### **Tools Made of Light-The Physics Nobel Prize 2018**

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#### Abstract

The Nobel Prize winners have successfully used those properties of lasers that have seldom been used previously. *Arthur Ashkin* used the property that light can exert pressure. The pressure exerted is proportional to the intensity of light. Therefore lasers with its high intensity could exert the pressure on tiny objects. *Gérard Mourou* and *Donna Strickland* used the property, that lasers are not strictly monochromatic. The spectral profile of the laser does have a fairly large bandwidth that can be manipulated. *Arthur Ashkin* realized that a laser would be the perfect tool for getting beams of light to move small particles. *Gérard Mourou* and *Donna Strickland* paved the way towards the shortest and most intense laser pulses created till date. The Royal Swedish Academy has honored the three physicists for their "ground breaking inventions in the field of laser physics". *Arthur Ashkin* [1] has been honored for his invention of optical tweezers, that trap and manipulate particles and living cells. *Gérard Mourou* and *Donna Strickland* together [2] have been honored for developing "chirped pulse amplification" (CPA) in which a laser pulse is stretched amplified and then compressed to increase its power.

# Keywords: Lasers, Ultra short Pulse, Chirped pulse, Stretcher/Compressor, Peak power, Optical tweezers, Light pressure, Spectral bandwith.

#### Introduction

he inventions being honored, is in the realm of laser physics. Since the invention of the laser in **1958**, the Nobel Prizes that have been awarded, for the work on lasers or for the work with lasers, is quite extensive. However, the full potential of lasers has not yet been realized. The **2018** Physics Nobel Prize is shared by three physicists (Arthur Ashkin, Gérard Mourou and Donna Strickland), who have proved beyond doubt that the laser is a fantastic tool made of light.

Lasers are presently being used routinely in scientific, military, medical and commercial applications. Some of the applications are laser cutting, welding and drilling. Lasers are used for photo-lithography, range finders, barcode readers, pointers and holography. In the entertainment industry lasers are used for lighting displays and other visual effects. In the medical field lasers are used for removing scar, tattoos and hair. The laser is used as a scalpel for soft tissue surgery. It is used

for the correction of myopia, and the removal of tumors. It is used in cancer treatment and in dentistry too. In scientific research, lasers are used as a spectroscopic tool, which is a must in all laboratories. Lasers are routinely being used for Raman spectroscopy, atmospheric remote sensing, holography, LIDAR ('light' and 'radar') applications, photochemistry and biochemistry. The high brightness, high intensity, high mono-chromaticity, and very low beam divergence and coherence are all properties which allow for these specialized applications. Lasers have penetrated every aspect of our lives. In fact we have forgotten that "laser" is not a word but an acronym (Light Amplification by Stimulated Emission of Radiation – LASER).

In the following paragraphs a flavor of the CPA technology will be presented. This technique has been researched and developed at BARC.

# Ultra short pulse and dispersion management

The idea of chirped pulse amplification (CPA) was proposed

many years earlier for a different problem altogether. It was used to solve the problem in radar systems. The main issue in designing a good radar system is the capability of the system to resolve, two tiny objects, at a long range with a very small separation between them. The technique of pulse compression is used for efficient radar transmission. By transmitting a wide pulse in which the carrier frequency is modulated and then by passing the received signal through a matched filter to accumulate the energy into a short pulse, a time compression is brought about. However transferring the idea from longer radio waves to shorter optical waves was not a trivial task. It was difficult in theory and in practice. The CPA technique enabled the emission of very intense ultra short pulses of light, using an elegant method, to avoid the risk of destroying the amplifying material. Gérard Mourou and Donna Strickland got the breakthrough, when a stretcher and a matched compressor were put together to obtain a very short and intense



Fig.1. The output optical signal, schematic, from a mode-locked laser oscillator. Electric field amplitude (E(v)) is a function of frequency v. E(t)is its fourier transform as a function of time t.  $\delta v$  is the mode spacing and  $\Delta v$ is the emission bandwidth, that is the full width at half maximum of the spectrum (top graph).

amplified pulse of light. Some of the issues that need to be understood are the phenomenon that govern the generation of an ultra-short optical pulse (of the order of pico-second and femto-second) and why these short pulses cannot be amplified directly and which processes prevent the direct optical amplification.

By the uncertainty principle, an ultra short pulse in the time domain must have a correspondingly broad spectrum in the spectral domain. It is therefore necessary to establish that the gain medium has a sufficiently broad bandwidth to amplify the short pulse, and other components (like mirrors, windows, lenses, modulators, etc) also are sufficiently broad band in their reflection or transmission responses, to transmit the pulses without filtering the pulse spectrum. Ultra short pulses are generated by the technique of modelocking and in general the radiation in a laser oscillator cavity resonates in discrete longitudinal modes. More than one longitudinal mode can extract energy from the oscillator

active (gain) medium. The finite number of oscillating laser modes are separated in frequency by  $\delta v = c/2L$ , where L is the oscillator cavity length and 'c' is the speed of light. The goal of mode locking is to ensure that the oscillating laser modes are locked in phase. Under these conditions the temporal output (Fig.1) will be a train of pulses separated by the cavity round trip time T. The duration of the pulse  $t_{p}$ , is related to the width ( $\Delta v$ ) of the laser emission, expressed as k. The factor k depends on the  $\Delta v t_n$ pulse shape. For Gaussian pulses k=0.441 and for hyperbolic secant pulses k=0.315. In order to generate ultra short pulses in the time domain, it is necessary to obtain mode-locked laser output with a broad spectral width in the frequency (or wavelength) domain. Therefore the shortest optical pulses are obtained from gain media with broad spectral ( $\nu = c/\lambda$  and  $\Delta \nu = (c/\lambda^2)\Delta\lambda$ ) gain profiles. Ti:Sapphire is a popular active media or gain media that is used in optical oscillators. The emission line width of such a medium is in the range of 170nm ( $\Delta\lambda$ ). Even Nd:glass is a frequently used medium for the generation of femto-second range mode locked pulses, though the emission line width is much smaller  $(\Delta\lambda=35nm).$ 

With mode-locking one may generate pico-second range pulses, but to generate pulses shorter than a picoseconds (femto-second range), the spectral profile of the pulse circulating in the oscillator cavity has to be adjusted or managed properly. Progress in ultra fast optics has relied extensively on the development of ways to characterize and manipulate dispersion. Dispersion is a phenomenon where the phase velocity of a wave depends on its frequency (or wavelength). Phase velocity ('v') in a uniform medium is written as v=c/n where 'c' is the speed

of light and 'n' is the refractive index of the material. For visible light, the refractive index, 'n', of most transparent materials decrease with increasing wavelength. That means  $1 < n(\lambda_{red}) < n(\lambda_{yellow}) < n(\lambda_{blue})$  or alternatively it means that  $dn/d\lambda < 0$ . Here the medium is said to have normal dispersion. If the refractive index increases with increasing wavelength (for example in the ultraviolet wavelengths) the medium is said to have anomalous dispersion. Another quantity that is required in the subject of dispersion is the group velocity. Group velocity of the wave is the rate at which, changes in the amplitude (the envelope of the wave) will propagate. The group velocity vg is expressed as  $v_{a}=v/[1-(\lambda/n)(dn/d\lambda)]$ . As can be seen, the group velocity is a function of the wave frequency or wavelength. This results in group velocity dispersion (GVD) which causes a short pulse of light to spread in time as a result of different frequency components of the pulse travelling at different velocities in a medium. Thus the consequence of dispersion manifests itself as a temporal effect. This phenomenon that causes different wavelengths in a wave packet to travel at different speeds/velocities, broadens the ultra short pulse temporally as it circulates in the cavity. The spectral width of the pulse is inversely proportional to the minimum temporal duration and so as pulses become shorter, they become more susceptible to GVD. Clearly excessive GVD will prevent the generation of short pulses and so it should be minimized.

Now in a laser oscillator cavity there is one more phenomenon taking place. Suppose that a laser is mode locked and each pulse in the train of pulses is about 1ps. The intra cavity pulse energy would be about  $10nJ-1\mu J$ , then the peak powers reach the range of





Fig.2. Schematic of the CPA concept. The oscillator produces a short pulse, which is then passed through an optical fiber where the pulse is stretched (1st communication by D. Strickland & G. Mourou) from femto-seconds to nearly a nano-second. The intensity is low enough to be amplified in an amplifier. Energy is extracted from the amplifier without pulse distortions or amplifier material damage. After energy extraction the pulse is compressed to nearly its original temporal width.

10KW to 1MW. Most cavity radiation is generally focused to about 100µm, making the intensity inside the cavity reach level of 10<sup>8</sup>-10<sup>10</sup> W/cm<sup>2</sup>. At these intensities the refractive index of the intra-cavity medium can become non-linear due to optical Kerr effect, and this gives rise to self phase modulation (SPM). SPM causes the pulse spectrum to broaden, which can increase the loss at any spectral filter in the laser oscillator cavity if it is not broad band enough. The added spectrum or frequency chirp, should make the circulating pulse shorter, but a shorter pulse is more prone to GVD and therefore detrimental to the generation of a short temporal pulse. The interaction of SPM and GVD may be exploited in such a way so as to obtain shorter pulses. The final duration of the pulse is determined by the interaction of SPM and GVD. This is usually achieved by including dispersive elements in the laser cavity which provide adjustable GVD of the opposite sign to the laser medium and other components. The prism is such a dispersive element. Brewster angled prism pair is inserted inside the oscillator cavity, to provide adjustable intra cavity GVD. Specially designed dielectric mirrors are also used. Using prism pairs or optically designed dielectric mirrors (chirped mirrors) to control the net cavity GVD, brings about the generation of ultra short pulse. Once mode locking has been achieved, to obtain the ultimate bandwidth limited pulse duration, the GVD on each cavity roundtrip should be close to zero.

# Chirped Pulse Amplification and dispersion control

Progress in ultrafast optics is dependent on the development of ways to characterize, measure, manipulate and manage dispersion and nonlinear interactions in the gain medium and other optical components. The means by which this can be accomplished in a laser oscillator is different from that in a laser amplifier. It is necessary to take into account the group velocity dispersion of the laser pulse as it traverses the amplification system. It is also imperative to measure and control the nonlinear optical effects that are bound to surface during this amplification process. Femto-second

laser pulses have very high peak powers and associated high electric fields and the peak power increases, even as the pulse amplifies and extracts a modest energy from the gain medium. This induces beam distortion and optical damage in the gain medium and the other optical components through which the beam propagates. Self focusing and SPM are responsible for these damages. For efficient extraction of energy from amplifiers, pulses should have fluences (pulse energy per unit area) close to the characteristic saturation fluence of the laser amplifier material, a requirement easily met by nanosecond pulse amplifiers, without the risk of inducing optical damage. Operation at those same fluences, with pulse duration in the femtosecond range, is not possible without inducing self focusing and self phase modulation, leading ultimately to severe damage to the material or the gain medium. One method of overcoming such beam intensity limitations of ultra short pulse amplification, is to increase the amplifier medium cross-section or aperture to accommodate a beam size,



Fig.3. The schematic of the basic structure of a stretcher and compressor based on gratings. G<sub>1</sub>, G<sub>2</sub> G<sub>3</sub> & G<sub>4</sub> are gratings with equal number of grooves or lines per mm. (a) The stretcher is a double pass stretcher. At the end of one pass through the stretcher the beam is collimated but spatially chirped (indicated by the elliptical beam on the mirror). At the end of the second pass through the stretcher the beam ideally becomes a circular cross sectioned beam with no spatial chirp, but chirped and stretched in time. (b) The input to the compressor is a stretched pulse. At the end of one pass through the compressor one gets a spatially chirped beam (elliptical beam on the mirror). After the second pass through the compressor the beam is ideally circular in cross-section, with no spatial chirp and compressed to an ultra short pulse.

that has been increased to proportionately reduced intensity. The required apertures would be impractically large and the laser system would be very inefficient. These are the limitations of direct amplification of ultra short pulses. In order to overcome this Donna Strickland and Gérard Mourou devised CPA, so that the short pulse can be manipulated in a controllable and reversible fashion. The amplifier medium never encounters a high peak power, high intensity short pulse. Therefore by stretching, amplifying and recompressing the ultra short pulse to nearly its original pulse duration, it is possible to circumvent the damage limitation of amplifiers and scale the ultra short pulse to very high peak powers.

The first CPA system used the positive GVD of a single mode fiber to

temporally spread the wavelength components of the ultra-short pulse. Donna Strickland and Gérard Mourou used a CW mode-locked, Nd:YAG oscillator [2] to generate 150ps pulses with 1.06µm as the centre wavelength of the spectrum. This was coupled into a 1.4km single mode fiber and the pulse that emerged was stretched to about 300ps. In the single mode fiber the red side of the infra-red wavelengths of the pulse travels faster than the blue side, resulting in positive GVD and therefore temporal stretching. It was then amplified in a Nd:glass regenerative amplifier before recompression in a pair of parallel diffraction gratings. A grating pair exhibits negative GVD [3] where the blue side of the spectrum travels faster than the red side. There was a problem in this kind of an

arrangement. The fiber stretcher and diffraction grating compressor did not have their dispersive characteristics exactly complementary to each other. In other words the dispersive characteristics or the GVD did not match, giving rise to temporal sidelobes to the main pulse. The compressed pulse had a central high peak, which was accompanied with wings (or pedestal) on either side. The parameter that quantifies such a pulse, is the contrast ratio. Temporal contrast is defined as the ratio of the intensity of the main pulse to the intensity of the pedestal or sub-peak pulse. In high intensity laser plasma physics experiments, poor temporal contrast ratio caused by pre-pluses (or background pedestal or side lobes) can change the properties of target before the arrival of the main laser pulse.

It wasn't long, before a pulse stretcher, constructed with the help of a telescope of magnification one, placed between two anti-parallel configured gratings [4] was devised to obtain positive GVD. In place of the optical fiber stretcher a grating based stretcher was employed. This dispersive device had the exact same function as the parallel pair of grating compressor but with opposite sign. This was the compressor's exact conjugate. This means that, in theory a short pulse can be stretched to any pulse duration, and then recompressed to its exact original shape, without wings or pedestals. It was demonstrated that a stretching factor of 10<sup>3</sup>-10<sup>4</sup> was achievable. Amplification in Nd:glass amplifiers and then compression led to the Table Top Terawatt (T<sup>3</sup>) system or a high peak power system that fits into a small laboratory. In general for CPA systems, grating based stretcher/ compressor design is used. The antiparallel grating configuration as

shown in **Fig.3** (a) can generate even negative GVD, depending on the placement of the gratings. If grating  $G_2$  is in the position shown in **Fig.3(a)** then the stretcher shows a GVD>0. If  $G_2$  is placed at the position marked with a 'yellow grating', then the GVD= 0. If  $G_2$  is placed at a position beyond the 'yellow grating' marker, then the GVD<0. An indigenously developed Nd:glass based CPA system at B.A.R.C [5][6] uses the pair of grating based stretcher/ compressordesign.

Many designs of the stretcher evolved over the years. The stretcher operates by introducing time delay for different spectral components of the ultra-short pulse. Therefore the output of the stretcher is a long chirped optical pulse. The dispersive element used could be either ruled gratings, holographic gratings, reflective or transmission type of gratings. For example in case of a Nd:glass based CPA system one can use holographic gratings with 1200 lines /mm. The unit magnification telescope in the stretcher [7] requires achromatic lenses. With this it is possible to stretch a 200fs optical pulse to 600ps and beyond. Some of the designs use all reflective optics [8] to provide high quality imaging at unity spatial and angular magnification. The stretchers need to have high spectral bandwidth and high fidelity. Retaining the entire band width is important because then the compressed pulse can be reduced temporally to the minimum possible. The performance of the stretcher is affected by the finite beam size, divergence, lateral walk-off of different spectral components and the aperture of the telescope. A well designed stretcher optimizes all these aspects of the beam along with the extent to which a temporal pulse can be stretched. The stretcher and the compressor design are generally in

the double pass mode. That means that the pulse encounters the gratings twice as schematically shown in **Fig.3**. This is because at the end of one pass the beam is spatially chirped. Only after the second pass, the spatial chirp becomes null. In this process of double passing, the temporal stretch (or compression) increases too.

The next step in the CPA system is the amplification. In the amplification process the regenerative amplifier is the first step in which a nano-Joule level energy pulse is amplified to an energy level of about a milli-Joule. After this the stretched pulse extracts energy from linear amplifiers, until the desired energy is reached. It is during this process that spectral narrowing occurs, the phenomenon that prevents the recompression, to revert the stretched pulse to its original temporal profile. The amplification in the gain media and also other optical components in the amplification system introduces, both amplitude and phase distortions, preventing the optimal recompression of the laser pulse. The compression grating pair, as a thumb rule, needs to have the same number of grooves as the stretcher gratings. Therefore, if gratings with 1200 lines/mm was used in the stretcher then the compressor gratings too should have 1200 lines/mm. The compression gratings have to be very large, because by this stage a very high energy level has been reached and peak power is also very high. This could damage the gratings if the beam does not have a large cross-section. Diffraction gratings are presently available with apertures of the order of one meter<sup>2</sup>, allowing direct recompression to one Peta-Watt peak power or more. Stretching and recompression over many orders of magnitude in pulse duration, is a process that requires high accuracies in the design and

manufacturing of the optical components and in construction of the compressor. Many designs of the compressor have been tried out and suggested [9], mainly to obtain high peak powers in the final pulse and also to obtain high temporal contrast. In all CPA systems the non negligible higher order phase terms associated with the material dispersion in the components of the laser system limits the fidelity of recompression. The compressor design could compensate these phase terms to obtain a near clean temporal pulse.

# High Peak Power Lasers and their applications.

Over the last three decades CPA has become the technique of choice for producing high peak power, ultra short pulses. High peak power lasers that fit into a small laboratory, can now reach focused intensities of the order of 10<sup>19</sup> W/cm<sup>2</sup>. Such lasers are widely being used in many types of laser plasma interaction experiments. Many of the "laser-matterinteraction" experiments depend on the high focused intensity, short pulse duration and a good pulse contrast ratio. For many experiments the required interactions of the main pulse with the target is strongly perturbed if there is a pre-pulse intensity on target. Therefore as the main pulse intensities are increased with improving system design so must the contrast ratio.

At modest intensity levels, pumpprobe experiments for chemistry, biology and material science, has opened up the door for ultrafast processes, not known before. Many applications have been motivated primarily because ultrafast laser pulses can interact with materials very differently from long pulses, enabling high precision removal of very small amount of material without melting, a property very useful in material

amplifier active medium could reach



Fig.4. Laser intensity versus year with various physical thresholds. The achievable laser intensity shows a plateau for about 20 years due to limitations caused by nonlinear effects. The development of the laser systems over the years shows a turning point at 1985 with the discovery of the CPA.

processing. In fact when a material is cut or drilled with long pulsed lasers, the surrounding material shows the effect of heat transfer, microcracking, aftermath of a shock wave and zones of irregular material. While in case of an ultra-short pulsed laser, the material that is processed, gets a clean smooth finish, because none of the effects described, happens. There is only dense plasma in the vicinity of the laser impinging on the material leading to the smooth finish of the material. High precision material removal is very interesting in medical applications, where minimal damage to surrounding tissue is the need for most surgical procedures. Citing its mission to recognize inventions that benefit humankind, the Royal Swedish Academy has highlighted how Gérard Mourou and Donna

Strickland's work made possible production of surgical stents and the use of lasers (LASIK- Laser Assisted in-Situ Keratomileusis) to correct vision.

It is interesting to see the evolution of laser peak powers over the years. First the lasers were free running with the pulse durations in the few microsecond (µs) range and peak powers in the kilowatt range. Then a few years later, with the introduction of quality factor modulation in the laser cavity, the same energy could be packed into a nano-second (ns) time scale, to produce megawatt peak power. Mode-locking enabled the laser pulse duration to be reduced to the picoseconds level, pushing the peak powers to Giga-watt level. It means that intensities inside the laser

several Giga-watts per centimeter square  $(GW/cm^2)$ . As described in the earlier sections, many nonlinearities show up at these intensities. A beam with a Gaussian radial intensity distribution, sees a larger index of refraction at the centre, than at the sides. All the optical elements in the path of the beam begin to behave as lenses, which unacceptably deform the beams wave-front quality. Therefore the only way to increase the peak power beyond the Giga-watt level was to increase the beam diameter and therefore the size of the gain medium and the size of all the other instruments. This not only increased the cost, but it was difficult to implement practically too. Although the pulse duration kept decreasing over the years, the intensity dependent non-linear effects kept the peak powers at a constant level, (Fig.4) for many years until CPA was invented. The years after the 1985 invention, saw a very quick rise in peak powers. Today it is possible to obtain powers in the Peta-watt range. Enormous intensities, of  $10^{20}$ - $10^{22}$  W/cm<sup>2</sup> is made available on target. The field strength at these intensities (I) is of the order of a Tera-volt per cm, or hundred times the Coulomb field binding the ground state electron in the hydrogen atom. The light pressure (P=I/c) at these intensities is extreme (order of Giga-bar to tera-bar). The laser interaction with matter generates energetic electrons and ions. With laser intensities of  $10^{18}$ – $10^{19}$  W/cm<sup>2</sup> it is possible to accelerate electrons to 80MeV-100MeV. These are nearly monoenergetic with an energy spread of a few percent. The electrons are accelerated by making them surf a laser driven plasma wave or the laser wake-field acceleration [10, 11] as it is popularly known. Analogous results

for ions too have been reached, with the production of quasi-monoenergetic protons. At intensities of  $10^{21}$  W/cm<sup>2</sup> the electric fields become so high that the electrons accelerate to relativistic velocities. Subsequent to the acceleration of electrons up to relativistic energies, protons and ions are accelerated by well controlled mechanisms in a laser plasma acceleration setup. With a Peta-watt laser pulse, the emitted proton bunch was reproducibly observed with energies between 20MeV and 40MeV [12] and with a twenty five percent energy spread.

In many ways the physical environment of extreme electric fields, magnetic fields, pressure, temperature and acceleration can be found in stellar interiors. An astrophysical environment can be created in a laboratory! Scientific research in the field of Phototransmutation of long lived nuclear waste is an ongoing endeavor, along with X-ray emission study and gamma-ray emission study. The exciting possibilities of using ultrahigh intensity lasers in a laboratory setting, opens the door to scientific research in areas of physical extreme. Even today there is still a challenge to make the pulse durations shorter and push the peak powers towards tens of Peta-watt and beyond.

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#### References

- A. Ashkin, "Acceleration and trapping of particles by Radiation Pressure", Physical Review Letters, Vol.24, No.4, 1970, 156.
- 2. Donna Strickland and Gerard Mourou, "Compression of Amplified Chirped optical pulses", Optics Comm., Vol. 56, No.3, 1985, 219.
- 3. E. B. Treacy, "Optical pulse compression with diffraction gratings", IEEE. J.Quant. Electronics.QE-5, 1969, 454.
- O.E. Martinez, "3000 Times Grating Compressor with a positive group velocity dispersion: A p plications to fiber compensation in 1.3-1.6μm region", IEEE, J. Quant. Elect. QE-23, 1987, 59.
- Paramita Deb, Kailash C. Gupta, Jayant K. Fuloria, L. Dhareshwar, V. Rajeshree and B.S. Narayan, "CPA Nd:glass laser system for intense laser matter interaction research", BARC Newsletter, February 2008.
- 6. Paramita Deb, Kailash C. Gupta and Jayant K. Fuloria, "Development of the chirped pulse

amplification technique for high peak power production with Nd: glass laser system", BARC/E/022/2011.

- 7. Paramita Deb, L.J. Dhareshwar and B.K.Godwal, "Design Aspects of a grating pair stretcher / Compressor", Proceedings of Golden Jubilee DAE-BRNS National Laser Symposium 2003.
- 8. A. Offner, U.S. patent, 3748015, 1971.
- 9. Nandan Jha & Paramita Deb, "Temporal contrast improvement in chirped pulse amplification systems by a four grating compressor and by spectral modifications", Optik 125, 2014, 2261-2266.
- 10. T. Tajima and J.M. Dawson, "Laser Electron Accelerator", Physical Review Letters, 43, 1979, 267-270.
- 11.C.G.R. Geddes, Cs.Toth,
  J. van Tilborg, E. Esarey,
  C.B. Schroeder, D. Bruhwiler,
  C. Nieter, J. Cary and
  W.P. Leemans, "High-quality
  electron beams from a laser
  wakefield accelerator using
  plasma-channel guiding", Nature,
  431,2004, 538-541.
- P. Hilz et al, "Isolated proton bunch acceleration by a Peta-watt laser pulse", Nature Communications, 2018, 9:423, 1-8.