensation along meridian and photon emission on the acupuncture points. *J Tradit Chin Med.* 1980;8:53–56.
- Kobayashi M. Modern technology on physical analysis of biophoton emission and its potential extracting the physiological information. In: Musumeci F, Brizhik LS, Ho M.-W, eds. Energy and Information Transfer in Biological Systems. London, England: World Scientific Publishing; 2003: 157–187.
- Van Wijk R, Kobayashi M, Van Wijk EPA. Spatial characterization of human ultra-weak photon emission. *J Photochem Photobiol B*. 2006;83:69–76.
- Van Wijk R, Van Wijk EPA, Schroen Y, van der Greef J. Imaging human spontaneous photon emission: historic development, recent data and perspectives. *Trends Photochem Photobiol.* 2013;15:27–40.
- Van Wijk E, Van Wijk R, Cifra M. Spontaneous ultraweak photon emission from human hands varies diurnally. In: *Proceedings of SPIE-OSA Biomedical Optics* (*Biophotonics* 2007: *Optics in Life Science*); June 17–21, 2007; Munich Germany, paper 6633\_54.
- 17. Cohen S, Popp FA. Biophoton emission of the human body. *J Photochem Photobiol B.* 1997;40:187–189.
- Cohen S, Popp FA. Low-level luminescence of the human skin. Skin Res Technol. 1997;3:177–180.
- Jung HH, Yang JM, Woo WM, Choi C, Yang JS, Soh KS. Year long biophoton measurements: normalized frequency count analysis and seasonal dependency. *J Photochem Photobiol B.* 2005;78:149–154.
- Kobayashi M, Kikuchi D, Okamura H. Imaging of ultraweak spontaneous photon emission from human body displaying diurnal rhythm. *PLoS One*. 2009;4:e6256.
- Jung HH, Woo WM, Yang JM, et al. Left-right asymmetry of biophoton emission from hemiparesis patients. *Indian J Exp Biol.* 2003;41:452–456.
- 22. Lee C, Yang JM, Yi SH, et al. Biophoton emission from patients with a cold. *J Int Soc Life Inf Sci.* 2004;22:362–365.
- 23. Zhao X, Van Wijk E, Yan Y, et al. Ultra-weak photon emission of hands in aging prediction. *J Photochem Photobiol B*. 2016;162:529–534.
- 24. Summer W. *Photosensitors—A Treatise on Photoelectric Devices and Their Application to Industry*. London, England: Chapman and Hall Ltd; 1957.
- Tarusov BN, Ivanov II, Petrusevich YM. Ultraweak Luminescence in Biological Systems. Moscow, Russia: Moscow University; 1967.
- Konev SV, Lyskova TI, Nisenbaum GD. Very weak bioluminescence of cells in the ultraviolet region of the spectrum and its biological role. *Biophysics (USSR)*. 1966;11:410–413; *Biofizika*. 11:361–363.
- Adam W, Cilento G. Chemical and Biological Generation of Excited States. 1st ed. New York, NY: Academic Press; 1982.
- 28. Cadenas E. Biological chemiluminescence. *Photochem Photobiol*. 1984;40:823–830.

- Tilbury RN, Quickenden TI. Spectral and time dependence studies of the ultraweak bioluminescence emitted by the bacterium *Escherichia coli*. *Photochem Photobiol*. 1988;47:145–150.
- Slawinska D, Slawinski J. Biological chemiluminescence. Photochem. Photobiol. 1983;37:709–715.
- Turrens JF. Mitochondrial formation of reactive oxygen species. J Physiol. 2003;552:335–344.
- Boveris A, Cadenas E, Reiter R, Filipkowski M, Nakase Y, Chance B. Organ chemiluminescence: noninvasive assay for oxidative radical reactions. *Proc Natl Acad Sci USA*. 1980;77:347–351.
- Boveris A, Cadenas E, Chance B. Ultraweak chemiluminescence: a sensitive assay for oxidative radical reactions. *Fed Proc.* 1981;40:195–198.
- Pospíšil P, Prasad A, Rác M. Role of reactive oxygen species in ultra-weak photon emission in biological systems. *J Photochem Photobiol B.* 2014;139:11–23.
- 35. Swinbanks D. Body light points to health. *Nature*. 1986;324 (6094):203.
- 36. Ives JA, Van Wijk EP, Bat N, et al. Ultra-weak photon emission as a non-invasive health assessment: a systematic review. *PLoS One.* 2014;9:e87401.
- Chinnery PF, Schon EA. Mitochondria. J Neurol Neurosurg Psychiatry. 2003;74:1188–1199.
- Wallace DC. A mitochondrial bioenergetic etiology of disease. J Clin Invest. 2013;123:1405–1412.
- 39. Picard M, Wallace DC, Burelle Y. The rise of mitochondria in medicine. *Mitochondrion*. 2016;30:105–116.
- Gorman GS, Chinnery PF, DiMauro S, et al. Mitochondrial diseases. Nat Rev Dis Primers. 2016;2:16080.
- Sondheimer N, Glatz CE, Tirone JE, Deardorff MA, Krieger AM, Hakonarson H. Neutral mitochondrial heteroplasmy and the influence of aging. *Hum Mol Genet*. 2011;20:1653–1659.
- Labbé K, Murley A, Nunnari J. Determinants and functions of mitochondrial behavior. *Annu Rev Cell Dev Biol*. 2014;30:357–391.
- Picard M, McEwen BS. Psychological stress and mitochondria: a conceptual framework. *Psychosom Med.* 2018;80:126–140.
- Picard M, Turnbull DM. Linking the metabolic state and mitochondrial DNA in chronic disease, health, and aging. *Diabetes*. 2013;62:672–678.
- 45. Picard M, McManus MJ, Gray JD, et al. Mitochondrial functions modulate neuroendocrine, metabolic, inflammatory, and transcriptional responses to acute psychological stress. *Proc Natl Acad Sci USA*. 2015;112:6614–6623.
- Anesti V, Scorrano L. The relationship between mitochondrial shape and function and the cytoskeleton. *Biochim Biophys Acta*. 2006;1757:692–699.
- 47. Pendin D, Filadi R, Pizzo P. The concerted action of mitochondrial dynamics and positioning: new characters in cancer onset and progression. *Front Oncol.* 2017;7:102.
- Moore AS, Holzbaur ELF. Mitochondrial-cytoskeletal interactions: dynamic associations that facilitate network function and remodeling. *Curr Opin Physiol.* 2018;3:94–100.

- 49. Sheu SS, Wang W, Cheng H, Dirksen RT. Superoxide flashes: illuminating new insights into cardiac ischemia/ reperfusion injury. *Future Cardiol*. 2008;4:551–554
- Wei L, Dirksen RT. Perspectives on: SGP symposium on mitochondrial physiology and medicine: mitochondrial superoxide flashes: from discovery to new controversies. *J Gen Physiol*. 2012;139:425–434.
- Ichas F, Jouaville LS, Mazat JP. Mitochondria are excitable organelles capable of generating and conveying electrical and calcium signals. *Cell*. 1997;89:1145–1153.
- 52. Murphy MP. How mitochondria produce reactive oxygen species. *Biochem J.* 2009;417:1–13.
- 53. Aon MA, Cortassa S, Marban E, O'Rourke B. Synchronized whole cell oscillations in mitochondrial metabolism triggered by a local release of reactive oxygen species in cardiac myocytes. *J Biol Chem.* 2003;278:44735–44744.
- 54. Zorov DB, Filburn CR, Klotz LO, Zweier JL, Sollott SJ. Reactive oxygen species (ROS)-induced ROS release: a new phenomenon accompanying induction of the mitochondrial permeability transition in cardiac myocytes. *J Exp Med.* 2000;192:1001–1014.
- 55. Fang H, Chen M, Ding Y, et al. Imaging superoxide flash and metabolism-coupled mitochondrial permeability transition in living animals. *Cell Res.* 2011;21:1295–1304.
- Glancy B, Hartnell LM, Malide D, et al. Mitochondrial reticulum for cellular energy distribution in muscle. *Nature*. 2015;523:617–620.
- 57. Adachi Y, Kindzelskii AL, Cookingham G, et al. Aberrant neutrophil trafficking and metabolic oscillations in

severe pyoderma gangrenosum. J Invest Dermatol. 1998;111:259–268.

- Adachi Y, Kindzelskii AL, Ohno N, Yadomae T, Petty HR. Amplitude and frequency modulation of metabolic signals in leukocytes: synergistic role of IFN-g in IL-6and IL-2-mediated cell activation. J Immunol. 1999;163:4367–4374.
- Levine JH, Fontes ME, Dworkin J, Elowitz MB. Pulsed feedback defers cellular differentiation. *PLoS Biol.* 2012;10:e1001252.
- Levine JH, Lin Y, Elowitz MB. Functional roles of pulsing in genetic circuits. *Science*. 2013;342:1193–1200.
- 61. Burgos RC, van Wijk EP, Van Wijk R, He M, van der Greef J. Crossing the boundaries of our current healthcare system by integrating ultra-weak photon emissions with metabolomics. *Front Physiol.* 2016;7:611.
- 62. Schroen Y, van Wietmarschen HA, Wang M, et al. East is East and West is West, and never the twain shall meet? *Science*. 2014;346:1569.
- 63. Van Wijk R, Van Wijk EP, Van Wietmarschen HA, Van der Greef J. Towards whole-body ultra-weak photon counting and imaging with a focus on human beings: a review. J Photochem Photobiol B. 2014;139:39–46.
- 64. Burgos RCR, Schoeman JC, Winden LJV, et al. Ultraweak photon emission as a dynamic tool for monitoring oxidative stress metabolism. *Sci Rep.* 2017;7:1229.
- Scheiffele E. Questioning one's "own" from the perspective of the foreign. In: Parkes G, ed. Nietzsche and Asian Thought. Chicago, IL: University of Chicago Press; 1991: 31–50.