



Scientific Background on the Nobel Prize in Physics 2018

## GROUNDBREAKING INVENTIONS IN LASER PHYSICS

OPTICAL TWEEZERS AND GENERATION OF HIGH-INTENSITY,  
ULTRA-SHORT OPTICAL PULSES

The Nobel Committee for Physics



## Groundbreaking inventions in laser physics

### *Optical tweezers and generation of high-intensity, ultra-short optical pulses*

#### General introduction

The very first paper describing the principle for an infrared or optical maser arrived to *Physical Review* [1] almost exactly 60 years ago (August 26, 1958) and was authored by Arthur L. Schawlow and Charles H. Townes, then at the Bell Telephone Laboratories in New Jersey. It represented an extension of the maser technique to the infrared and optical regions. This paper provided the blueprint for how to construct an optical maser, and it was Theodor H. Maiman [2] who in 1960 was the first to demonstrate coherent stimulated optical emission. The optical maser became known to a broader audience interested in popular science when Schawlow published an article in *Scientific American* in 1961 [3].

The name “optical maser” was initially used in technical literature, and also in Schawlow’s popular science article [3]. However, “optical maser” had already been replaced by “laser” (light amplification by stimulated emission of radiation) when the Royal Swedish Academy of Sciences awarded the 1964 Nobel Prize in Physics to Townes, Nicolay G. Basov and Aleksandr M. Prokhorov “for fundamental work in the field of quantum electronics, which has led to the construction of oscillators and amplifiers based on the laser-maser principle”.

The field of laser physics and its applications grew rapidly after the first discoveries. Laser light has unique properties such as coherence, directionality, monochromaticity and intensity, which are very useful properties both in science and in everyday life. Clearly, in the early years of the laser, the principal driver was the desire to have a device that would generate light waves of the same purity as radio waves. The first lasers were operated in short bursts, but there was a need for continuous operation. The development of continuous-wave, frequency-sharp lasers was a prerequisite for high-resolution laser spectroscopy, which has generated several Nobel Prizes in Physics.

Another important development in laser physics was the production of short pulses of light, thanks in particular to the inventions of laser Q-switching [4] and mode locking [5-9], which made it possible to produce a repetitive train of intense, short laser pulses. Together with the development of dye lasers [10, 11], this set off a new direction towards shorter and shorter optical pulses [12-17]. The access to short optical pulses, with durations matching the time-scale for atomic motion in molecules, led to new research fields in chemistry, and the possibility to study, in real time, transition states in chemical reactions. These breakthroughs were recognized by the Nobel Prize in Chemistry in 1999 to Ahmed Zewail.

This year’s Nobel Prize in Physics recognizes two inventions in laser physics that have opened new frontiers and generated important applications beneficial to the general public. One of them uses continuous, monochromatic lasers, whereas the other one concerns pulsed lasers.

One half goes to **Arthur Ashkin** for his invention of the optical tweezers and their application to biological systems.

The other half goes jointly to **Gérard Mourou** and **Donna Strickland** for their method of generating high-intensity, ultra-short optical pulses.

## Brief history of optical tweezers

Optical tweezers are a laser-based method for trapping and manipulating particles, which takes advantage of the ability of light to exert force, or radiation pressure. The idea that light could exert pressure was put forward in 1619 by Johannes Kepler, who postulated that the pressure of light explains why comet tails always point away from the Sun. In 1873, James Clerk Maxwell showed theoretically that light can exert pressure, based on his theory of electromagnetism. The existence of radiation pressure was finally verified experimentally in the early 1900s, by Pyotr Lebedev, Ernest F. Nichols and Gordon F. Hull. The time it took before its verification is a reminder of how extraordinarily weak such radiation pressure is under everyday circumstances. With the advent of lasers in the 1960s, it became possible to study radiation pressure using intense, collimated beams of light. A pioneer in this field was Arthur Ashkin, whose efforts led to the invention of the optical tweezers.

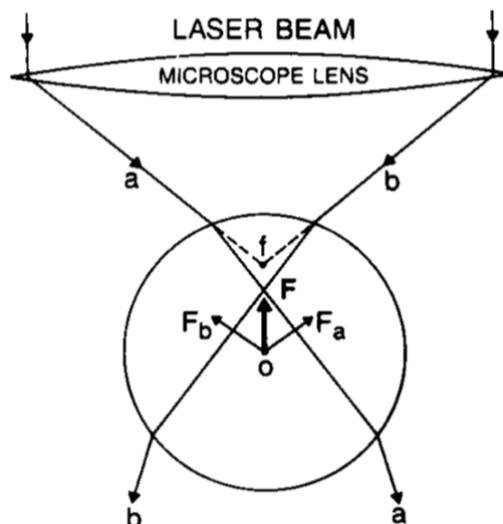
An early milestone was Ashkin's demonstration in 1970 that optical forces, generated by laser light focused into narrow beams, could displace small dielectric particles in both air and water [18]. The particles were accelerated in the direction of propagation of the light beam, as intended, by forward scattering forces. In addition, particles having a refraction index higher than the surrounding environment were drawn to the centre of the Gaussian beam by a transverse force in the direction of the intensity gradient, a so-called gradient force. Finally, having made this observation, Ashkin went on to demonstrate that three-dimensional trapping of particles could be achieved by using two counter-propagating laser beams [18].

This work was soon followed by Ashkin's construction of the first single-beam three-dimensional trap, the optical levitation trap in air [19]. With this method, particles are trapped at a point where the upward scattering force from a single vertical laser beam is balanced by gravity. However, this method becomes impractical in situations where the gravitational force is weak and Brownian motion dominates.

In 1986, Ashkin and coworkers were the first to implement an all-optical single-beam trap [20]. Originally called the single-beam gradient force optical trap, it soon became known as optical tweezers. This method traps particles by sending a laser beam through an objective lens; this creates a component of the gradient force that is opposite to the direction of propagation of the beam (see Figure 1). For trapping to occur, this force component must be sufficiently strong to balance the forward scattering force, which requires the use of a high numerical aperture, or large angle of convergence in the beam, provided in practice by a microscope objective lens. It was demonstrated that this method could trap dielectric particles in water, ranging in size from a few tens of nanometres up to tens of micrometres [20].

The optical tweezers scheme was originally suggested for the trapping of atoms [22]. Soon after its first implementation for dielectric particles [20], it was also employed in atom cooling and trapping experiments [23]. However, Ashkin immediately realised and began to investigate its potential applicability to biological systems. In groundbreaking studies, he demonstrated that optical tweezers could trap and manipulate viruses and living cells, switching from a green to an infrared laser for reduced damage from the intense optical beam [24, 25]. Further applications included manipulating subcellular components of plant cells [26], and estimating the force driving organelle transport along microtubules (part of the cytoskeleton) in amoeba cells [27].

Ashkin's pioneering studies of viruses and living cells were soon followed by new applications of the optical tweezers method to biological systems by other scientists. An early study by Steven M. Block, David F. Blair and Howard C. Berg investigated the mechanics of bacterial flagella [28], which consist of a helical filament connected to a rotary motor that serve to propel the bacterium. By twisting the bacterium about a tethered flagellum, and calibrating the optical force against viscous drag, they could measure the torsional compliance of the flagellum.



**Figure 1:** Qualitative ray optics description of the restoring backward force in an optical tweezers trap, for a dielectric sphere that is located below the focus  $f$  and assumed to be large compared with the wavelength of the light. Rays of light carry momentum and are bent by refraction when passing the dielectric sphere. By conservation of momentum and Newton's second law, the momentum change of the refracted rays results in an oppositely directed force on the sphere. A typical pair of rays,  $a$  and  $b$ , gives rise to a net force  $F$  on the sphere, directed towards the focus  $f$ . In the so-called Rayleigh regime, where the particle is instead small compared with the wavelength, the optical force can be calculated by treating the particle as a point dipole. The force obtained can be decomposed into two forces: a scattering force, which is in the direction of propagation of the beam and is proportional to the intensity, and a gradient force, which is proportional to the intensity gradient and is directed toward higher intensity. Source: reference [21].

## Molecular-level applications

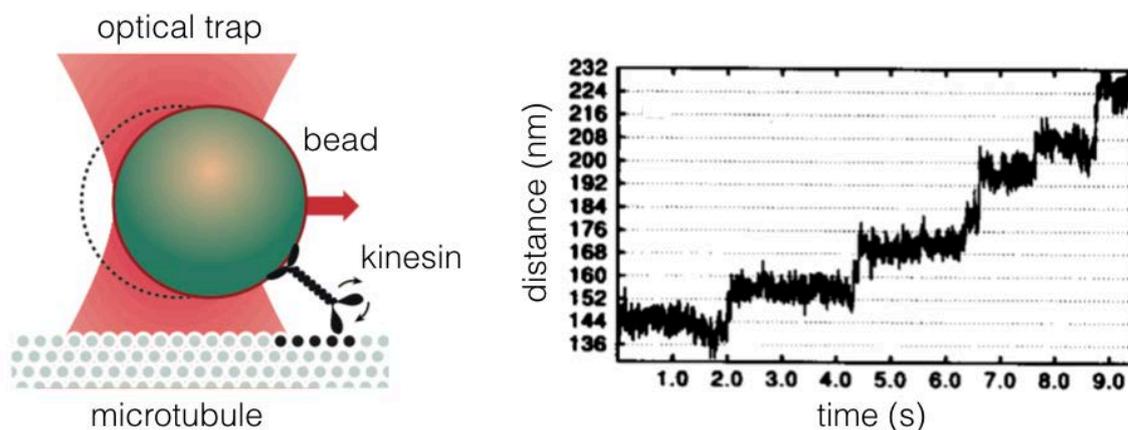
Optical tweezers are now a widely used tool in biological physics and related areas, and continue to find new applications. The method is used for non-invasively trapping and manipulating objects such as single cells and organelles and for performing single-molecule force and motion measurements. The study of single molecules is made possible by linking them to “handles” that can be easily trapped with the tweezers, such as micron-sized polystyrene or silica beads. The beads also act as probes to monitor motion and force.

A basic optical tweezers instrument for trapping micron-sized objects is a relatively simple tool. However, accurate monitoring of the motion of trapped objects, in aqueous solution at room temperature, is a challenge that requires advanced instrumentation [29], which may involve the use of dual traps holding, for instance, the respective ends of a protein or DNA molecule. Progress in this area has brought single-molecule optical trapping experiments to a level where single base-pair steps along DNA can be detected [30], corresponding to a spatial resolution at the Ångström level.

Early subjects for single-molecule studies with optical traps were the physical properties of DNA, such as relaxation, elasticity and the occurrence of a sharp force-induced transition to an extended form of DNA [31-33]. Related work was performed using magnetic tweezers [34] and glass micro-needles [35]. Another optical tweezers-based study demonstrated reversible unfolding of small

RNA molecules under mechanical force [36]. Force-extension curves for an RNA molecule were subsequently used for the first experimental test [37] of Jarzynski's equality in stochastic thermodynamics, which relates nonequilibrium work distributions to equilibrium free energy differences [38].

An area in which optical tweezers have proven particularly valuable is the kinetics and mechanics of molecular motors. These motors convert chemical energy into linear or rotary motion. One group of molecular motors consists of linear motor proteins that play an essential role in intracellular transport, muscle contraction and cell division, for example. Basic parameters of a linear motor include its step size, dwell times and the force generated, which are not directly accessible with ensemble methods. With optical tweezers, it has been possible to determine trajectories of single linear motor proteins with sufficient resolution to resolve their stepwise motion, and thereby obtain information on step size and dwell times, including the role of fluctuations. A breakthrough was the first direct observation of the stepping motion of kinesin [39], which transports cellular cargo along microtubules (see Figure 2). A step size of 8 nm was observed, which corresponds to the length of the repeating unit along microtubules, and the maximum force produced by kinesin molecules (about 5 pN) could be measured [39]. Related work analysed the interaction of single myosin molecules with actin filaments [40, 41]. The myosin-actin interaction generates a relative sliding of myosin and actin filaments for muscle contraction.



**Figure 2:** (Left) Sketch of the kinesin-microtubule system studied with optical tweezers in reference [39]. An optically trapped bead carries a single kinesin molecule that walks along an immobilized microtubule filament. (Right) Displacement versus time graph for a bead, which shows that the kinesin molecule executes a walk, pulling the bead forward in a stepwise manner. Sources: reference [39].

Since these pioneering studies, major advances have been achieved in the precision of optical trapping experiments, which have enabled studies of an increasingly wide range of molecular machines. A landmark was the resolution of one-base-pair steps along DNA by the motor RNA polymerase, which copies DNA into mRNA in the process of transcription [30]. This corresponds to a step size of 3.4 Å, or about 20 times shorter than that of kinesin mentioned above. The process of translation, where ribosome machines synthesise proteins based on mRNA transcripts, has also been studied by optical tweezers experiments, in which the codon-by-codon translation of a single mRNA molecule by a single ribosome could be followed [42]. Optical tweezers-based experiments have also provided insight into how proteases use mechanical force to unfold substrate proteins during targeted protein degradation [43, 44]. These examples illustrate the use of optical trapping techniques to gain unique insight into the mechanics of fundamental biomolecular processes.



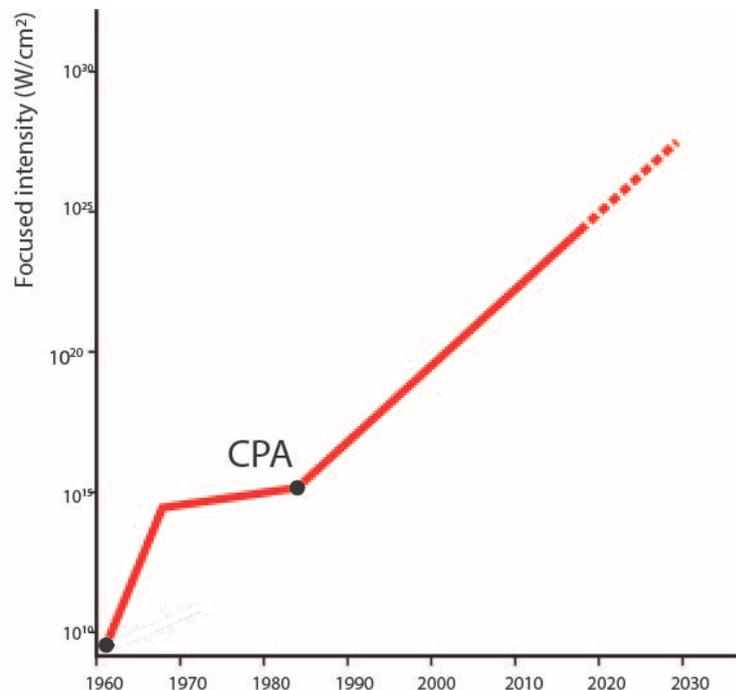
## Concluding remarks for optical tweezers

The emergence of physical techniques to probe individual molecules, such as single-molecule fluorescence, single-molecule fluorescence resonance energy transfer, atomic force microscopy, magnetic tweezers and optical tweezers, has opened up a new window through which we can view the molecular foundations of biology. Ashkin's idea of using radiation pressure to trap and manipulate particles, his invention of the optical tweezers and his pioneering applications of this method to biological systems were central to this development. His groundbreaking invention was before its time: its potential would be explored with subsequent improvements to the supporting technologies for optical tweezers, as well as the development of a surrounding array of methods that might be used in tandem with them.

## Generation of high-intensity, ultra-short optical pulses

As described in the introduction, the development of optical pulses of short duration was not followed by a large increase in peak power or energy per pulse. Although the pulses became shorter, owing in particular to several innovative developments of mode-locked lasers [13-17], the number of photons in each pulse increased only marginally between 1970 and 1985 (see Figure 3). Nanojoule pulses from a mode-locked oscillator could be amplified to the millijoule level, a six-order-of-magnitude increase. Larger amplification was hindered by damage to the amplifier material and optical components of the laser.

Circumventing this problem required increasing the beam diameter, thus decreasing the intensity experienced by the amplifier medium and preventing damage. This resulted in huge and costly laser installations that could only be realised by national research institutes. Moreover, these large lasers operated at low repetition rates, as little as a few shots per day, in order to give the amplifiers sufficient time to cool between shots.



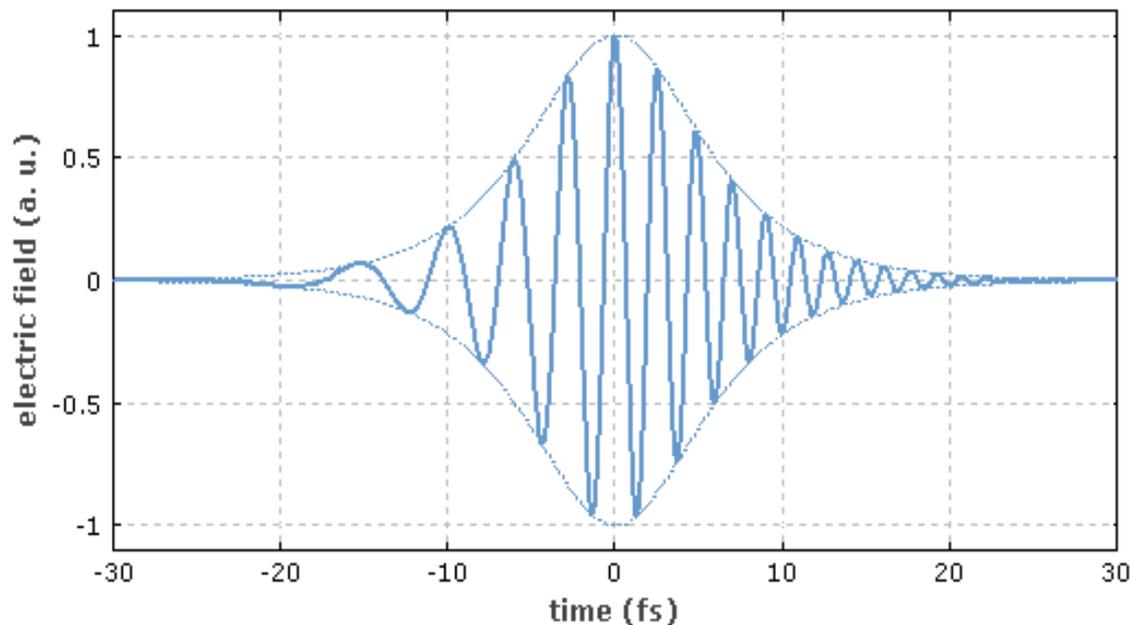
**Figure 3.** The history of pulsed laser technology in terms of peak intensity. After an initial increase in intensity during the 1960s, as described in the text, only an incremental increase occurred during more than a decade. The invention of the CPA technique for optical pulses by Strickland and Mourou in 1985 [45] dramatically changed the situation. The values on the y-axis are indicative because the intensity depends on how sharply the laser beam is focused.

The breakthrough came in 1985, when Donna Strickland and Gérard Mourou invented the chirped pulse amplification (CPA) technique for optical pulses [45]. The inspiration came from radar technology, just as Townes had benefitted from his experience in radar systems when inventing the maser, as well as in research related to optical communication [46, 47].

The CPA technique proceeds in three steps: 1) an ultra-short laser pulse is stretched in time by several orders of magnitude, so that its peak power is correspondingly reduced, 2) it is amplified in a laser material without damaging it, 3) it is compressed in time back to its original duration, resulting in very high peak power. In the original implementation of Strickland and Mourou [45],

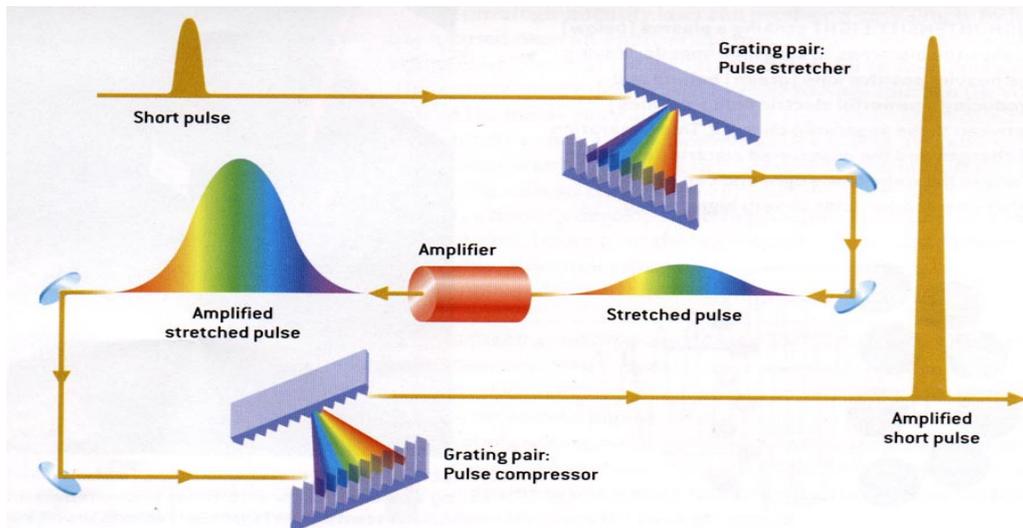
in the first step, a short, low-energy, nanojoule pulse from a mode-locked Nd:YAG laser was coupled into a single-mode optical fibre and stretched to a duration of about 300 ps. The pulse was linearly chirped (see Figure 4) in the fibre by group velocity dispersion and self-phase modulation (a nonlinear optical effect inducing a varying refractive index) [48]. The dispersion in the fibre was positive, so that the low-frequency (red) part of the pulse propagated faster than the high-frequency (blue) part. In the second step (see Figure 5), Strickland and Mourou then amplified the chirped pulse in a Nd:glass regenerative amplifier. In the final step, the long chirped pulse was compressed by a double grating compressor [49] to 2 ps; the energy of the amplified pulse was 1 mJ.

The CPA concept and further progress beyond the original demonstration were presented at the *Conference on Lasers and Electro-Optics* in San Francisco, June 9-13, 1986 [50] and at the *Fifth OSA Topical Meeting, Snowmass, Colorado*, June 16-19, 1986 [51]. Shortly after the breakthrough paper [45], CPA-based lasers with peak powers exceeding 1 TW were constructed [50–53].



**Figure 4.** Chirped optical pulse, with the electric field plotted against time. The chirp of the pulse is the time dependence of its instantaneous frequency. The pulse is up-chirped, which means that the frequency increases with time. (Reproduced from <http://rp-photonics.com/chirp.html>.)

The first improvement of the CPA-technique occurred very soon after the breakthrough paper, when the fibre used to stretch the pulse was replaced by a pair of diffraction gratings [54-56]. Amplification of pulses from nanojoule to joule level was demonstrated [53], i.e. a nine-orders-of-magnitude increase in energy per pulse. A standard CPA configuration is shown in Figure 5. The invention of the CPA technique enabled a giant leap in the intensity of optical pulses; see Figure 3.



**Figure 5.** The standard CPA configuration. The chirp is illustrated with colours. Initially the gain medium (amplifier) was Nd:glass, whereas today, another common gain medium is Ti:sapphire. (Reproduced from Center for Ultrafast Optical Science, University of Michigan in Ann Arbor.)

Several new areas of research and practical applications followed the invention of CPA. CPA technology and important offspring, such as the Optical Parametric CPA [57], were used in the push for higher intensities (see Figure 3). Soon after the invention of CPA [45], the acronym  $T^3$  emerged, to describe a tabletop terawatt laser. Typical parameters for the first Nd:glass systems were 1 J/pulse and a pulse duration of about 1 ps. Shorter pulses, below 100 fs, were obtained using Ti:sapphire [58]. Soon the vision of a petawatt laser system emerged [52], which took a decade to be realised at the Lawrence Livermore National Laboratory in 1999 [59].

Figure 3 (displaying *focused* intensity) shows that peak power or intensity have continued to grow at a rapid pace over many years. The development is also strikingly illustrated by two reviews separated by nearly two decades [60, 61]. While the first review was written at about the time the first petawatt laser was constructed [59], the latter review described no fewer than 50 petawatt-class lasers worldwide, either currently operational, under construction or in the planning phase [61].

One petawatt is no longer an upper limit. Many projects now aim for higher power and intensity and are in various stages of development. For example, the Extreme Light Infrastructure (ELI) Beamlines facility in Prague, Czech Republic, will include a 10-PW laser system. Focused intensity levels exceeding  $10^{23}$  W/cm<sup>2</sup> are anticipated, opening new fields of research. High-field physics could open windows to new extreme states of matter such as radiation-dominated ones, high-pressure quantum ones, warm dense matter (WDM) and ultra-relativistic plasmas. High-energy-density physics (HEDP) is of fundamental importance for research in the field of laboratory astrophysics and inertial confinement fusion.

A second aspect of equal importance to the frontier of high-intensity physics was that CPA technology led to laser systems with high peak power due to short pulse duration, but modest pulse energy, thus enabling high repetition rates. Affordable tabletop lasers ( $T^3$ ) that fit university groups' budgets could deliver pulses at a rate of 10 Hz with peak power equal to that of the few shots per day delivered by the very large and expensive lasers used in inertial confinement experiments for nuclear fusion. These tabletop systems opened new research areas such as strong-field physics, attosecond science, and laser-plasma acceleration, described below.

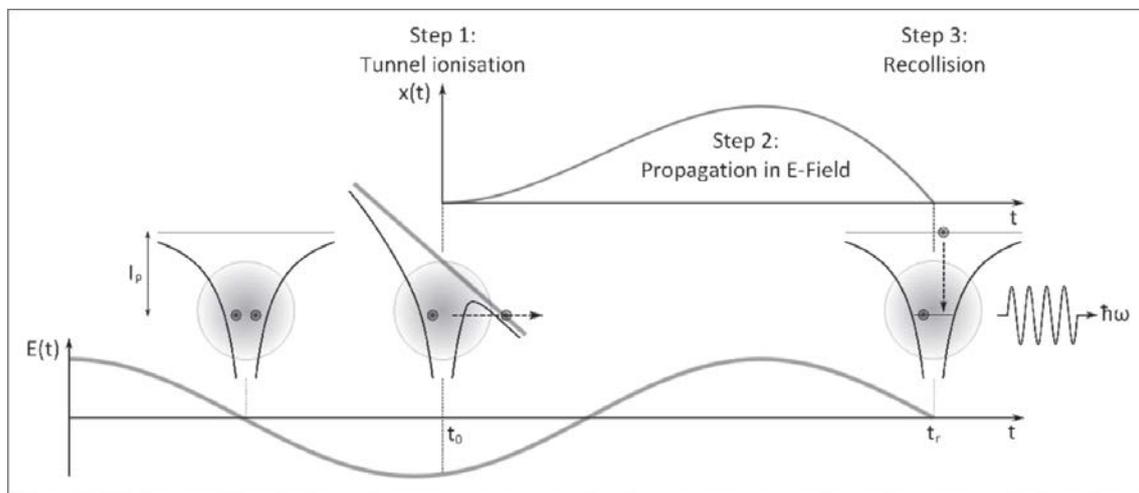
## Applications

A third and very practical aspect of CPA technology was the fact that it became possible to construct compact and user-friendly, high-power, ultra-short laser systems suitable for industrial and medical applications, in addition to basic physics research. The CPA technology opened up a wide range of research areas due to the widespread availability of high-power, ultra-short pulse lasers with high repetition rates.

### *Strong-field physics and attosecond science*

Atoms and molecules exposed to low-intensity light do not change their properties as a consequence of the interaction. If the light is tuned to be in resonance with a transition, an excitation can occur, and if the photon energy is sufficiently high, an electron may be liberated in the process of ionization. An interesting regime occurs when the light field strength becomes comparable to that needed to bind electrons in atoms or molecules. This is called the strong-field regime of atomic physics [62-70].

Several interesting physical phenomena follow the ionization process in a strong laser field. The atom can be ionized by absorbing many more photons than required, leading to the ejection of electrons with very high kinetic energy, a process called above-threshold ionization (ATI) [69, 70]. High Harmonic Generation (HHG) of the laser light [66, 67] was initially discovered without CPA technology, but the widespread exploration of strong-field physics that followed was a direct consequence of CPA. Detailed experimental studies of HHG using CPA-based femtosecond lasers led to the elaboration of an intuitive semi-classical interpretation of the physics in strong laser fields [70-72], presented in Figure 6.



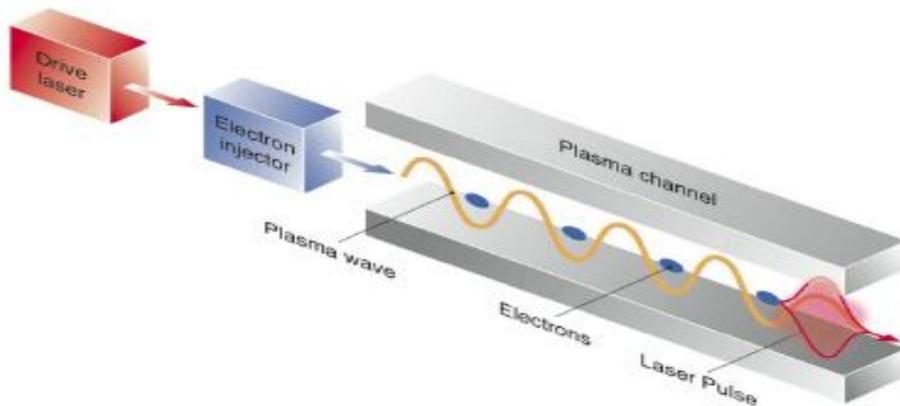
**Figure 6.** Illustration of the three-step recollision model of HHG. In the first step, the laser field causes tunnelling ionization; in the second step, the laser field first accelerates the electron. When the field reverses in the next half-cycle, the free electron may return back to the ion and recombine. In this third step, an extreme ultraviolet photon is emitted. (Reproduced from J.P. Marangos and M. Oppermann, *Attosecond generation and high field physics*, in *Ultrafast Non-Linear Optics* (Scottish Graduate Series), R. Thomson, ed., Springer, New York, p. 45 (2013).)

However beautiful, the femtosecond laser technology developed during the 1960s, 1970s and 1980s was unable to break the 1-fs-pulse-duration limit. Shortly after the first experimental realisations of high harmonics, it was suggested that, in analogy with mode locking, high-order harmonics could lead to pulses shorter than 1 fs [73]. A decade later, after building on many improvements and insights into HHG by means of CPA-based lasers, the first attosecond pulses were experimentally observed [74, 75]. This was the birth of a new research field – attosecond science. For the first time, the electron dynamics inside atoms, molecules and matter in the condensed phase could be probed [76].

### *Laser-plasma acceleration*

Accelerator technology is still totally dominated by radiofrequency (RF) accelerators operating in a frequency range from 100 MHz up to several gigahertz. This technology is mature, robust and serves the operating requirements for many accelerators. However, it has some disadvantages. If the goal is construction of an accelerator at the high-energy frontier, the limited acceleration gradient requires the accelerator to be very large and hence very expensive. When high-energy particles (most often protons) are needed for radiation therapy of tumours, for example, a heavy and bulky RF accelerator is difficult to fit into a hospital environment.

Researchers suggested in 1979 that an intense laser could generate a plasma wave (the wakefield) that could accelerate electrons to 1 GeV over a distance of 1 cm [77]. The key to this very high acceleration gradient is having a high-power laser. Figure 7 illustrates the principle for laser-plasma acceleration.



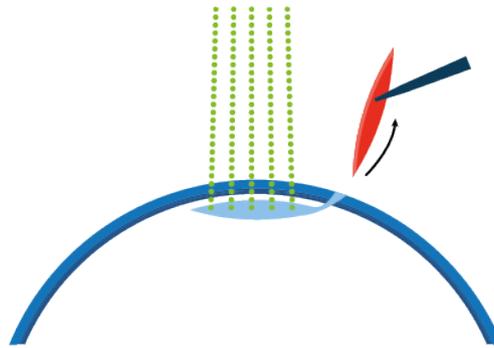
**Figure 7.** Schematic illustration of laser-plasma acceleration. An intense laser pulse drives a plasma wave (wake) in a plasma channel, which also guides the laser pulse and prevents diffraction. Plasma background electrons injected with the proper phase can be accelerated and focused by the wake. (Reproduced from W.P. Leemans (2010), White Paper of the ICFA-ICUIL Joint Task Force – High Power Laser Technology for Accelerators, [http://icfa-bd.kek.jp/WhitePaper\\_final.pdf](http://icfa-bd.kek.jp/WhitePaper_final.pdf).)

At Lawrence Berkeley National Laboratory in California, a petawatt-class laser at the Berkeley Lab Laser Accelerator (BELLA) facility is used to accelerate electrons to 4.2 GeV over a distance of 9 cm [78]. This is an acceleration gradient of at least two orders of magnitude higher than what can be obtained with RF technology. That there are many remaining challenges before laser accelerators can be used for medical applications is well understood [79].

### *High-intensity lasers in industry and medicine*

High-intensity, ultra-short laser pulses are very powerful when high precision is needed because of the minimal thermal energy deposition in materials, resulting in negligible collateral damage beyond the desired interaction volume. The CPA technology has made it possible to build compact and user-friendly laser systems suitable for industrial and medical applications. The intensity level can be adjusted to be optimal for different applications: for example, lower levels for heat treating and higher for material removal. High-aspect-ratio holes that are required for stents can be drilled with femtosecond lasers.

In recent years, femtosecond lasers have become available for clinical use in refractive surgical procedures to treat myopia and astigmatism worldwide. In LASIK (laser-assisted in situ keratomileusis; see Figure 8), a femtosecond laser offers high precision for making the corneal flap, which is required for the excimer laser to have access to and reshape the corneal stroma. With the introduction of an all-in-one femtosecond laser procedure [80], which does not require the creation of a flap, a very small incision of about 4 mm or less is created in order to remove the photo-ablated refractive lenticule. Removing the lenticule changes the shape of the cornea, so that the desired refractive correction is obtained. Typical femtosecond pulse energies are 120 nJ [81].



**Figure 8.** Schematic illustration of an all-in-one femtosecond laser refractive surgical procedure. The green dotted lines represent the beams from a CPA-based femtosecond laser operating at fairly low pulse energies of 120 nJ/pulse, but at a high repetition rate of more than 100 kHz. The laser beam is continuously moved in circles with decreasing radii, as in a spiral moving inwards. The femtosecond laser creates a small lens-shaped bit of tissue to be removed, a lenticule, within the cornea. The laser is also used to create a small incision in the cornea through which the lenticule is mechanically removed. The laser is focused to a few micrometres, so that the laser ablation process creating the lenticule can be positioned with high precision. The lenticule is typically 6 mm in diameter and 100  $\mu\text{m}$  in thickness in the centre. By removing the lenticule, the focal length is prolonged, so that focus is moved to the retina and myopia corrected.

### **Concluding remarks for generation of high-intensity, ultra-short optical pulses**

The invention by Mourou and Strickland of the CPA technique has opened many avenues for researchers both in basic and applied science, resulting in beneficial applications. Expanding the frontiers of CPA is an ongoing endeavour.



## References

- [1] A.L. Schawlow and C.H. Townes, *Infrared and optical masers*, Phys. Rev. **112**, 1940 (1958)
- [2] T.H. Maiman, *Stimulated optical radiation in ruby*, Nature **187**, 493 (1960)
- [3] A.L. Schawlow, *Optical masers*, Scientific American **204** (6), 52 (1961)
- [4] F.J. McClung and R.W. Hellwarth, *Giant optical pulsations from ruby*, J. Appl. Phys. **33**, 828 (1962)
- [5] L.E. Hargrove, R.L. Fork and M.A. Pollack, *Locking of He-Ne laser modes induced by synchronous intracavity modulation*, Appl. Phys. Lett. **5**, 4 (1964)
- [6] M. DiDomenico Jr., *Small-signal analysis of internal (coupling-type) modulation of lasers*, J. Appl. Phys. **35**, 2870 (1964)
- [7] A. Yariv, *Internal modulation in multimode laser oscillators*, J. Appl. Phys. **36**, 388 (1965)
- [8] H.W. Mocker and R.J. Collins, *Mode competition and self-locking effects in a Q-switched ruby laser*, Appl. Phys. Lett. **7**, 270 (1965)
- [9] A.J. DeMaria, D.A. Stetser and H. Heynau, *Self mode-locking of lasers with saturable absorbers*, Appl. Phys. Lett. **8**, 174 (1966)
- [10] P.P. Sorokin and J.R. Lankard, *Stimulated emission observed from an organic dye, chloro-aluminum phthalocyanine*, IBM J. Res. Dev. **10**, 162 (1966)
- [12] F.P. Schäfer, W. Schmidt and J. Volze, *Organic dye solution laser*, Appl. Phys. Lett. **9**, 306 (1966)
- [13] E.P. Ippen, C.V. Shank and A. Dienes, *Passive mode locking of the the cw dye laser*, Appl. Phys. Lett. **21**, 348 (1972)
- [14] C.V. Shank and E.P. Ippen, *Subpicosecond kilowatt pulses from a mode-locked cw dye laser*, Appl. Phys. Lett. **24**, 373 (1974)
- [15] I.S. Ruddock and D.J. Bradley, *Bandwidth-limited subpicosecond pulse generation in mode-locked cw dye lasers*, Appl. Phys. Lett. **29**, 296 (1976)
- [16] R.L. Fork, B.I. Greene and C.V. Shank, *Generation of optical pulses shorter than 0.1 psec by colliding pulse mode locking*, Appl. Phys. Lett. **38**, 671 (1981)
- [17] W.J. Tomlinson, R.H. Stolen and C.V. Shank, *Compression of optical pulses chirped by self-phase modulation in fibers*, J. Opt. Soc. Am. B **1**, 139 (1984)
- [18] A. Ashkin, *Acceleration and trapping of particles by radiation pressure*, Phys. Rev. Lett. **24**, 156 (1970)
- [19] A. Ashkin and J.M. Dziedzic, *Optical levitation by radiation pressure*, Appl. Phys. Lett. **19**, 283 (1971)
- [20] A. Ashkin, J.M. Dziedzic, J.E. Bjorkholm and S. Chu, *Observation of a single-beam gradient force optical trap for dielectric particles*, Opt. Lett. **11**, 288 (1986)



- [21] A. Ashkin, *Force of a single-beam gradient laser trap on a dielectric sphere in the ray optics regime*, Biophys. J. **61**, 569 (1992)
- [22] A. Ashkin, *Trapping of atoms by resonance radiation pressure*, Phys. Rev. Lett. **40**, 729 (1978)
- [23] S. Chu, J.E. Bjorkholm, A. Ashkin and A. Cable, *Experimental observation of optically trapped atoms*, Phys. Rev. Lett. **57**, 314 (1986)
- [24] A. Ashkin and J.M. Dziedzic, *Optical trapping and manipulation of viruses and bacteria*, Science **235**, 1517 (1987)
- [25] A. Ashkin, J.M. Dziedzic and T. Yamane, *Optical trapping and manipulation of single cells using infrared laser beams*, Nature **330**, 769 (1987)
- [26] A. Ashkin and J.M. Dziedzic, *Internal cell manipulation using infrared laser traps*, Proc. Natl. Acad. Sci. USA **86**, 7914 (1989)
- [27] A. Ashkin, K. Schütze, J.M. Dziedzic, U. Euteneuer and M. Schliwa, *Force generation of organelle transport measured in vivo by an infrared laser trap*, Nature **348**, 346 (1990)
- [28] S.M. Block, D.F. Blair and H.C. Berg, *Compliance of bacterial flagella measured with optical tweezers*, Nature **338**, 514 (1989)
- [29] T.T. Perkins, *Ångström-precision optical traps and applications*, Annu. Rev. Biophys. **43**, 279 (2014)
- [30] E.A. Abbondanzieri, W.J. Greenleaf, J.W. Shaevitz, R. Landick and S.M. Block, *Direct observation of base-pair stepping by RNA polymerase*, Nature **438**, 460 (2005)
- [31] T.T. Perkins, S.R. Quake, D.E. Smith and S. Chu, *Relaxation of a single DNA molecule observed by optical microscopy*, Science **264**, 822 (1994)
- [32] S.B. Smith, Y. Cui and C. Bustamante, *Overstretching B-DNA: the elastic response of individual double-stranded and single-stranded DNA molecules*, Science **271**, 795 (1996)
- [33] M.D. Wang, H. Yin, R. Landick, J. Gelles and S.M. Block, *Stretching DNA with optical tweezers*, Biophys. J. **72**, 1335 (1997)
- [34] S.B. Smith, L. Finzi and C. Bustamante, *Direct mechanical measurements of the elasticity of single DNA molecules by using magnetic beads*, Science **258**, 1122 (1992)
- [35] P. Cluzel, A. Lebrun, C. Heller, R. Lavery, J.L. Viovy, D. Chatenay and F. Caron, *DNA: an extensible molecule*, Science **271**, 792 (1996)
- [36] J. Liphardt, B. Onoa, S.B. Smith, I. Tinoco Jr. and C. Bustamante, *Reversible unfolding of single RNA molecules by mechanical force*, Science **292**, 733 (2001)
- [37] J. Liphardt, S. Dumont, S.B. Smith, I. Tinoco Jr. and C. Bustamante, *Equilibrium information from nonequilibrium measurements in an experimental test of Jarzynski's equality*, Science **296**, 1832 (2002)
- [38] C. Jarzynski, *Nonequilibrium equality for free energy differences*, Phys. Rev. Lett. **78**, 2690 (1997)

- [39] K. Svoboda, C.F. Schmidt, B.J. Schnapp and S.M. Block, *Direct observation of kinesin stepping by optical trapping interferometry*, Nature **365**, 721 (1993)
- [40] J.T. Finer, R.M. Simmons and J.A. Spudich, *Single myosin molecule mechanics: piconewton forces and nanometre steps*, Nature **368**, 113 (1994)
- [41] J.E. Molloy, J.E. Burns, J. Kendrick-Jones, R.T. Tregear and D.C.S. White, *Movement and force produced by a single myosin head*, Nature **378**, 209 (1995)
- [42] J.D. Wen, L. Lancaster, C. Hodges, A.C. Zeri, S.H. Yoshimura, H.F. Noller, C. Bustamante and I. Tinoco Jr, *Following translation by single ribosomes one codon at a time*, Nature **452**, 598 (2008)
- [43] M.E. Aubin-Tam, A.O. Olivares, R.T. Sauer, T.A. Baker and M.J. Lang, *Single-molecule protein unfolding and translocation by an ATP-fueled proteolytic machine*, Cell **145**, 257 (2011)
- [44] R.A. Maillard, G. Chistol, M. Sen, M. Righini, J. Tan, C.M. Kaiser, C. Hodges, A. Martin and C. Bustamante, *ClpX(P) generates mechanical force to unfold and translocate its protein substrates*, Cell **145**, 459 (2011)
- [45] D. Strickland and G. Mourou, *Compression of amplified chirped optical pulses*, Opt. Commun. **56**, 219 (1985)
- [46] J. Desbois, F. Gires and P. Turnois, *A new approach to picosecond laser pulse analysis shaping and coding*, IEEE J. Quant. Electron. QE-**9**, 213 (1973)
- [47] R.L. Fork, O.E. Martinez and J.P. Gordon, *Negative dispersion using pairs of prisms*, Opt. Lett. **9**, 150 (1984)
- [48] B. Nikolaus and D. Grischkowsky, *12x pulse compression using optical fibers*, Appl. Phys. Lett. **42**, 1 (1983)
- [49] E. Treacy, *Optical pulse compression with diffraction gratings*, IEEE J. Quant. Electr. QE-**5**, 454 (1969)
- [50] D. Strickland, P. Maine, M. Bouvier, S. Williamson and G. Mourou, *Picosecond pulse amplification using pulse compression techniques*, in *Conference on Lasers and Electro-Optics*, G. Bjorklund, E. Hinkley, P. Moulton and D. Pinnow, eds., OSA Technical Digest (Optical Society of America, 1986), paper THL1
- [51] D. Strickland, P. Maine, M. Bouvier, S. Williamson and G. Mourou, *Picosecond pulse amplification using pulse compression techniques*, in *Ultrafast phenomena V: Proceedings of the Fifth OSA Topical Meeting, Snowmass, Colorado, June 16-19, 1986*. G.R. Fleming and A.E. Siegman, eds., (Berlin, Heidelberg, New York, Springer Verlag, 1986), p. 38
- [52] P. Maine, D. Strickland, P. Bado, M. Pessot and G. Mourou, *En route vers le Petawatt*, Rev. Phys. Appl. (Paris) **22**, 1657 (1987)
- [53] P. Maine, D. Strickland, P. Bado, M. Pessot and G. Mourou, *Generation of ultrahigh peak power pulses by chirped pulse amplification*, IEEE J. Quantum Electron. QE-**24**, 398 (1988)
- [54] O.E. Martinez, *Grating and prism compressors in the case of finite beam size*, J. Opt. Soc. Am. B **3**, 929 (1986)



- [55] O.E. Martinez, *3000 times grating compressor with positive group velocity dispersion: Application to fiber compensation in the 1.3-1.6  $\mu\text{m}$  region*, IEEE J. Quant. Electron. QE-**23**, 59 (1987)
- [56] M. Pessot, P. Maine and G. Mourou, *1000 times expansion/compression of optical pulses for chirped pulse amplification*, Opt. Commun. **62**, 419 (1987)
- [57] A. Dubietis, G. Jonusauskas and A. Piskarskas, *Powerful femtosecond pulse generation by chirped and stretched pulse parametric amplification in BBO crystal*, Opt. Commun. **88**, 437 (1992)
- [58] P. Moulton, *Ti-doped sapphire: tunable solid-state laser*, Opt. News **8**, 9 (1982)
- [59] M.D. Perry, D. Pennington, B.C. Stuart, G. Tietbohl, J.A. Britten, C. Brown, S. Herman, B. Golick, M. Kartz, J. Miller, H.T. Powell, M. Vergino and V. Yanovsky, *Petawatt laser pulses*, Opt. Lett. **24**, 160 (1999)
- [60] S. Backus, C.G. Durfee III, M.M. Murnane and H.C. Kapteyn, *High power ultrafast lasers*, Rev. Sci. Instrum. **69**, 1207 (1998)
- [61] C. Danson, D. Hiller, N. Hopps and D. Neely, *Petawatt class lasers worldwide*, High Power Laser Science and Engineering, vol. 3, p. 1 (2015)
- [62] L.V. Keldysh, *Ionization in the field of a strong electromagnetic wave*, Sov. Phys. JETP **20**, 1307 (1965)
- [63] F.H.M. Faisal, *Multiple absorption of laser photons by atoms*, J. Phys. B **6**, L89 (1973)
- [64] H.R. Reiss, *Effect of an intense electromagnetic field on a weakly bound system*, Phys. Rev. **22**, 1786 (1980)
- [65] M.V. Ammosov, N.B. Delone and V.P. Krainov, *Tunnel ionization of complex atoms and atomic ions in an alternating electric field*, Sov. Phys. JETP **64**, 1191 (1986)
- [66] M. Ferray, A. L'Huillier, X.F. Li, L.A. Lompre, G. Mainfray and C. Manus, *Multiple-harmonic conversion of 1064 nm radiation in rare gases*, J. Phys. B **21**, L31 (1988)
- [67] X.F. Li, A. L'Huillier, M. Ferray, L.A. Lompré and G. Mainfray, *Multiple-harmonic generation in rare gases at high laser intensity*, Phys. Rev. A **39**, 5751 (1989)
- [68] S. Augst, D. Strickland, D.D. Meyershofer, S.L. Chin and J.H. Eberly, *Tunneling ionization of noble gases in a high-intensity laser field*, Phys. Rev. Lett. **63**, 2212 (1989)
- [69] P. Agostini, F. Fabre, G. Mainfray, G. Petite and N.K. Rahman, *Free-free transitions following six-photon ionization of xenon atoms*, Phys. Rev. Lett. **42**, 1127 (1979)
- [70] K.J. Schafer, B. Yang, L.F. DiMauro and K.C. Kulander, *Above threshold ionization beyond the high harmonic cutoff*, Phys. Rev. Lett. **70**, 1599 (1993)
- [71] K.C. Kulander, K.J. Schafer and J.L. Krause, *Dynamics of short-pulse excitation, ionization and harmonic conversion*, in *Super-Intense Laser-Atom Physics*, NATO ASI Series (Series B: Physics), **316**, 95 (1993)
- [72] P.B. Corkum, *Plasma perspective on strongfield multiphoton ionization*, Phys. Rev. Lett. **71**, 1994 (1993).



- [73] Gy. Farkas and Cs. Tóth, *Proposal for attosecond light pulse generation using laser induced multiple-harmonic conversion processes in rare gases*, Phys. Lett. A **168**, 447 (1992)
- [74] P.M. Paul, E.S. Toma, P. Breger, G. Mullot, F. Augé, Ph. Balcou, H.G. Muller and P. Agostini, *Observation of a train of attosecond pulses from high harmonic generation*, Science **292**, 1689 (2001)
- [75] M. Hentschel, R. Kienberger, C. Spielmann, G.A. Reider, N. Milosevic, T. Brabec, P. Corkum, U. Heinzmann, M. Drescher and F. Krausz, *Attosecond metrology*, Nature **414**, 509 (2001)
- [76] F. Calegari, G. Sansone, S. Stagira, C. Vozzi and M. Nisoli, *Advances in attosecond science*, J. Phys. B **49**, 062001 (2016)
- [77] T. Tajima and J.M. Dawson, *Laser electron accelerator*, Phys. Rev. Lett. **43**, 267 (1979)
- [78] W.P. Leemans, A.J. Gonsalves, H.-S. Mao, K. Nakamura, C. Benedetti, C.B. Schroeder, Cs. Tóth, J. Daniels, D.E. Mittelberger, S.S. Bulanov, J.-L. Vay, C.G.R. Geddes and E. Esarey, *Multi-GeV electron beams from capillary-discharge-guided subpetawatt laser pulses in the self-trapping regime*, Phys. Rev. Lett. **113**, 245002 (2014).
- [79] U. Linz and J. Alonso, *What will it take for laser driven proton accelerators to be applied to tumor therapy?*, Phys. Rev. ST Accel. Beams **10**, 094801 (2007)
- [80] W. Sekundo, K.S. Kunert and M Blum, *Small incision corneal refractive surgery using the small incision lenticule extraction (SMILE) procedure for the correction of myopia and myopic astigmatism: results of 6 month prospective study*, Br. J. Ophthalmol. **95**, 335 (2011)
- [81] F. Lin, Y. Xu and Y. Yang, *Comparison of the visual results after SMILE and femtosecond laser-assisted LASIK for myopia*, J. Refract. Surg. **30**, 248 (2014)