

Supplementary Material

Physics Essentials Enable Deeper Understanding in Signaling and Crosstalk of the Carcinogenesis Paradigm “*Epistemology of the Origin of Cancer*”

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Supplementary Material

Physics general aspects

The term “*physics*” derives from the Greek word ἡ φύσις, meaning “*nature*”. Physics is a natural science, dealing with fundamental phenomena and laws based on observations, measurements, and experiments that have enabled the explanation of many such phenomena. Philosophy is one origin of physics, as astronomy is inseparable from natural philosophy. Traditional physics (classical physics) includes mechanics, thermodynamics, electricity, optics, atomic and nuclear physics, and energy. In addition, areas such as biophysics and physical chemistry have developed in close connection with other natural sciences. Physics includes atomic, nuclear and particle physics, quantum theory, relativity theory, and solid-state physics. In Physics, direct observations are often impossible, and in some cases, very complex experiments are necessary. Of course, it is impossible to map every individual scientific revolution that fundamentally changed our thinking and promoted the concept of science as a subject. Even the scientific revolution of the 20th Century, including the Special and General Theories of Relativity [1, 2] (FIG. 1) and quantum mechanics [3, 4] (FIG. 2 & 3), is based on earlier research.

The discovery of radiation and its influence on understanding carcinogenesis extends back to before the 19th Century. From a scientist’s point of view, it is necessary to explore the origin of light waves in science, the wave theory of light in the 19th Century, electromagnetic radiation in the 19th and 20th Centuries, quantum physics, background radiation, nuclear fission and atom splitting, and radiocarbon dating.

Origins of light in science before the 19th century

At the end of the 19th Century, there was an ongoing dispute in science regarding whether light follows the corpuscular or wave theory. This debate extends far back in time. According to Hartmut Römer, Aristotle (384–322 BC) wrote in his “*De Anima*” II,7” and the Senses “*De Sensu III*” that “*light is not a substance or body but a quality,*” the “*visible quality of objects is their color,*” and light should behave like the waves of the sea [reviewed in 5]. However, light was long viewed as a material entity.

The Greek scientist, Empedocles of Acragas (approximately 492 BC to approximately 432 BC), a pupil of the Pythagoreans, proposed that the moon “*gets its light from the sun*” [page 65 in 6] and “*that the light of the sun comes from the opposite hemisphere*” [page 67 in 6]. “*Empedocles recognized that it takes time for light to travel and is not seen, as thought by Gomperz and others - remarkable from a scientific point; it is simply an obvious accompaniment of the view that light is material*” [page 68 in 6].

Leonardo di ser Piero da Vinci (1452–1519) presented a wave concept of light in his manuscripts: “*Just as the stone thrown into water becomes the centre and cause of various circles, and sound made in the air spreads out in circles, so every body placed within the luminous air spreads itself out in circles and fills the surrounding parts with an infinite number of images of itself, and appears all in all and all in each part*” [Manuscripts by Leonardo da Vinci at the Library of the Institut de France, reviewed in 7-9].

In 1543, the astronomer Nicolaus Copernicus (1473–1543) published the book “*De Revolutionibus Orbium Coelestium*” (*On the Revolutions of the Heavenly Spheres*), proposing a heliocentric model of the universe with the sun in the center, circled by planets [10]. It is no coincidence that this book alone has a current market value of more than £1.5 million British pounds. Two months after the book was released, Copernicus died, and it is assumed that

Copernicus was hesitant about publishing this book at an earlier time due to the reaction of the Catholic Church, which was powerful in those days. "*De Revolutionibus Orbium Coelestium*" was later rejected by the Catholic Church and even by Martin Luther, suggesting that Luther was a revolutionary thinker only in terms of theology. Another milestone was Johannes Kepler's (1571–1630) theory of vision, reported in 1604 [11].

The Dutch astronomer and mathematician Willebrord Snellius (1580–1626) is generally credited for establishing the law of refraction in 1621; this law remained unpublished until it was mentioned and recognized by René Descartes (1596–1650) in his book "*Dioptrics*" (French: "*La dioptrique*"), published in 1637 [12]. The law of refraction was also mentioned by the astronomer and physicist Christiaan Huygens (1629–1695) in a lecture presented to the *Royal Académie des Sciences* in Paris in 1678. Based on the phenomena of polarization and Huygens' mathematical calculations, the "*Huygens Principle*" suggested that light is based on wave motion. Huygens published his book "*Treatise on Light*" (French: *Traité de la Lumière*) in 1690 [13], which was translated by the physicist Silvanus Philips Thompson (1851–1916) in 1912 [14]. The mathematician and historian Professor Roshdi Rashed reconstructed parts of a book from the Iraqi Ibn Sahl (Abu Sad al-Ala ibn Sahl, (Persian: *بن جعفر بن علی بن حسن علی ابو*: ماکولا, approximately 940–1000) from 984 and attributed the discovery of the law of refraction to Ibn Sahl some 600 years before Snellius [15, 16].

Between the 1630s and 1660s, Pierre de Fermat (1601–1675) stated and discussed the "*principle of the least time*," in which light travels from one point to another via the quickest path [17, 18], and "*provided a mathematical proof that the straight line is not the fastest way for light to traverse between two optical media*" [19], explaining that light moves slower in denser media. The United States physicist Richard P. Feynman (1918–1988) visualized Fermat's principle: "*One may imagine Romeo discovering his great love Juliet at some*

distance from the shore of a shallow, leisurely flowing river, struggling for her life in the water. Without thinking, he runs straight toward his goal – although he might have saved valuable time if he had taken the longer route, running the greater part of the distance on dry land, where he would have achieved a much higher speed than in the water” [20].

In 1663, Otto von Guericke (1602–1686) created static electricity using a sulfur ball and a wooden cradle, which spun while rubbing against another object. Afterwards, Guericke also observed electroluminescence [21 reviewed in 22, 23]. Benjamin Franklin (1706–1790) used two rubber objects together to induce static electricity and exchanged this information with the British botanist, Peter Collinson (1694–1768) [24].

In 1665, the Jesuit Francesco Maria Grimaldi (1618–1663) observed the diffraction of light and mathematically demonstrated that light exhibits wave motion [25]. In 1667, Robert Hooke (1635–1703) stated that light consists of rapid vibrations, by which he attempted to explain refraction and colors [26 reviewed in 27, 28]. The velocity of light was determined by Ole Rømer (1644–1710) who presented his findings to the French Academy of Sciences on 21 November 1676. Rømer published these findings on 7 December 1676 [29 reviewed in 30]. In 1704, Sir Isaac Newton (1642–1726) suggested that light is corpuscular or particle-like, e.g., in Prop II, he stated that “...all the lightis reduced into very small particles, and then they become transparent” [31]. The force of the interaction between electric charges is named after Charles–Augustin de Coulomb (1736–1806), who discovered these charges in 1785 [32].

In 1780, Luigi Galvani (1737–1798) conducted experiments on frogs and observed that their legs contracted when exposed to electric sparks, which he interpreted as a type of animal electricity [33 reviewed in 34]. In 1791, based on his own experiments, Alessandro Giuseppe Antonio Anastasio Volta (1745–1827) suggested that every body contains electricity in a type

of homeostasis and that rubbing against metal results in a new equilibrium. Thus, Volta coined the term “*metallic electricity*” [35].

Wave theory of light in the 19th century

Thomas Young (1773–1829) discovered light interference and presented his findings at *The Bakerian Lecture* on 12 November 1801. Young proposed a wave theory [36], but this theory was ignored. On 15 October 1815, the engineer Augustin Jean Fresnel (1788–1827) presented a lecture to the Academy of Sciences in Paris [37] after conducting Young’s experiment with some modifications. He demonstrated that bright and dark bands of light were caused by the diffraction of an object, thus proving Young’s wave theory. Fresnel’s work was published a year later [38]. In 1819, Fresnel presented his wave theory of diffraction to the French Academy of Sciences [39] and published his interpretation of refraction and reflection in polarized light [40–44 reviewed in 180, 181]. In 1814, Joseph von Fraunhofer (1787–1826) observed that the spectrum of sunlight passing through a prism is divided by fine black lines [45].

Hans Christian Ørsted (1777–1851) discovered that magnetic fields are created by electric currents in 1820 [46 reviewed in 47]. In September 1820, François Arago (1786–1853) presented a lecture on Ørsted’s electromagnetic effect to the French Academy in Paris. Among the audience was André–Marie Ampère (1775–1836), who had found in the same month that electricity flows in the same direction for two nearby wires [48]. Ampère reported the effect between two electric currents, which lead to the study of electromagnetism [49] and further research [50].

During a speech in April 1846, Charles Wheatstone (1802–1875) suffered from an attack of stage fright, and Michael Faraday (1791–1867) filled the time after this interruption. Faraday presented his theory on the origin of light: “*On the Structure of the Aether, and the nature of action at a distance,*” which was later published [51, 52]. In 1822, Faraday reported magnetic rotation based on the Ørsted principle [53]. The theory and equations of James Clerk Maxwell (1831–1879), presented in 1865 [54], brought together the earlier works of Fresnel and Young, indicating that light acts as a wave rather than a particle. In 1859, Julius Plücker (1801–1868) observed cathode rays and their deflection by a magnetic field [55]. This effect was also shown by Johann Wilhelm Hittorf (1824–1914) in 1869 who attributed the effect to negatively charged particles [56]. Johann Heinrich Wilhelm Geißler (1814–1879) constructed instruments for Plücker, and his tubes were shown to hold a stronger vacuum [57]. Helmholtz’s pupil, Gotthilf–Eugen Goldstein (1850–1930), reported the phenomenon of isolated gas discharge in his doctorate research in 1879 and discovered canal rays (“*kanalstrahlen*”) in 1886 [58].

At a meeting in Belfast in 1874, George Johnstone Stoney (1826–1911) postulated that charges or elemental units of electricity could exist within atoms. He published his theory in 1881 and coined the term “*electron*” in 1891 [59-61 reviewed in 62]. In 1883, Thomas Alva Edison (1847–1931) showed that electrons from a heated metal (thermionic emission) flow in a vacuum to a cooler plate (*Edison effect, U.S. patent 307,031*). Joseph John Thomson (1856–1940) proved that electrons were the cause of the Edison effect and validated Stoney’s suggestion from 1897 that cathode rays are corpuscular with a negative charge, which he termed ‘*corpuscles*’ [63-65 reviewed in 66]. In 1878, Sir William Crookes (1832–1919) modified the Geissler apparatus by creating a vacuum (Crookes tube) [67].

In 1878, Albert Abraham Michelson (1852–1931) measured the speed of light in water and found that it was lower than that for air by a factor of exactly 1.33 [68-70]. In 1887, Albert Michelson and Edward Morley (1838–1923) performed an interferometer experiment disproving the existence of luminiferous ether, which was widely supported at the time [71]. In a series of experiments from 1887 to 1893, Heinrich Rudolf Hertz (1857–1894), who was a student of Hermann Ludwig Ferdinand von Helmholtz (1821–1894), showed that charged particles are emitted if light shines on a metal in a vacuum; these particles were shown to be electrons by Thomson (*see above*). Hertz also demonstrated that Maxwell's theory and equations were correct, thereby verifying the existence of electromagnetic waves [72-82]. By this, Maxwell's work and earlier works by Faraday and others were also validated [83].

In 1892, with his pupil Philipp E. A. Lenard (1862–1947), Hertz inserted a thin aluminum foil with a window (*Lenard window*) in a cathode ray tube that was closed airtight; he then stabilized the tube with grit. By this, electrons could exit the tube only through the Lenard window; subsequently, the electrons penetrated the metal foil and exhibited fluorescence. Here, the absorption coefficient was almost proportional to the density of the foil, meaning that the beam attenuation depended on the mass of the irradiated sample (*Lenard's law of mass absorption*) and the deflection of cathode rays by magnetic forces [84-86].

In 1895, Hendrik Antoon Lorentz (1853–1928) developed equations based on the idea that it may be possible to convert partial or temporal coordinates from one inertial system to another [87, 88]; this idea was later correctly interpreted by Albert Einstein. In 1899, George Francis FitzGerald (1851–1901) published his assumption that all moving objects shorten in their direction of motion, which explained the results of Michelson and Morley [89]. According to Harvey R. Brown, FitzGerald, together with Michelson and Lorentz, established the basis of the origins of relativity [90]. Lorentz was the first Conference President in 1911 of the

renomeed Solvay Conference (French: *Conseils Solvay*) at the Hotel Metropole in Brussels, Belgium to discuss the fundamental problems of contemporary physics (**FIG. 4**). Chemistry was added in 1922 and the Solvay Conference of Physics is followed by a gap year with the Solvay Conference of Chemistry.

Electromagnetic radiation in the 19th and 20th centur

Uraninite (pitchblende) was reported by Petrus Albinus (1543–1598) in 1590 [*page 549 in 91*]. Initially, pitchblende was mistaken for zinc ore. The unequivocal demonstration of uranium as a metal was achieved by Eugène–Melchior Péligot (1811–1890) in 1841. Péligot reduced potassium to anhydrous uranium tetrachloride and isolated uranium [*92–97 reviewed in 98*] which was a precondition of later discovery of radioactivity and the photoelectric effect. Between 1888 and 1891, the Russian physicist Alexander Grigorievich Stoletov (1839–1896) demonstrated that the intensity of light is directly proportional to the induced photoelectric effect (*Stoletov's Law*) [*99-102*].

The discovery of electromagnetic radiation (X-rays/Röntgen rays) on 8 November 1895 was fundamental [*103*] and is attributed to the German engineer and physicist Wilhelm Conrad Röntgen (1845–1923) [*104–106*], for which he received the Nobel Prize in Physics in 1901. Röntgen did not graduate from high school: he was accused of drawing a caricature of his school teacher, but did not want to reveal the actual culprit. Therefore, he left school in 1863. Röntgen passed the examination needed to enter the Polytechnic Institute at Zürich, Switzerland, and graduated in mechanical engineering in 1869. After being appointed as an assistant professor at the University of Würzburg, Germany, and Strasbourg University, France, he became a professor in 1875 at Hohenheim in Württemberg, Germany. In 1876, Röntgen returned to Strasbourg, France, as a professor of physics. He became the physics

chair at the University of Giessen in 1879, the University of Würzburg in 1888, and the University of Munich in 1900, where he remained for the rest of his life. In 2020, scientists celebrated the 125th anniversary of Röntgen's discovery and the 175th anniversary of his birthday, 27 March 1845. Röntgen's discovery had a fundamental influence on our understanding of various scientific fields, such as medicine, surgery, pneumology, physics and astrophysics, chemistry, molecular biology including X-ray diffraction of DNA and structural protein analysis through X-ray crystallography, imaging technologies and modern image processing, engineering, and materials analysis, as well as art history and archeology. However, the precondition of Röntgen's discovery goes back over three centuries and the resulting concept of electrons and their discovery were not isolated developments [107]. Earlier studies investigated the phenomenon in which an electrical current at very high voltage passing through a tube filled with noble gas at extremely low-pressure results in a glowing beam. Such studies were very important for Röntgen's discovery [reviewed in 108, 109].

It is assumed that Nikola Tesla (1856–1943) observed Röntgen's later findings in 1894, although this cannot be proven because Tesla's laboratory was completely destroyed by fire shortly afterward. After Röntgen presented his findings on X-rays, Tesla sent Röntgen his 1894 photographs, for which Röntgen congratulated him in terms of his precision [reviewed in 110, 111]. However, after Röntgen's discovery, the media became very focused on X-rays [reviewed in 112].

Antoine Béchère (**FIG. 5a & 5b**) studied infectious diseases and immunology and his thesis in 1882 dealt with measles [113]. After Röntgen's discovery of X-rays in 1895 (**FIG. 6a & 6b**), Béchère strongly supported the use of its medical application [reviewed in 114, 115]. He investigated a new diagnostic approach for improving the diagnosis of thoracic diseases [116].

In 1899, Bécère published a book about the use of radiology in tuberculosis [117, 118] and in 1906 Bécère together with Joseph AC Belot (1876-1953) and George Haret (1874-1932) presented their results on the application of radium for radiotherapy in cancer patients [119], which is why Bécère is known as one of the founders of radiotherapy [120]. For this, Bécère received the Daudet award of the Académie Française de Médecine and in 1931 he became its President. Antoine Bécère worked with Marie Curie to provide special radiological ambulances for frontline use in WWI and developed training courses for military radiologists, nurses, and medical students [121].

In 1891, the Polish *Marie Skłodowska* left Warsaw to study in Paris. With the support of her brother-in-law, she matriculated at the Sorbonne and passed her examination [reviewed in 121, 122]. *Marie Skłodowska* was introduced by Professor Gabriel Lippmann (1845–1921) to Pierre Curie (1859–1906), who was very impressed by her. Pierre Curie wished to marry *Skłodowska*, who initially declined. However, they married in 1895 and worked together (FIG. 7).

The discovery of electromagnetic radiation (X-rays/Röntgen rays) on 8 November 1895 was a fundamental discovery that influences us today. This discovery is attributed to the German engineer and physicist Wilhelm Conrad Röntgen (1845–1923) [104–106], for which he received the Nobel Prize in Physics in 1901. This development occurred accidentally when Röntgen covered a cathode tube to investigate whether such rays would pass through glass with a heavy black cardboard layer. Röntgen observed a green fluorescent light glowing on a platinum aquarium screen 9m away. He found that even a thick book or wood could not block the rays, and after placing his hand on the screen, he saw the bones of his hand as shadows. In contrast to today's commercialized science, Röntgen did not patent his discovery. At this time, it was not known that the glowing beam was caused by electrons; thus, the beam was named

“*cathode radiation*.” Röntgen’s discovery resulted from the work of brilliant thinkers and researchers over three centuries: the resulting concept of electrons and their discovery were not isolated developments [107].

After learning about Röntgen’s achievement in 1886, *Antoine Henri Becquerel* (1852–1908) investigated uranium salts. He exposed these salts to sunlight, placed them on photographic plates, and observed emitted rays. Initially, Becquerel thought that the rays were due to absorbed energy from the sun. On one occasion, Becquerel performed the experiment in Paris while it was cloudy and thought that the experiment had failed. However, by accident, he found strong images on the photographic plates, meaning that the uranium sulfate emitted radiation rather than the sun: by this, Becquerel discovered spontaneous radioactivity from uranium salts in 1896 [124, 125 reviewed in 126]. Becquerel also published about the influences of a magnetic field on the radiation emitted by radioactive substances [127]. Marie Curie read a paper in *Comptes Rendus* based on Henri Becquerel’s discovery and stated to her husband “...*that she doubted that uranium should be the only element emitting the new type of rays*.” The very next day, she began investigating one element after another.

However, on 12 April 1898, it was Lipman who reported Curie’s results on the radioactivity of pitchblende and copper uranium phosphate mineral chalcocite to the Paris Academy of Sciences. Marie Curie named the bismuth-like element polonium (in honor of her native Poland) and coined the term “*radioactivity*” to describe the new phenomenon. Together with Gustave Bémont (1857–1937), Marie Curie published the discovery of polonium that she had extracted from pitchblende and presented a lecture to the French Academy of Sciences on 18 July 1898 [128, 129]. In her doctoral dissertation, Marie Curie described the investigation and the new radioactive substances in greater detail [130] and together with Becquerel [131].

In 1899, Julius Elster (1854–1920) and Hans Geitel (1855–1923) used electrometers and found that the discharge of an electrically charged body occurs much more rapidly if a radioactive sample is brought close to this body; moreover, the discharge time is dependent on the level of radioactivity. They published these findings in 1900 [132]. Because Elster and Geitel concluded that the spontaneous discharge was due to the presence of ions in the atmosphere, scientists began to investigate radioactivity with the help of ionization, but not vice versa [133].

In 1900, Ernest Rutherford (1871–1937) observed that conductivity can be reduced by placing a lead shield around the measuring device [134]. In 1898, he laid a thin aluminum foil over uranium and found that one type of radiation was readily absorbed while another type was more penetrating. Rutherford termed these radiation types α - and β -rays, respectively [134, 135]. One year later, Friedrich Oskar Giesel (1852–1927) demonstrated that β -rays (which had been shown by Thomson and Pierre to be identical to cathode rays) can be easily deflected by a magnetic field [136], which was also reported by Becquerel for α -rays. Between 1900 and 1902, Rutherford with Frederick Soddy (1877–1956) showed how atoms of a radioactive element (thorium in this case) spontaneously transform into another element, radium. Initially, scientists did not believe these results, but publications followed [137-141].

The discovery of the positively charged α -rays and the negatively charged β -rays, combined with the finding that radioactive elements can transform into other elements, led to the Nobel Prize in Chemistry for Rutherford in 1908. In particular, the phenomenon of one element transforming into another led to a revolution within the world of physics. Non-charged γ -rays were discovered by Paul Villard (1860–1934) in 1900, which he termed “*X-rays emitted by radium*” [142, 143]. Rutherford later coined the term γ -rays [reviewed in 144]. In 1903, Sir William Ramsay (1852–1916) and Soddy reported that helium gas can be produced by the

radioactive decay of radium, although they could not explain how one chemical element could emanate from another. For this work, the Nobel Prize in Chemistry was awarded to Ramsay in 1904 and Soddy in 1921 [145, 146].

In 1903, Max von Laue (1879–1960) described the wave nature of X-rays in his doctoral thesis, which was partially published in 1904 in the *Annals of Physics* and as a book [147,148]. Later, von Laue together with Walter Friedrich (1883–1968) and Paul Knipping (1883–1935) showed, that X-ray irradiation of a copper sulfate crystal resulted in regular patterns of dark points on a photographic plate [149]. Max von Laue received the Nobel Prize in Physics in 1914 for his discovery of the diffraction of X-rays on crystals and for proving Einstein's photoelectric effect. Later, these experiments prompted the work of Sir William Henry (1862–1942) and Sir William Lawrence Bragg (1890–1971), for which both received the Nobel Prize in 1915. Due to their work, the X-ray diffraction images of DNA acquired by Rosalind Franklin in 1952 were possible. In 1906, Rutherford showed that α -particles deviate slightly while passing through matter and afterward undergo a scattering process [150].

In 1908, Hans Geiger (1882–1945) found a way of counting α -particles [151], which later led Geiger and his student Walther Müller (1905–1979) to perform experiments using the Geiger–Müller tube counter for measuring radioactivity [152]. These two scientists worked with Sir Ernest Marsden (1889–1970) from 1908 to 1913 (Geiger–Marsden experiment) on experiments in which α -beams impinged on a thin gold foil: the majority of the particles passed through the foil undisturbed, but particles close to the nuclei of gold atoms were deflected at a wide angle [153-155]. Based on the Geiger–Marsden experiments, Rutherford discovered the atomic nucleus [156] and developed an atomic model similar to the solar system (*Rutherford atomic model*) [157], suggesting a massive positively charged nucleus in

the center surrounded by an opposite charge. Niels Bohr (1885–1962), James Chadwick (1891–1974), and later Robert Oppenheimer (1904–1967) also worked with Rutherford.

Bohr modified Rutherford's atomic model and included the quantum theory [158], which clashed with classical physics during this time. Although Bohr's model conflicted with Rutherford's atomic model, Rutherford supported Bohr throughout his work. After some time, the Bohr–Rutherford model was accepted in physics, although no one could explain the quantum jumps of electrons [reviewed in 159]. Bohr received the Nobel Prize in Physics in 1922.

George de Hevesy (1885–1966) was an unpaid research assistant in Rutherford's laboratory from 1911 to 1912. Rutherford gave him a problem to solve: *“My boy, if you are worth your salt, you try to separate Radium-D from all that lead.”* De Hevesy failed to solve this problem, but he proposed the idea of radiotracers in 1912 during a lecture to the Bunsen Society (German: *Deutsche Bunsen-Gesellschaft für Physikalische Chemie e.V.*) in Germany. He suggested that radioactive indicators (radioisotopes) might be used for probing atoms in electrochemical measurements [reviewed in 160, 161]. Hevesy and Fritz Paneth (1887–1958) determined the chemical and electrochemical identity of lead and radium-D [162, 163]. In 1943, Hevesy received the Nobel Prize in Chemistry *“for his work on the use of isotopes as tracers in the study of chemical processes.”*

In 1914, Rutherford's former pupil, Chadwick, found that β -emission was continuously distributed [164]. In 1932, he discovered the neutron [165], providing an important puzzle piece for quantum physics [166]. Chadwick received the Nobel Prize in Physics in 1935.

Quantum age

On 14 December 1900, Max Planck (1858–1947) presented a hypothesis to the Physical Society of Physics in Berlin, stating that energy at each wavelength is composed of N identical finite “*energy quanta*.” Planck heuristically presented blackbody radiation to the German Physical Society; this concept conflicted with Newton’s mechanics as well as Faraday’s and Maxwell’s electromagnetic equations, which gave birth to quantum physics [167]. In general, Planck applied the concept of thermodynamic equilibrium (*homeostasis*) and described the equation of temperature-dependent radiation emission based on very small packages of emitted energy, which he termed “*quanta*.” Planck received the Nobel Prize in Physics in 1918.

In 1887, Heinrich Hertz discovered the photoelectric effect [72-74], and Albert Einstein published his explanation of the light-quantum hypothesis. Einstein theorized that electromagnetic radiation (light) does not have an arbitrary amount of energy; rather, the energy is quantized [168]. At this time, Einstein’s theories were rejected, as Maxwell’s electromagnetic theory was viewed as valid for interference and diffraction. In 1905, Einstein published “*Zur Elektrodynamik bewegter Körper*” (English: On the electrodynamics of moving bodies”) [1], which was later named “*Special relativity theory*.” This theory is today known by the equation, $E=mc^2$ due to the equivalence of mass and energy, which are directly proportional to one another. Afterward, Einstein developed his theory of general relativity, which he published in 1916 [169]. Just one year later, Einstein published a book about both theories [170]. In 1921, Einstein received the Nobel Prize in Physics, which was presented to him in 1922.

Pierre Auger (1899–1933) demonstrated Lisa Meitner’s discovery of 1922 in regard to the influence of X-rays on matter, the so-called “*Auger effect*.” This phenomenon led to an

interpretation of the photoelectric effect in which a radiation-less transition of an excited atom can occur [171].

In 1923, Arthur Holly Compton (1892–1962) demonstrated the particle nature of radiation via the scattering of a photon by charged particles, the so-called “*Compton effect*” [172], for which he received the Nobel Prize in Physics in 1927. Max Born (1882–1970) had previously worked on quantum mechanics [173, 174]. In 1925, Werner Heisenberg (1901–1976), Max Born, Pascual Jordan (1902–1980), Paul Dirac (1902–1984), and Erwin Schrödinger (1887–1961) provided the intellectual and mathematical (and philosophical) basis for quantum mechanics. Together, Born, Heisenberg, and Jordan delved deeper into the matter and reported the first complete formulation of quantum mechanics [175].

In 1926, Brillouin developed a basic equation of wave mechanics [176]. Meanwhile, Heisenberg attempted to establish a basis for theoretical quantum mechanics [3]. Originally, the term “*matrix mechanics*” was not included in his publications, although this term was used later [reviewed in 177]. Paul Adrien Maurice Dirac completed this work and described how the “*Compton effect*” could be addressed [178]. In 1926, Erwin Schrödinger developed a wave equation [4] following de Broglie’s work from 1924, for which he received the Nobel Prize in Physics in 1933. In 1927, Heisenberg published his famous “*uncertainty principle*” (German: *Unschärferelation*), which states that two complementary properties of a particle cannot be determined at the same time (e.g., position and momentum) [179]. This development was followed by the “*Copenhagen interpretation*” as the first complete interpretation of quantum mechanics by Bohr and Heisenberg. These scientifically fruitful years provided a basis for describing the phenomena of atomic physics, solid-state physics, and nuclear and elementary particle physics.

De Broglie expanded Schrödinger's work by incorporating the quantum mechanics of Heisenberg, Born, and Jordan in 1929 [180, 181]. De Broglie received the Nobel Prize in Physics "for his discovery of the undulatory nature of electrons," which demonstrated that electrons behave like waves [182].

In 1932, Ernest Orlando Lawrence (1901–1958) and Milton Stanley Livingston (1905–1986) published a paper on the production of high-speed lightweight ions, which enabled the later production of radionuclides within a cyclotron. For this work, Lawrence received the Nobel Prize in 1939 [183]. Later, Lawrence was also responsible for uranium-isotope separation during the *Manhattan Project*. In 1934, Irène and Frédéric Joliot-Curie discovered artificial radioactivity in isotopes (the impingement of α -particles from polonium on an aluminum sheet was not instantaneous) [184], for which both received the Nobel Prize in Chemistry in 1935. Technetium-99m (atomic number 43) was discovered in 1937 by Carlo Perrier (1886–1948) and Glenn Theodore Seaborg (1912–1999) [185-187] and isolated by Seaborg and Emilio Gino Segre (1905–1989) [188, 189]. Seaborg received the Nobel Prize in Chemistry for this work in 1951. Segre was part of the *Manhattan Project* and received the Nobel Prize in Physics in 1959. One aspect to consider when evaluating the biological effects of radiation is background radiation. Due to these achievements, we now have the complete electromagnetic spectrum (FIG. 8) [adapted from 190].

Background radiation

In 1909, the German physicist and Jesuit priest Theodor Wulf (1868–1946), studied penetrating radiation in Germany, Holland, and Belgium. Aiming to improve Elster and Geitel's electrometer, he constructed an apparatus for measuring radiogenic ionization with a large-volume measuring chamber by keeping the capacity of the measuring arrangements as

low as possible. Wulf thought of using the threads of his electrometer as a discharge body, resulting in very low capacities. He presented a hypothesis, which was very bold at the time, that if radioactivity originated from Earth, its intensity would decrease with height [191, 192]. He took his electroscope to the top of the Eiffel Tower and found that the radiation was lower at a height of approximately 300m. Today, we know that his findings were caused by the radioactive metal of the Eiffel Tower. However, according to Wulf's interpretation, his findings indicated that the radioactivity came from outside the earth's atmosphere.

In 1910 and 1911, the Swiss physicist Albert Gockel (1860–1927) performed experiments in Europe, Turkey, and North Africa in underground caves and tunnels, lakes, and seas. He also performed experiments via balloon flights on mountains and the glaciers of the Alps in Jungfrauoch, Switzerland [193, 194]. Gockel was the first to use Wulf's apparatus in balloon experiments. Gockel *"took an enclosed electroscope up in a balloon with him to a height of 13,000 feet and reported that he found the "penetrating radiation" about as large at this altitude as at the earth's surface, and this despite the fact that Prof. Eve, of McGill University, had calculated that it ought to have fallen to half its surface value in going up 250 feet"* [195, 196]. Gockel coined the term *"kosmische Strahlung"* (cosmic radiation) [197].

On 20 October 1910, the Italian physicist Domenico Pacini (1878–1934), observed a reduction in radioactivity on a ship at sea compared with land measurements, concluding that a proportion of radiation must be independent of emission from the Earth's crust. He also showed that the radiation occurring three meters below the sea surface is approximately 20% lower than that at the surface [198]. The Austrian physicist, Victor Franz Hess (1883–1964), discovered *"extraterrestrial radiation"* (cosmic rays) by measuring radiation at various altitudes. Hess found that the radiation levels at altitude increased by up to two-fold compared with those at sea level. Therefore, he concluded that the radiation originated from outer space

[198-200]. This finding provided the basis for our current understanding of background radiation exposure [*see later*] and was confirmed in 1925 by the American physicist Robert Andrews Millikan (1868–1953), who originally coined the term “*cosmic rays*” [195]. The Nobel Prize in Physics was awarded to Millikan in 1923 for his measurements of the photoelectric effect, and to Hess in 1936 for his investigations of ionizing radiation in the atmosphere.

Hess performed measurements on a balloon flight up to 5,300 meters on 7 April 1912 during a near-total eclipse of the Sun. He found that the ionization of the atmosphere did not decrease during the eclipse. Thus, he concluded that the radiation must come from outer space rather than the sun. The German physicist Werner Kolhörster (1887–1946), repeated Hess’s experiments during 1913 and 1914. On 28 June 1914, he reached 9,300 meters and confirmed Hess’s findings [201, 202]. From these experiments, scientists began to better understand background radiation.

In 1964, Robert Woodrow Wilson (1936) and Arno Allan Penzias (1933) discovered cosmic background radiation by accident (Nobel Prize in Physics, 1978) [203, 204]. Here Natural background radiation (NBR) exposure and High background radiation (HBR) exposure needs to be differentiated as provided in the main manuscript.

Nuclear fission and atom splitting (1938–1946)

In 1938, Otto Hahn (1879–1968), Lise Meitner (1878–1968), and Fritz Strassmann (1902–1980) (FIG. 9) [205] provided proof of nuclear fission in uranium, in which the nucleus of an atom splits into smaller parts [206–216]. One year later, the interpretation of these results was developed by Meitner (1878–1968) and her nephew Otto Frisch (1904–1979) [215, 216]. Otto

Hahn received the Nobel Prize in Chemistry in 1944. In honor of Lise Meitner, the element 109 was named after her in 1997, Meitnerium (Mt). Both Meitner in 1938 and Frisch in 1939 had to emigrate because of their Jewish ancestry during the Nazi regime. Meitner never received the Nobel Prize, although she was nominated and supported by Max Planck, Max Born, and Niels Bohr. Enrico Fermi (1901–1954), who worked on the Manhattan Project and discovered the trans-uranium elements [217-219], for which he received the Nobel Prize in Physics in 1938.

Prior to this time, it was generally believed that the nucleus of a heavy atom splits into two lighter nuclei. Qian Sanqiang (钱三强), also known as Tsien San-Tsiang (1913–1992), was a Chinese nuclear physicist who worked in the Curie Laboratory of the Radium Institute in Paris under the supervision of Marie Curie's daughter, Irène Joliot-Curie, and her son-in-law, Frédéric Joliot-Curie, from 1937 (the year in which Marie Curie passed away) to 1947. San-Tsiang obtained his French national doctorate in 1940 and became a professor at Tsinghua University in 1947. San-Tsiang is known as the father of the Chinese atomic bomb (16 October 1964). With Irène Joliot-Curie, Tsien San-Tsiang published a comparison of radiation for radioactive isotopes from uranium and thorium [220]; he also investigated the emission of proton groups by α -rays from polonium and the intensity of γ -rays from radioactinium [221, 222]. Together with his wife, He Zehui (1914–2011) (FIG. 10) [223], and two French students, Raymond Chastel and Leopold Vigneron, Tsien San-Tsiang demonstrated “*the existence of ternary fission from the measurement of fission tracesand predicted the mass spectrum of the fragments*” [224-226 reviewed in 223]. Tsien San-Tsiang was awarded the Henri de Parville Award by the French National Academy of Sciences in 1946. Tsien San-Tsiang served as President of Zhejiang University from 1979 until 1982.

Radiocarbon dating (1939–1946)

Serge Alexander Korff (1906–1989) used a Geiger–Müller tube to count cosmic rays at altitudes up to 116,000 feet [227, 228]. In 1939, he showed that neutrons are produced by cosmic rays in the atmosphere and stated that the reaction of such neutrons with nitrogen-14 produces radiocarbon (carbon-14) [229, 230]. Samuel Ruben (1913–1943) and Martin Kamen (1913–2002) confirmed the existence of radiocarbon in 1940 [231]. In 1946, Willard Libby (1908–1980) reported on the concept of carbon-14 dating. Cosmic rays transform nitrogen-14 into carbon-14, which has a half-life of approximately 5730 years, within the atmosphere. The carbon-14 is absorbed by organisms through carbon dioxide, and once an organism dies, the carbon decays at a predictable rate to nitrogen-14 [232-235] (Nobel Prize in Chemistry in 1960).

Research from the end of the 19th and the beginning of the 20th Century led to research at Los Alamos for the Manhattan Project. The completion of the above content is provided within the main body manuscript.

Measurement parameters (see Table 1, main manuscript)

Sievert

In 1979, the ionizing radiation dose equivalent was designated by the “*International Bureau of Weights and Measures*” (French: *Bureau international des poids et mesures*, BIPM) at the “*General Conference on Weights and Measures*”, which is the basis for the International System of Units (Système international [d'unités], SI); this unit was denoted as the Sievert (Sv) in honor of the Swedish physicist, Rolf Maximilian Sievert (1896–1966). The BIPM is supervised by the “*International Committee for Weights and Measures*” (French: *Comité international des poids et mesures*, CIPM), which is a Board of 18 members that meet

biannually. According to the CIPM, the Sv is defined by $H = Q \times D$, where "*the quantity dose equivalent H is the product of the absorbed dose D of ionizing radiation and the dimensionless factor Q (quality factor) defined as a function of linear energy transfer (LET) by the International Commission on Radiation Units and Measurements (ICRU)*" [236-239]. According to the International Commission on Radiological Protection (ICRP), "*The Sievert is the special name for the SI unit of equivalent dose, effective dose, and operational dose quantities. The unit is joule per kilogram.*" One Sievert is equal to one joule/kilogram body weight. Based on this definition, exposure to 1 Sv corresponds to a 5.5% chance that a person will develop cancer over a lifetime of exposure.

Gray

The CIPM established the unit *Gray (Gy)* for absorbed doses in honor of the British physicist Louis Harold Gray (1905–1965), stating that "*in order to avoid any risk of confusion between the absorbed dose D and the dose equivalent H , the special name for the respective units should be used, that is, the name gray should be used instead of joules per kilogram for the unit of absorbed dose D and the name Sievert instead of joules per kilogram for the unit of dose equivalent H .*" Accordingly, one Gray is an absorbed dose of one joule of radiation energy per kilogram of matter or tissue ($1 \text{ Gy} = 1 \text{ J/kg}$) [236].

Radiation in living organisms

The French physician, Jean Alban Bergonié (1857–1925), and the physician and dermatologist Louis Tribondeau (1872–1918) investigated the effects of radiation on the testes of rats [240] and established the Bergonié–Tribondeau law in 1906 which states that

“Immature cells and cells in an active state of division are more sensitive to the X-rays than are cells which have already acquired their fixed adult, morphological or physiological characters” [241 reviewed in 242–246]. The authors noted that the “biological effect can thereby be studied both in dividing and in nondividing tissues of the same morphological and physiological cell types” [245]. Today it would be considered relevant if a cell line or type is stimulated or not as there are significant differences between the lymphoid and the myeloid lineages plus additional differences of cell subtypes, e.g. high radioresistance of macrophages and dendritic cells [247].

Development during embryology

Knowledge of embryogenesis and fetogenesis, as well as the process of differentiation of the three germ layers into various tissues, is required to understand the different effects of radiation (TABLE 1). Age determination of embryos is uncertain if the starting point of development is unclear [248]. Until the beginning of the 20th Century, the prevailing understanding was that ovulation coincided with menstruation or very soon afterward [249–251 reviewed in 248]. From 1919 to 1922, Kyusako Ogino (1882–1975) investigated 65 female patients. In 1923, the findings were published in the *Hokuetsu Medical Journal*, stating that ovulation is related to the subsequent menstruation rather than the previous menstruation [252]. In 1929, Hermann Knaus (1892–1970) showed an association between the ovarian corpus luteum and the sterile period [253], and Ogino provided a more detailed view on the ovulation and sterile period [254]. Both researchers provided more details demonstrating that the menstrual period in females occurs 14 (\pm 2) days after ovulation. However, ovulation is influenced by cohabitation, and thus, this rule does not apply to all humans [reviewed in 248].

The below-mentioned political events may be – especially during today’s time – seen as important, influencing the (Zeitgeist) cultures during these times and reflecting both societies and scientists.

Time in context World War I (WWI) and interwar times

WWI was a global war, although the Germans did not use the term “*world war*”. Instead, they preferred the term “*the Great War*” [255], with a farewell to the bourgeois era and the European Peace Order that had been in place since 1871. Occurring between 1914 and 1918, WWI was the “*great seminal catastrophe*” of the 20th Century, a term coined by George F. Kennan [256–266]. At the beginning of the 1920s, the world was attempting to handle the dreadful consequences of WWI with its casualties, wounded soldiers and citizens, and destroyed cities and countries. Estimates of WWI casualties vary greatly. According to the Robert Schuman European Centre (Centre européen Robert Schuman, CERS) in Scy-Chazelles, France, 40 million casualties occurred in WWI, including 20 million killed (9.7 million military personnel, approximately 10 million civilians) and 21 million wounded [267].

The Treaty of Versailles was signed on 28 June 1919 on the fifth anniversary of the assassination of Archduke Franz Ferdinand (28 June 1914 in Sarajevo), who was shot with his wife Sophie by the Serbian nationalist, Gavrilo Princip. This Treaty officially ended WWI, with the defeat of Germany and the acceptance of territorial changes, territories surrendered to the control of allied states, military restrictions, and reparations [268]. The Allied Powers consisted of the Entente Powers or Triple Alliance of the French Third Republic, the British, and the Russian Empire plus Japan, the United States, Serbia, Belgium, Greece, Montenegro, and Romania [258].

Gustav Stresemann (1878–1929) suggested treaties to the British Foreign Minister, Sir Austen Chamberlain (1863–1927), promising post-war borders. On 5–6 October 1925, the WWI Western European Allied powers, together with the new states of Central and Eastern Europe, created a post-WWI territorial settlement at Locarno, Switzerland (Locarno Treaties). These Treaties were signed on 16 October 1925 [269]. The Dawes Plan presented by the Dawes committee under chair Charles G. Dawes (1865–1951) regulated the agreement between the reparation commission and the German government. This plan was signed on 9 and 30 August 1924 [270, 271 reviewed in 272] and determined the WWI reparations to be paid by Germany. For this work, Dawes received the Nobel Peace Prize in 1925. Germany entered the League of Nations in 1926 as a permanent member.

The French Foreign Minister, Aristide Briand (1862–1932), who had previously laid the foundation of friendly relations between France and Germany in Locarno in 1925 [reviewed in 273], was one of the prime movers of the German candidacy to the League of Nations, which was initially dismissed. Stresemann applied again on 8 February 1926 [274], and on 8 September 1926, Germany was admitted to the League and given a permanent seat on the Council, based on a unanimous vote of the League of Nations Assembly [275].

For this work, the leading negotiators and foreign ministers Sir Austen Chamberlain, Gustave Stresemann, and Aristide Briand received the Nobel Peace Prize in 1926. Consequently, the United States Secretary of State Frank B. Kellogg (1856–1937) and French Foreign Minister Aristide Briand proposed that war not be used for resolving conflicts, resulting in an international agreement known as the *General Treaty for Renunciation of War as an Instrument of National Policy* or the *Kellogg–Briand Pact*. This Treaty was signed on 27 August 1928 by the United States, France, and Germany, followed by other countries [276, 277]. In 1929, Kellogg received the Nobel Peace Prize for his work in this regard.

The following period was characterized by increased nationalism, perhaps without profound changes in political thinking [278], as well as transitory economic recovery and upheaval. Parallels to today may be recognized. The 1920s are generally referred as the roaring twenties, the "*années folles*" (crazy years), or the Jazz Age; during that time, jazz was often seen as arrhythmical [279]. In addition, during the 1920s, the practice of laboratory medicine and pathology evolved to become what we recognize today [280]. Unfortunately, many scientists developed a type of enthusiasm for war; however, this attitude, which is only partially worked up, was held only among some scientists, particularly famous scientists.

If one were to study the background and incidents of a given war, one might conclude that war reflects the inability of people to interact due to their lust for power and oppression. Because these desires occur naturally in humans, one must assume – unfortunately – that there will always be wars. However, history clearly reveals that post-war periods result in many terrible acts; thus, intelligent scientists should refrain from any kind of enthusiasm for war.

Although WWI was officially over, many wars and riots occurred worldwide, such as the May Fourth Movement in Beijing, China (4 May 1919), the Spartacist uprising in Berlin, Germany (5–12 January 1919), the Berlin March Battles (1919), the Bavarian Council Republic (1919), the Hamburg Sülz riot (June 1919), the "*biennio rosso*" in Italy (1919/1920), the Broken Hill in New South Wales, Australia (1919/2910), and the Red Summer in the United States (1919). The year after WWI ended, 1919, was an extremely turbulent year worldwide, as other uprisings and disasters occurred: the Russian Civil War (1917–1922) as a consequence of the Russian Revolution in 1917, the Polish–Soviet War (1919–1920), Semana Trágica (Tragic Week) in Buenos Aires, Argentina (7–14 January 1919), the annexation of Transylvania by Romania, the Estonian War of Independence (1918–1920), the Anglo–Irish War (1919–1921), British "Bloody Friday" (Battle of George Square, 31 January 1919), the

Pinsk massacre in Poland (5 April 1919), the Amritsar massacre (Jallianwala Bagh massacre, 13 April 1919), the Greek occupation of Smyrna with the Greco–Turkish War (1919–1922), the War of Independence in Afghanistan (1919), and the Armistice Day Riot (11 November 1919) [281–290].

In 1918, the last year of WWI ended with the pandemic of the “*Spanish flu*” [291–296]. The time at which this pandemic originated and the temporal behavior of the spread are controversial. One German thesis stated that this disease arose in the end of 1917 and the beginning of 1918, with possible places of origin in China, France, and the United States. Others stated that the infected cook Albert Gitchell at Fort Riley, Kansas, United States, spread the disease around the military camp, and from there the spread continued to France, followed by Europe and the rest of the world [297–300 reviewed in 301].

The interwar years (1919 to 1939) until World War II [WWII]) started with many scientific discoveries; for example, the term “*covalence*” was introduced in relation to chemical bonding [302]. Scientifically, the first few decades of the 20th century can be declared of Physics.

This period provided the initiation of social media, with the world's first commercial radio station (Pracht Concerten Gratis Geven) developed by the Dutch scientist and radio pioneer Hanso Schotanus at Steringa Idzerda (6 November 1919) in Den Haag, Netherlands [303].

Time in context European Vision

In September 1929, the French Foreign Minister Aristide Pierre Henri Briand (1862–1932) gave a remarkable speech at the 10th session of the League of Nations where he called for federal bonds across Europe: “*I think that among peoples constituting geographical groups*

like the peoples of Europe, there should be some kind of federal bond...” [304]. Similarly, a call was made for the organization of a federal European union, which was supported by Gustav Stresemann. However, many countries, such as the United States, questioned this vision and dismissed it; moreover, the vision became *ad absurdum* due to the rise of the Nazi regime and the subsequent WWII.

The term “*United States of Europe*” is attributed to Victor Marie Hugo (1802–1885), who was a French poet, intellectual, statesman, and member of the French assembly (French: Académie Française) since 1841. In his speech during the 2nd General Peace Congress in Paris in August 1849 (during his exile against Napoleon III), Hugo stated, “*A day will come when those two immense groups, the United States of America and the United States of Europe, shall be seen placed in presence of each other, extending the hand of fellowship across the ocean, exchanging their produce, their commerce, their industry, their arts, their genius, clearing the earth, peopling the deserts, improving creation under the eye of the Creator, and uniting, for the good of all, these two irresistible and infinite powers, the fraternity of men and the power of God*” [305].

On 19 September 1946, Sir Winston Leonard Spencer Churchill (1874–1965) declared, “*Our constant aim must be to build and fortify the United Nations Organization. Under and within that world concept we must recreate the European family in a regional structure called, it may be, the United States of Europe, and the first practical step will be to form a Council of Europe*” for the “*United States of Europe*” [306].

Originally a German citizen, the French statesman Jean-Baptiste Nicolas Robert Schuman (1866–1963) stated, “*Today we are laying the foundations of a spiritual and political co-operation from which there will arise the European spirit, the promise of a broad and lasting supranational union*” on 5 May 1949 in London, United Kingdom. Schuman is credited for

establishing the name *European Community* [307]. On 5 May 1949, the Council of Europe with two main bodies, the Committee of Ministers and the Parliamentary Assembly, was founded via the London Treaty Pact by Belgium, Denmark, France, Ireland, Italy, Luxembourg, the Netherlands, Norway, Sweden, and Great Britain, with its headquarters in Strasbourg, France. The Organization's statute entered into force on 3 August 1949 [308].

The *Schuman Declaration* followed on 9 May 1950, presented by Jean-Baptiste Nicolas Robert Schuman (1866–1963) [309]. A treaty establishing the European Coal and Steel Community was signed in Paris by Belgium, France, Italy, the Federal Republic of Germany, Luxembourg, and the Netherlands on 18 April 1951 in Paris, France [310]. On 25 March 1957, 'The Treaties of Rome' establishing the European Economic Community and a treaty establishing the European Atomic Energy Community (EAEC or EURATOM) were signed. The first European Parliamentary Assembly was held on 19 March 1958 [311].

Here, we recognize the enormous input of France's creation of the European Community. Today, it seems a tragic paradox that one of the most important British statesmen of the 20th century established the vision of creating the European Community, while at the beginning of the 21st century on 31 January 2020, the United Kingdom signed the British exit (Brexit) after the referendum of 29 March 2017 [312].

Legend to figures

Figure 1 TITLE

Albert Einstein, about 1905

Figure 1 LEGEND

Albert Einstein at the patent office in Bern, Switzerland, from about 1905 [*Picture from 313, Page 93*].



Figure 2 TITLE

Werner Heisenberg, about 1927

Figure 2 LEGEND

Werner Heisenberg [*Picture from 313, Page 139*].



Figure 3 TITLE

Erwin Schrödinger, 1926

Figure 3 LEGEND

Erwin Schrödinger, 1926 [*Picture from 313, Page 139*].



Figure 4 First Solvay Conference, in 1911

Figure 4 LEGEND Photograph of participants of the first Solvay Conference, in 1911, Brussels, Belgium. [*Picture from 313, Page 107*].

- Standing from left to right: Robert Goldschmidt, Max Planck, Heinrich Rubens, Arnold Sommerfeld, Friedrich Lindemann, Louis de Broglie, Martin Knudson, Fritz Hasenöhl, Georges Hostelet, Édouard Herzen, James H. Jeans, Ernest Rutherford, Heike Kammerlingh Onnes, Albert Einstein, Paul Langevin.
- Seated from left to right: Walther Nernst, Léon Brillouin, Ernest Solvay*, Hendrik Antoon Lorentz, Emil Warburg, Jean Perrin, Wilhelm Wien, Marie Skłodowska-Curie, Henri Poincaré.

* Ernest Solvay was not present when the group photo was taken and his portrait was afterwards glued onto the group picture.

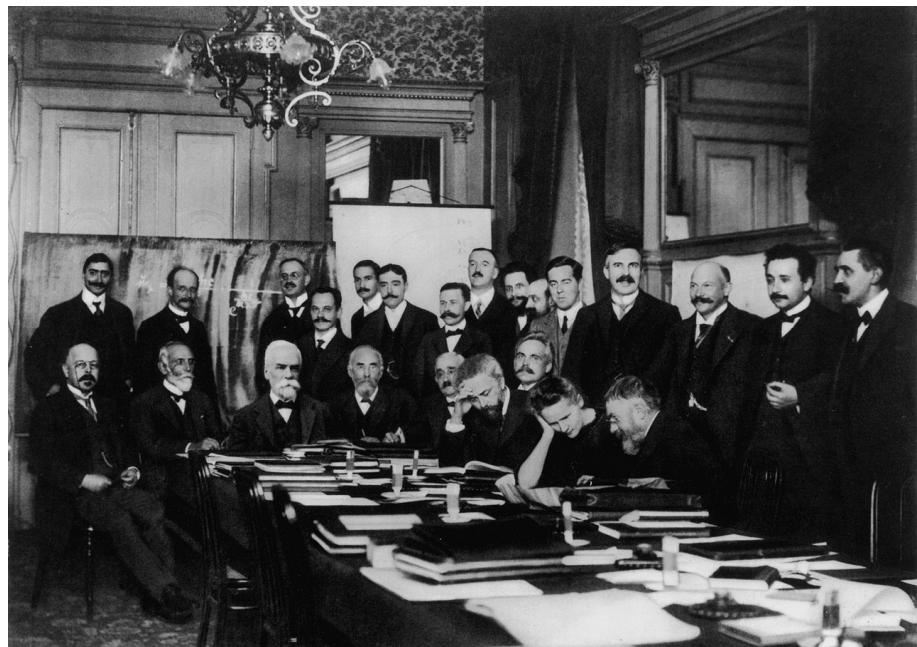


Figure 5a

Antoine Béclère, 1896

Figure 5a LEGEND

Antoine Béclère, 1896 [*Picture from 115*].



Figure 5b TITLE

Antoine Béclère

Figure 5b LEGEND

French postal stamp-Antoine Béclère, 1957

[Picture from 115].

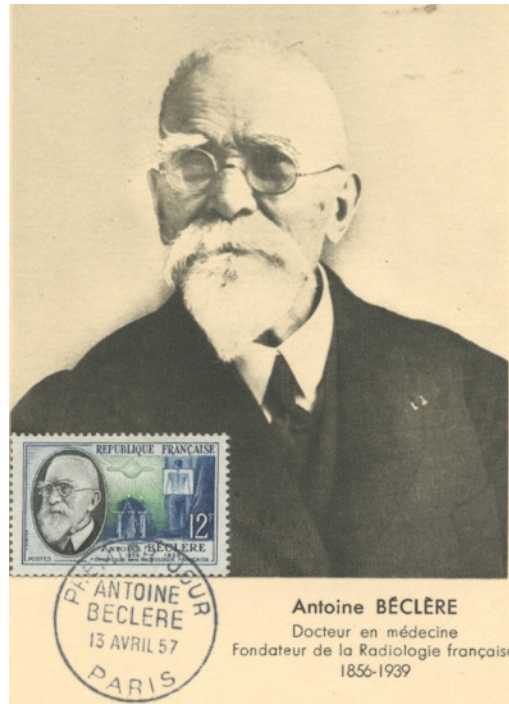


Figure 6a

Mrs. Röntgen's hand, first X-ray photograph, 1895

Figure 6a LEGEND

Mrs. Röntgen's hand, first X-ray photograph, 1895

[*Picture from 103*] from Courtesy National Library of Medicine, NIH



Figure 6b TITLE

Wilhelm Konrad Röntgen, 1906

Figure 6b LEGEND

Wilhelm Konrad Röntgen in a laboratory, 1906

[*Picture from 103*] from Courtesy National Library of Medicine, NIH



Figure 7 TITLE

Marie and Pierre Curie, 1900

Figure 7 LEGEND

Marie and Pierre Curie in the lab, about 1900

[Picture from 313, Page 39].



Figure 8 Electromagnetic spectrum.

Figure 8 LEGEND Complete electromagnetic spectrum with spectral subdivisions of the visible waveband [*adapted from 190*].

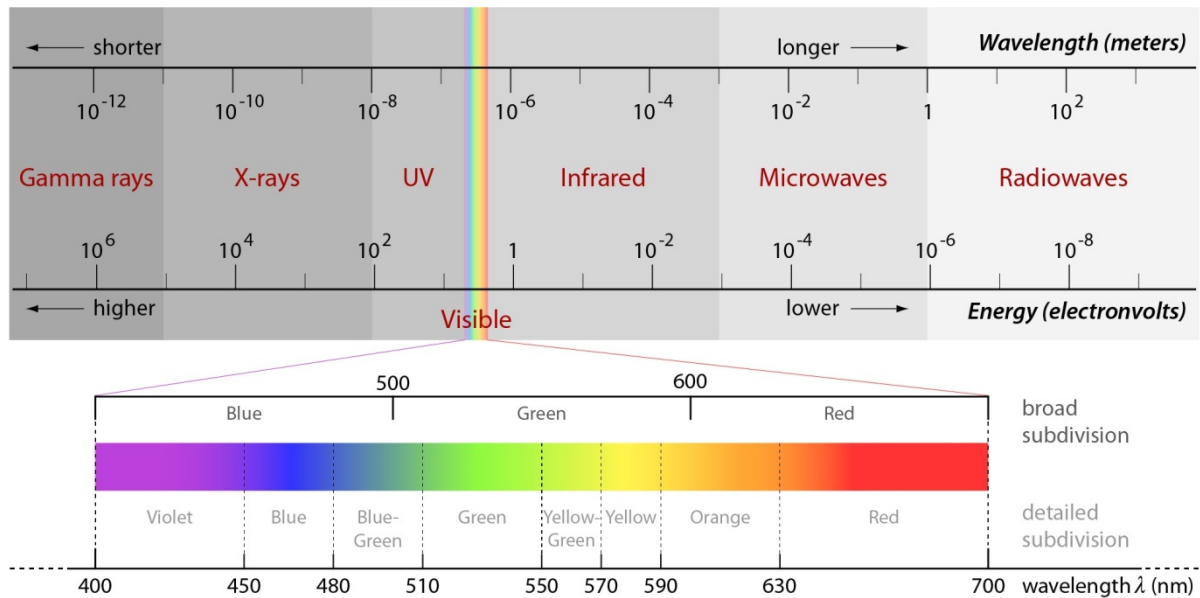


Figure 9

Fritz Strassmann, Lise Meitner and Otto Hahn, 1956

Figure 9 LEGEND

Fritz Strassmann, Lise Meitner and Otto Hahn, at the Max-Planck-Institute for Chemistry, Mainz, Germany 1956,

[205] from Courtesy Archiv zur Geschichte der Max-Planck-Gesellschaft, Berlin



Figure 10

Qian Sanqiang and his wife He Zehui, 1946

Figure 10 LEGEND

Qian Sanqiang and his wife He Zehui, 1946 (second and third from right) at the International Conference on Fundamental Particles and Low Temperatures held in Cambridge, UK in July 1946 [223], Image credit: Qian family.



Table Legends

Table 1 The three germ layers and their differentiation into various tissues.

Endoderm	Gastrointestinal tract & organs	Foregut	GI tract	Mouth & pharynx	
				Esophagus	
				Stomach	
				First part of small intestine	Duodenum (up to ampulla)
			Endocrine organs	Thyroid & parathyroid	
				Thymus	
				Pancreas	
			Other organs	Liver & gall bladder	
				Spleen	
		Respiratory tract	Trachea, bronchi, alveoli		
		Auditory	Auditory tube & tympanic cavity		
		Urinary	Bladder & urethra		
		Midgut	GI tract	Small intestine	Duodenum (distal half)
					Jejunum
					Ileum
				Colon	Cecum
			Appendix		
			Ascending colon		
			Transverse colon (proximal 2/3)		
Hindgut	GI tract	Colon	Transverse colon (distal 1/3)		
			Sigmoid		
			Rectum		
		Portal-venous system			
Mesoderm	Connective tissue	Fibers & ground substance	Elastic	Extracellular matrix	
			Collagenous	Tendons, ligaments, etc.	
			Reticular	Bone marrow	
		Cells	Fibroblasts, adipocytes, macrophages, mast cells, leukocytes		
		Muscles	Striated muscles	Cardiac & skeletal muscles	
			Smooth muscles	Gut organs, bladder, uterus, circulatory system	
		Bones & cartilage			
		Circulatory system	Vascular, lymphatic, mesenteries		
		Genitourinary system		Kidney, gonades	
		Serous membranes		Body cavities (thorax, abdomen): peritoneum, pleura	
		Spleen			
Red blood cells					
Ectoderm	Nervous system	Peripheral nervous system, brain, spinal cord			
	Tooth enamel, hair	Teeth & nails			
	Skin cells	Epidermis, melanocytes, sebaceous glands			
	Eye	Lens, cornea, retina			
	Rathke pouch	Hypophysis			

Nomenclature of abbreviations

AAAS American Association for the Advancement of Science; **AAPC** average annual percent change; **BEIR** Committee on the Biological Effects of Ionizing Radiation; **BIPM** Bureau international des poids et mesures (International Bureau of Weights and Measures); **CERS** Centre européen Robert Schuman, Robert Schuman European Centre; **CIPM** Comité international des poids et mesures (International Committee for Weights and Measures); **DOX** doxorubicin; **dsDNA** double-stranded DNA breaks; **EAEC** European Atomic Energy Community, EURATOM; **EC** European Community; **EDP Sciences** Édition Diffusion Presse Sciences; **ENU** N-ethyl-N-nitrosourea; **ESPCI** Ecole de Physique et Chimie Industrielles; **EURATOM** European Atomic Energy Community, EAEC; **Gy** Gray; **HBR** High background radiation; **HBRA**s high-background-radiation areas; **IAEA** International Atomic Energy Agency; **ICRP** International Commission on Radiological Protection; **ICRU** International Commission on Radiation Units and Measurements; **LD50** lethal dose for 50% of an exposed population; **LD50/30** lethal dose of radiation which is expected to cause death in 50% of an exposed population within 30 days; **LET** linear energy transfer; **LNT** linear no-threshold model; **LSS** Life Span Study; **MEF** mouse embryonic fibroblasts; **NAS** National Academy of Sciences; **NRC** Nuclear Regulatory Commission; **RBE** relative biological effectiveness; **ROS** reactive oxygen species; **SEER** United States Surveillance Epidemiology and End Results registry; **SFP** Société Française de Physique; **SI** Système international [d'unités] (International System of Units); **SMT** somatic mutation theory; **ssDNA** single-stranded DNA breaks; **Sv** Sievert; **UNSCEAR** United Nations Scientific Committee on the Effects of Atomic Radiation; **USNRC** United States Nuclear Regulatory Commission; **WGA** whole genome amplification; **WHO** World Health Organization; **WWI** World War I; **WWII** World War II.

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