Jan Evangelista Purkinje: Visual Physiologist

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Johann Evangelista Purkinje was an experimental physiologist whose investigations encompassed a wide radius of interests including subjective sensory phenomena, visual physiology, anatomy, and pharmacology. His prodigious scientific investigations, which, spanned a segment of the nineteenth century, left an enduring legacy of insight and innovation that, even today, inspires various subspecialties. His discoveries facilitated the development of new scientific disciplines such as the field of neuroscience and cellular physiology. He tenaciously pursued the doctrine that scientific knowledge should be predicated on experimental observations in the laboratory and not theoretical speculations. Because of his methods of investigation, he was generally considered the founder of experimental physiology. Purkinje was both a dedicated and admired teacher and an innovator in the development of original mechanical devices that facilitated new discoveries. On a personal note, he was known for his superb intellect, his excellence as a teacher, and both his kindly and generous behavior. Purkinje had a talent for music and both sang in a church choir and played the violin (Fig. 1).

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Jan, or Johann, Purkinje was born on December 17, 1787 in Libochovice, a small village in northern Bohemia (then part of the Austrian-Hungarian Empire and subsequently the Czech Republic). Purkinje was the first son of Josef Purkinje and Rosalia Safranek. His father suddenly died in 1793 when Jan was only 6 years old.

In 1797, at 10 years of age, he was sent to a Piarist order monastery at Mikulov in Moravia. Their curriculum, unlike the Jesuit schools of that time, taught natural sciences including math, physics, and biology, all of which helped to prepare Purkinje for his future career. Although Purkinje's original intent was to follow the priesthood and teach, he left the Piarist order in 1807 "*to be more free and to deal more freely with science*." To satisfy this goal, he entered the Department of Physiology in Prague as a student where he developed his interest in the natural sciences. It was this interest in science that subsequently led to his acceptance in medical school in 1813 at the Charles-Ferdinand University in Prague when he was 26 years old. His doctoral thesis for graduation from medical school was defended in 1818 and published in 1819. It was entitled "Contributions to the Knowledge of Vision in its Subjective Aspects." This thesis led to the interest and support of the accomplished poet and scientist Johann Wolfgang von Goethe, who shared similar interests. After completing his MD degree in 1818, he did not consider a clinical

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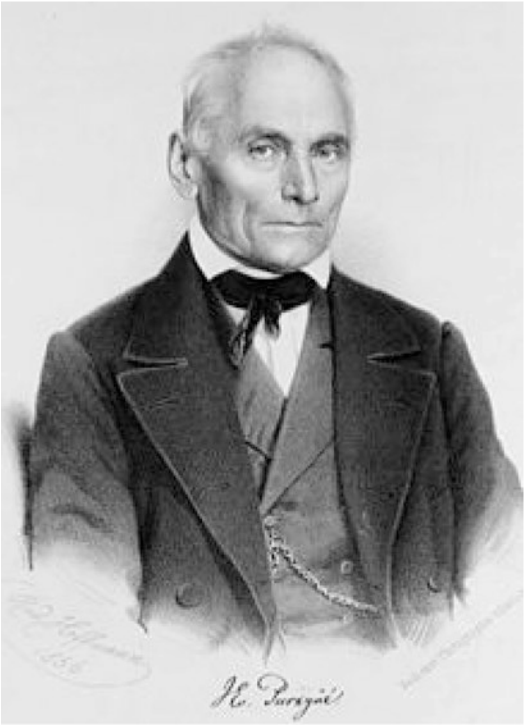

Fig. 1 Lithograph of Purkinje by Rudolph Hoffman, 1856, after a photograph by Bertsch and Aaraud in Paris. From: Wikipedia.org and monoskop.org (public domain)

medical practice but rather chose to pursue a career in experimental physiology and pharmacology. Five years later, in 1823, he accepted an appointment as Professor of Physiology and Pathology in Breslau, Prussia, where his scientific career ultimately flourished and where he founded the world's first independent, experimental, Physiological Institute in 1839 (Fig. 2).

His appointment at Breslau was contentious. With the influence of Goethe, as well as others, including his future father-in-law, Karl Asmund Rudolphĭ (1771–1832), Berlin Professor of Anatomy and Physiology, Purkinje was chosen over another candidate who was favored by the Breslau faculty. Initially Purkinje encountered appreciable resistance. As a Czech nationalist, he was an outlier in a land where Germanization of the populous was beginning to accelerate. The upper class segment of the population, such as those who were professors at the University of Breslau, were most often of German decent. Certain professors were particularly aggressive in hindering his research and adjustment to his new surroundings. In the end, Purkinje succeeded in spite of their hindrance. Nonetheless, he was often treated with

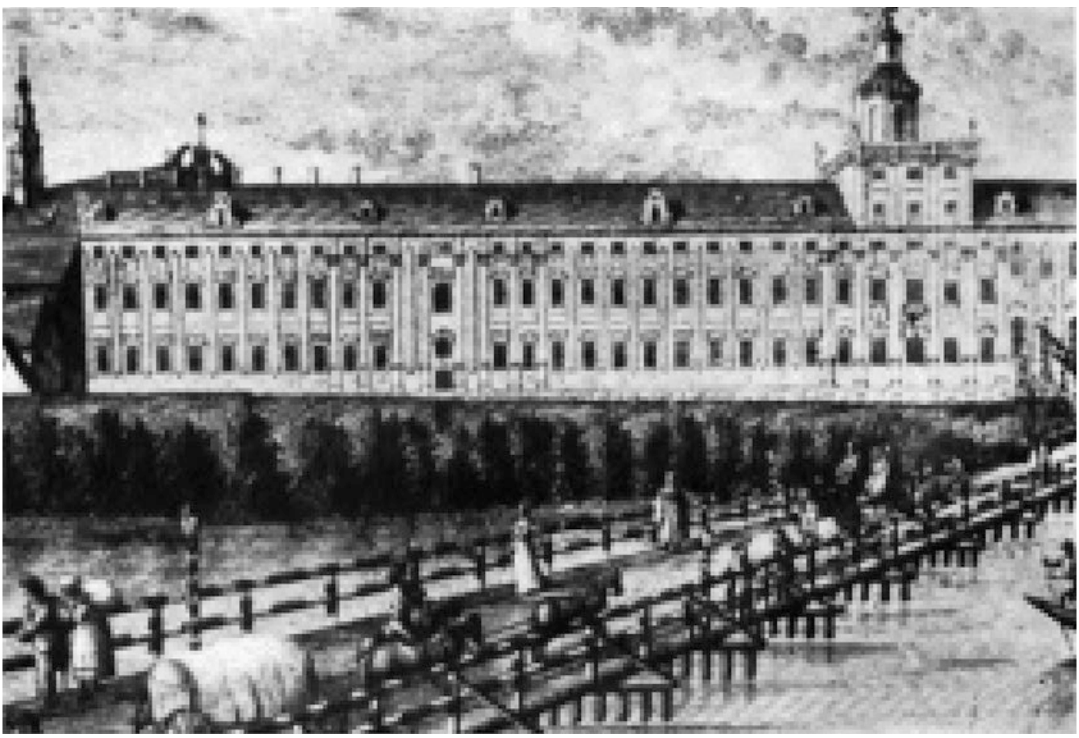

Fig. 2 University of Breslau. From: http://monskop.org/Jan_Evangelista_Purkyně (public domain)

Fig. 3 Physiological institute in Prague. From: http://monoskop.org/Jan_Evangelista_Purkyně (public domain)

suspicion and followed by the Breslau police [1]. In comparison, his devotion to this fatherland in Prague was limitless. He supported nationalistic issues aggressively. Purkinje participated in promoting Czech poetry, literature, and scientific publications so that his countrymen would be recognized and respected [1]. In April, 1850, he left Breslau and returned to Prague where he became the Chair of Physiology at the University. One of his primary goals at Prague University was to establish a physiological institute which he accomplished in October, 1851 (Fig. 3).

While Jan's native language was Czech, the scope of his linguistic talents included Latin, Greek, German, Polish, French, English, Hungarian and Italian, among others. He used the Germanic version of his name (Purkinje) while in Germany and in most of his scientific publications and the Czech version (Purkyně) in his correspondence with Czechs and subsequent to his return to Prague in 1850.

In 1827, at 40 years of age, Purkinje married his wife Julia Rudolph. They had two daughters, Rosalie and Johanka, and two sons, Karel Purkyně and Emmanuel von Purkyně. Tragically, both daughters died from cholera in 1832 during an epidemic in Breslau. In 1835, his wife Julia, died of either typhoid fever or a disease that affected her central nervous system, possible meningitis. He never remarried.

The study of overall visual function was both Purkinje's initial and his most sustained scientific interest throughout his diverse scientific pursuits. He continued his interest in various objective and subjective optical phenomena during the latter part of his career. His inaugural lecture at the University of Breslau in 1825 included discussions that related to his research on accommodation, peripheral vision, and "long and short" sightedness. Also included were topics on strabismus, the Purkinje shift, motion after images, and vertigo. While Purkinje pursued his study of vertigo in an experimental setting, the development of vertigo continues to be used as a clinical test for vestibular function. Purkinje helped to define a new era of study, that being subjective visual phenomena such as stroboscope patterns, effects of galvanic stimulation, pressure figures, visibility of retinal blood vessels and blood flow, other entoptic phenomena, and after images, among others. He was curious and highly motivated to identify the objective, physiological explanations of these subjective impressions. In so doing, he impacted upon the advancement of contemporary neuroscience (Fig. 4). Purkinje's initial studies of vision were conducted prior to when the accelerated development of various investigational instruments had occurred and thus his early experimental observations of visual phenomena were made without the use of more sophisticated laboratory equipment [2]. Nevertheless, his observations had a sizable impact on the study of sensory physiology.

Purkinje had a notable difference in visual acuity between his two eyes, the right eye being considerably better than his left. The later was defective since childhood. It is estimated that his right eye was myopic and his left hyperopic and slightly astigmatic. In his 30s, his right eye was alleged to require four diopters of correction [2]. This ocular asymmetry in vision was a hindrance for obtaining precise measurements during various investigations as it was necessary to predominantly use his right eye. In spite of this infirmity, he was yet capable of being accurate in his experimental observations.

Fig. 4 Portrait of Purkinje from an illustration in Posoinrěková (1955), included on page 27 in reference #2. From: http://www.pinterest.com/pin/154740937166756935/ Explore these ideas and more (public domain)

The scope of Purkinje's scientific interests was wide [3]. While some of his observations had also been made previously by other investigators, his investigations often resulted in more precise and comprehensive descriptions of various phenomena. In general, Purkinje's scientific interests can aptly be categorized into broad topics including investigations in subjective sensory phenomena, physiology, anatomy, and pharmacology. Within these categories reside many of Purkinje's contributions to ophthalmic science. Some of those with the strongest interest and importance are selected for further discussion. They represent only a small sample of his interests and productivity in the above topics of sensory phenomena and physiology.

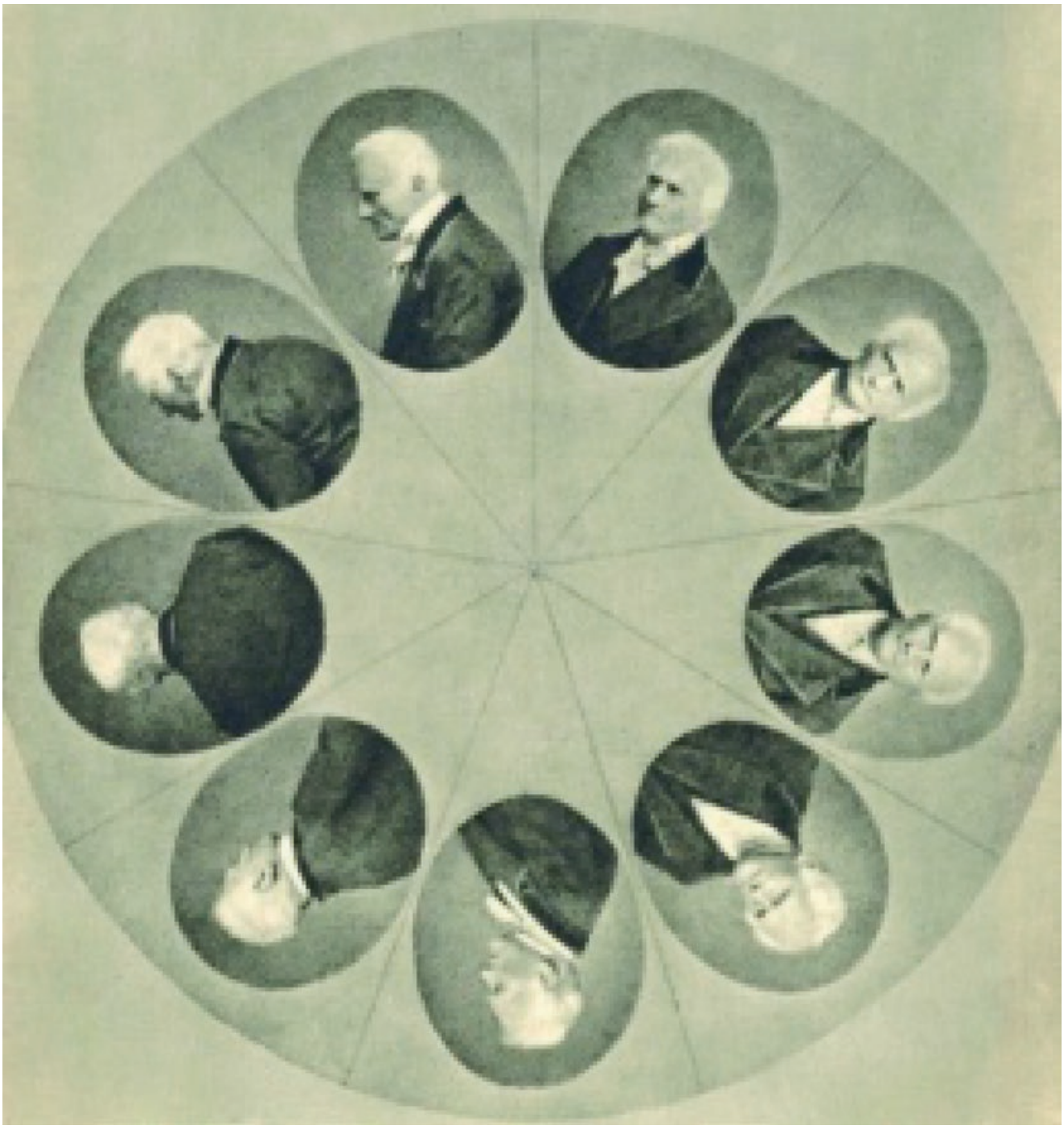

Fig. 5 Purkinje kinesiscope disc showing portraits of Purkinje, 1865. From: http://monoskop.org/Jan_Evangelista_Purkyně (public domain)

Development of the Ophthalmoscope and Other Clinical Instruments

In his 1823 academic acceptance dissertation, published while he was at Breslau, Purkinje was the first to describe a method for illuminating the interior of the eye. It was therefore Purkinje who discovered the illuminating principle ultimately used by Helmoltz in his ophthalmoscope, as well as the principles by which an ophthalmoscope operates. Using these principles, he examined the interior of the dog, cat, and human eyes. His work was published in Latin by Breslau University and preceded by 27 years, nearly three decades, Helmholtz's description of the ophthalmoscope [4, 5]. While Purkinje recommended his method for clinical use, he did not follow through with further development and promotion of his instrument. As a consequence, 24 years later, Ernest Brücke of Vienna, and E. von Erlach

[6] rediscovered the same method of illuminating the eye and provided Helmholtz the necessary information for his development of the ophthalmoscope. It is noteworthy that in an article by Thau it is cited that the word ophthalmoscope was first said to have been used by Anagnostakis who constructed an instrument with a similar purpose in 1854 [7].

Purkinje is also credited with having developed the first stroboscope and kinesiscope (Fig. 5). The stroboscope he initially constructed in the 1830s and an improved version in 1840 that he called the phorolyt. It consisted of two revolving cylindrical drums that produced moving pictures of the heart muscle and heart valves, among other images. A version of his kinesiscope was manufactured in Prague in 1860. It consisted of a rotating drum upon which drawings were placed. Purkinje used this instrument in his lectures to demonstrate animal movements. It also demonstrated the opening and closing of the heart valves in addition to the contraction of the auricles and ventricles of the heart. He was thus a pioneer of scientific cinematography.

Purkinje additionally laid the foundation for the development of an ophthalmometer, ultimately credited to Helmholtz. This instrument facilitated the measurement of changes in the curvature of the cornea as well as the anterior and posterior surfaces of the lens. This measurement helped to resolve several contradictory theories as to the process of accommodation. He also developed a simplified perimeter that facilitated a more precise estimate for the boundaries of peripheral visual fields. With this instrument, he determined the peripheral field limits of color vision and observed that yellow and blue colors were visible at slightly greater peripheral locations than were red and green and he discovered that all colors were more visible in the temporal compared to the nasal field.

Description of a Shift in Light Sensitivity of the eye during Dark-Adaptation (Purkinje Shift)

It was in 1825 that Purkinje described the effects of ambient illumination on the visibility of spectral colors and their apparent brightness

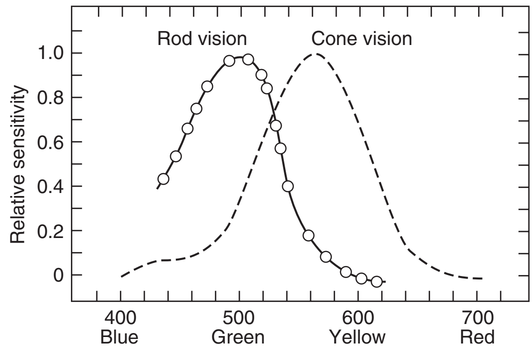

Fig. 6 Rod and cone light sensitivity curves on which the Purkinje shift is based. From: http://www.csus.edu/indiv/w/wickelgren/psyc103/classvisionone.html. The Visual System: Neuron to Higher Level Processing (public domain)

which he originally published in German. The Purkinje shift, or Purkinje effect, refers to the observation that reduction in luminance from daylight (photopic) levels to night (scotopic) levels results in a measurable change in visual spectral sensitivity as blue light becomes more readily perceived than red. This observation implicated a duplex organization of the retina (Fig. 6). During daylight, vision is mediated by the cone spectral sensitivity function while night vision is mediated by the rod spectral sensitivity function [8, 9].

Purkinje himself did not attribute great significance to the phenomenon [2]. He noticed its occurrence by chance while walking in the Bohemian fields when he noticed that his favorite flowers appeared a bright red on a sunny afternoon but very dark at dawn. He surmised that the eye has two different systems for the perception of colors, one for bright intensity light, and another for dusk and dawn. The term "Purkinje phenomenon" was coined by two French physicians, J.M. de Lepinay and W. Nicati, in 1882 [10]. Earlier recognition of a similar phenomenon were said to have already been made by both Aristotle and Leonardo da Vinci, although not with the same comprehensive clarity and sophistication as defined by Purkinje [11]. Reference to this observation can also be found in the Koran where it is described that there are times when a red and subsequently a blue thread will become more visible [12]. In the earlier part of the nineteenth century, Mathias Koltz had observed a difference in color vision under different levels of illumination [13].

Description of Visual Entoptic Images

Purkinje was not the first to observe the negative shadows cast on the retina by the retinal blood vessels when elicited by a moving source of light that illuminates the retina when directed through the sclera. In 1803, Sir Charles Bell (1774–1842) realized that the shadow phenomenon was related to the retinal blood vessels. Purkinje specified the characteristics of the phenomenon in greater detail and illustrated the appearance of the blood vessel shadows [2]. As such, the phenomenon became referred to as the "Purkinje tree."

This technique continues to have a useful application. The Purkinje test has been used to pre-operatively evaluate the visual potential for eyes undergoing surgery for a cloudy or opaque media. When a vascular pattern is observed, there is a good probability that reasonably substantial macular function is present, while if no vascular pattern is seen, it is more probable that the eye will have reduced macular function [14].

Based on personal observations with his own eyes, Purkinje also made observations referable to floaters, which were termed *mouches valantes*. He reported seeing several at the same time and described their motion as that of "falling stars." Purkinje also described and illustrated the circulation of blood in the retinal blood vessels, previously observed in 1703 by Boerhaave and in 1789 by Robert Doiven. Purkinje, however, better described and illustrated this entoptic phenomenon [2]. His interest in entoptic phenomena lead him to investigate the findings that prolonged pressure applied to the eyeball produced small patches of light referred to as phosphenes. This phenomenon was noted even in darkness. Purkinje explained this sensation as occurring from oscillations from the interior of the eye. It had previously been described by Alemaeon approximately 2500 years earlier and by several others, such as Descartes, Newton, and Morgagni, with various interpretations as to their origin [2].

Description of Catoptric Images

In 1823 while in Breslau, with the use of the flame from a candle, Purkinje observed four reflected images from the refracting surfaces of the eye (Purkinje images). These reflections arose from the anterior and posterior surfaces of both the cornea and lens (Fig. 7). An understanding of these catoptric images contributed to the development of the keratometer. Additionally, Purkinje suggested that the reflected image from the cornea could be used to measure its curvature, a principle that was a basis for development of the ophthalmometer.

In 1837, Sanson, a Parisian oculist, without prior knowledge of Purkinje's discovery, independently described these images. As such, there are those who prefer the term Purkinje-Sanson to describe this phenomenon. These images had previously been observed by Thomas Young (1773–1801) and, considerably later, comprehensively investigated by Helmholtz and were the basis for his investigations into the refraction of light by the eye.

Motion Aftereffects

In 1820, Purkinje reported on a type of apparent motion that was dependent on visual stimulation. It can be elicited by observing, for an extended period of time, a sequence of spatially distinct objects such as a long parade, moving water, or

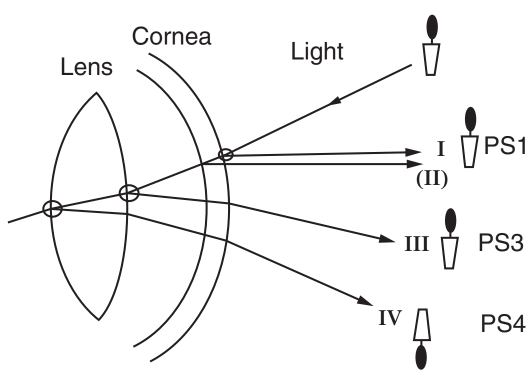

Fig. 7 Diagram illustrating the basis for the Purkinje images from the surfaces of the cornea and lens. From Internet: Purkinje Images by Kevin L. Ferguson. Typecast. How Can Film Speak of Writing? (public domain)

the spokes of a wheel not moving too quickly. When the movement of the objects stop and the observer fixates on a stationary object, this object will appear to move in the opposite direction [2].

Motion aftereffects had previously been described by both Aristotle and Lucietius. Purkinje provided an interpretation of the direction in which the aftereffect motion was observed to occur opposite to that of the prior motion. The motion aftereffect phenomenon had a subsequent impact on more modern day research relating to visual motion and as such was seen as having an impact on linking the psychology of vision to its underlying neurophysiology. Other notable nineteenth century figures in visual science, such as Müller, Helmholtz and Mach added knowledge to a better understanding of motion aftereffects [2].

Additional Contributions

In addition to contributions on ocular related investigations, Purkinje pursued an abundance of work on non-ophthalmic topics that fall under the rubric of anatomy and pharmacology. Four of these of particular interest are discussed.

Purkinje capitalized on the use of the achromatic microscope that had become available to him in 1832 over the protestations of colleagues who saw no reason why a physiologist should need such a device [15]. This instrument incorporated an achromatic lens that was added to a compound microscope notably improving its efficiency that facilitated greater visibility of small anatomical structures of both human and animal tissues. This enhanced magnification led to the identification of the Purkinje cells of the brain and Purkinje fibers of the heart. Purkinje is credited for the first lucid description of nerve cells and their processes in the brain and spinal cord. The Purkinje cells of the brain, discovered in 1837, are large neurons with branching dendrites that were identified in the cerebellar region of the brain. The Purkinje fibers or "network" identified an important intraventricular conduction system within the heart. These fibers, discovered in 1839, conduct electrical impulses from the atrioventricular node to the ventricles of the heart. Purkinje made two other meaningful contributions to the field of cardiology including the role of the heart on venous blood return and the description of the effect of digitalis on the heart in humans.

The physiological mechanism as to how digitalis blurred vision [16] was among Purkinje's extensive pharmacological studies. Following graduation from medical school, he worked for 5 years as an assistant in anatomy and physiology at the medical school in Prague. During this period he began his research activities experimenting with several medicinal substances that were in use for various conditions.

Purkinje was dissatisfied with medical research on drugs. At the time, knowledge of the effect and dosage of various drugs were in their very early stages and quite inadequate as they were all too often based on the use of experimental animals or a speculative approach rather than a rational, experimental verification basis. For these reasons, as well as his interest in the sensory and mental effects of various drugs [16, 17], Purkinje decided to experiment on himself, experiencing considerable discomfort and potential risk. Among his most noteworthy studies were his experiments with digitalis.

Over a 4 day period, Purkinje deliberately ingested an overdose of digitalis, the equivalent of nine times the lethal dose for a cat. For 15 days he experienced photopsias and black spots in his vision. His heart rate slowed and skipped beats. Purkinje also studied the effects of several extracts of ipecac (emetine). He additionally instilled drops of belladonna in his eyes and described the blurred vision that resulted. Further, he swallowed it and experienced its systemic effect [17].

In additional experiments Purkinje studied the toxic systemic effects for the self-administration of turpentine, nutmeg, ether, opium, and camphor to experience their sensory and general mental effects [2, 17]. After taking different doses of camphor, on one occasion he became totally unconscious for about half an hour. It took an additional full day before he regained his sense of time and awareness of his environment [17].

Purkinje conducted these experiments when he was a third year medical student. He visited a pharmacy in Prague owned by the father of a friend who provided him with the various substances [16, 17]. In total, he performed 35 experiments on himself [2]. His willingness to experiment on himself caused Goethe to refer to Purkinje as the martyr.

Purkinje's self-experimentation in pharmacology had lasting value beyond his various descriptions of the actions of individual drugs. He helped introduce a more sound basis for prescribing drugs and was possibly the first to describe the principle of drug interactions [17].

Although both the Babylonians and the ancient Chinese used fingerprints to sign documents, and the Chinese to identify criminals [18], Purkinje was the first to introduce a system of fingerprint classification and provided its detailed description. His systematic classification was introduced in 1823. In his system the papillary lines on the skin of the fingers were divided into nine parts based on their geometric arrangement [18]. Purkinje outlined how fingerprints could be used as a means of identifying individuals. This did not become recognized internationally for several years [18]. Nonetheless, his description and illustration of the furrows in the distal portion of the fingers subsequently led to the development of the science of dermatoglyphics.

Purkinje also conducted experiments on hearing, vertigo, made observations on the anatomy of human teeth, discovered the sweat glands in humans, studied the physiology of sleep, and developed a procedure by which, for the first time, photographic images could be obtained on microscopic material. In 1838, he observed cell division, and in the subsequent year he was the first to use the term "protoplasm" in the scientific literature. The diversity of his interests is underpinned by his additional investigations on the germinal vesicle in the yolk of birds' eggs [2]. These, and other, various investigations contributed to development of the cell theory, considered as likely one of the most important theories relevant to the rapid progress of both biology and medicine of the nineteenth century. Purkinje provided the basis upon which the cell theory would subsequently be developed [1]. The cellular theory was subsequently comprehensively formulated by Schwann and Schleiden.

Legacy

It was most unfortunate that his many investigations received less recognition than they deserved. Perhaps because of the accelerated rate and sheer volume of his productive investigations, he did not have enough time, or perhaps motivation, to adequately disseminate his observations. A likely more cogent reason is that his findings were frequently not appreciated because of the manner in which they became available. A majority of his publications were in the reports of the Silesion Society and other Czech publications. They also were contained in the Latin dissertations for the medical degrees of his pupils and in the summaries of various scientific congresses. Purkinje was continually experimenting and was seemingly not primarily motivated by personal gain or recognition [1]. He was more focused on stimulating thought and careful observation of details rather than following up on his observations. His discovery of a principle for an illumination source used for viewing the retina prior to Helmholtz and his subsequent pivotal invention of an ophthalmoscope is a vivid example [7].

Purkinje's collected works (*Opera Omnia*) have been published in 13 volumes. They are not assembled in chronological sequence. In 1918, the first portion of Purkinje's Opera Omnia was published in Latin. This volume contained his investigations relevant to ophthalmology as well as other studies [19]. The final volume appeared in 1985. These 13 volumes included Purkinje's various scientific contributions that appeared in journals and books. A list of Purkinje's scientific contributions, in addition to responses to them, was assembled by Kruta in 1969 [20].

Jan Evangelista Purkinje was a modest, inquisitive, courageous and visionary Czech physiologist whose vast interests and astute observations fostered a legacy of accomplishments that, even

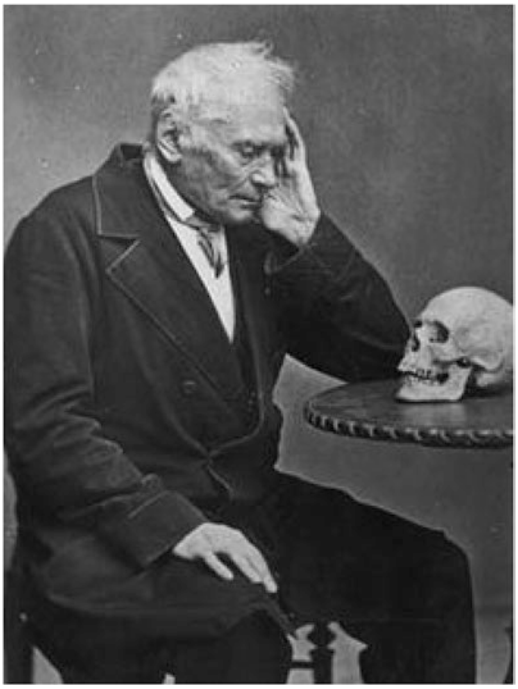

Fig. 8 Purkinje, in a reflective pose. From: http://www.pinterest.com/pin/154740937166756933/ Explore these ideas and more (public domain)

today, still impact our understanding for several aspects of visual science, general medicine, and biology (Fig. 8). It was said that "he found physiology a speculative study and left it an experimental science." [21] "Although he was not always thoroughly appreciated by his professional contemporaries, Purkinje was greatly respected, admired and loved by his Czech associates and countrymen. At his death … Purkyně was mourned by people of every class in Bohemia" [15]. It is a sad commentary that, because of limited financial means, a man such as Purkinje often could not afford to attend scientific meetings and had to work up until nearly the end of his life. He died on July 28, 1869 at age 81.

His humility and self-effacing manner are clearly in evidence in his own words, reported to have been said in 1869, just shy of 7 months before he died.

> "*I have indeed discovered various things, but, as for immortality of my name, this should not be taken literally. A hundred years hence perhaps only a few will know who Purkinje was, but that makes no difference. For indeed we do not know who discovered the plow, and yet it serves all humanity. The cause remains the same, but not the name—and that is the important thing.*" [22]

More than a century after his death, we can still appreciate the value of his substantial contributions to both visual science and clinical ophthalmology.

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