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Optical Biopsy XII

Robert R. Alfano
Stavros G. Demos
Editors

4–5 February 2014
San Francisco, California, United States

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Robert W. Boyd, University of Ottawa (Canada)

Introduction

The conference "Optical Biopsy XII," part of the SPIE Photonics West BiOS symposium, was held on February 4-5, 2014 in San Francisco. The conference consisted of seven oral sessions and hosted 33 papers with 21 of these from international contributions and four posters. In addition, the program included a special session entitled "45 Years of Supercontinuum Generation" consisting of seven invited presentations by world experts and pioneers to give an overview on the field of supercontinuum. The new non planar twisted form of light with orbital angular momentum and polarization was reviewed. We hypothesize that this method may provide a new tool for probing the structure and status of tissues. The slides from the "Ultimate ultrafast white light's first observations: early discovery circa 1970" presentation can be found in this volume.

As in previous years, the quality of the presentations was very high and included the presentation of novel approaches as well as the most recent developments in well established methods. Most presentations were concentrated in three main thematic areas: a) Light scattering; Tissue diagnosis with optical spectroscopy and spectral imaging; microscopy methods, Raman, and native fluorescence (auto–fluorescence). b) Imaging at the cell level for pathological assessment; scattering of complex structure light. c) Novel instrumentation and techniques for in vivo diagnosis.

Major advances in biomedical optics have been presented on: Tryptophan as a key cancer marker in aggressive cancers; enhancing the penetration depth in two photon microscopy using the second singlet state S2 of contrast agents in brain tissue so both the exciting and emission wavelengths are in therapeutic window; introduction of Resonance Raman in brain cancer; and the introduction of a 3rd optical window at 1650nm to 1800nm in tissue to reduce scattering and blurring effects in tissues.

It was worth noting that for another year there was a contribution on the detection of disease using optical spectroscopy signatures of body fluids such as urine or blood plasma. As the field of metabolomics continues to grow, it is possible that "optical metabolomics" may be a future growth area in the field of optical biopsy. The trend of increasing focus on translational research that was observed in previous years continued this year with nearly all speakers using part of their time to explain how the method and results presented can be implemented in a clinical setting. This trend is expected to continue as the field continues to mature and the medical community starts recognizing that some of these techniques will be a major part of medical practice in the near future.

We wish to thank Hamamatsu Corporation, Energy Research Company, Bay Spec, Inc., PerkinElmer Inc., and Intuitive Surgical, Inc. for support of Optics Biopsy

sessions, and Coherent Inc., LEUKOS, Corning Inc., NKT Photonics A/S, Fianium Ltd. and ThorsLabs, Inc. for support of the Supercontinuum session. We also thank the help of the session chairs, program chairs and SPIE staff for their help in making this successful conference.

Robert R. Alfano
Stavros G. Demos

ANNIVERSARY SESSION: 45 YEARS OF SUPERCONTINUUM GENERATION ABSTRACTS

Ultimate ultrafast white light's first observations: early discovery circa 1970 [8940-32],
Author(s): Robert R. Alfano, The City College of New York (USA)
Abstract: The first discovery and mechanism of super continuum generation with ultrashort pulses in solids (glasses and crystals) and rare gas media will be presented. How the observation of the white light over 6000cm-1 was unraveled for the first time with excitation of ultrashort pulses 45 years ago.

Evolution of the supercontinuum source [8940-33]
Author(s): James Roy Taylor, Imperial College London (United Kingdom)
Abstract: Spectral broadening and the generation of new frequencies were initially observed in pulsed laser systems in the mid-1960s as an inherent feature of the uncontrollable nonlinear process such as self-focusing and self-phase modulation occurring primarily in the gain media and were looked upon as deleterious rather than a resource. With the advent of mode locked lasers to generate picosecond pulses new effects were observed. Developed by the Alfano group in bulk media external to the laser in the 1970s the supercontinuum or "white light" source has now evolved into a commercially successful and highly compact source that can readily extend over more than three octaves with spectral power densities exceeding 100mW/nm. In this presentation I will describe this remarkable evolution.

Supercontinuum generation in optical fibers and its biomedical applications [8940-34]
Author(s): Govind P. Agrawal, Univ. of Rochester (USA)
Abstract: A microstructured optical fiber was first used in 2000 for supercontinuum generation. Since then, enormous progress has been made in understanding, controlling, and marketing fiber-based supercontinuum sources. In particular, biomedical applications of such sources are revolutionizing the field of medical imaging. In this talk I review the recent progress in this area and describe how a supercontinuum can be employed for biomedical imaging using the techniques known as coherent anti-Stokes Raman scattering, stimulated emission-depletion microscopy, and optical coherence tomography.

White light for the fast lane: supercontinuum generation in all-normal dispersion fibers for ultrafast photonics [8940-35]
Author(s): Alexander M. Heidt, Univ. of Southampton (United Kingdom)
Abstract: This talk will give an overview of the unique properties of supercontinuum generation (SCG) in all-normal dispersion (ANDi) fibers pumped by ultrashort pulses and the possibilities they offer for ultrafast photonics applications. In contrast to their anomalously pumped counterparts, the SCG process in ANDi fibers conserves a single ultrashort pulse in the time domain, completely suppresses soliton formation and decay, and avoids noise-amplifying nonlinear dynamics. The resulting spectra combine the best of both worlds – the broad, more than octave-spanning bandwidths usually associated with anomalous dispersion pumping with the high temporal coherence, pulse-to-pulse stability and well-defined temporal pulse characteristics known from the normal dispersion regime.

These characteristics are ideally suited for ultrafast photonics, and I will present application examples including the generation of high quality single-cycle pulses and their amplification, as well as ultrafast spectroscopy. This talk will also explore the exciting new possibilities enabled by extending this approach into the mid-IR spectral region using novel soft glass fiber designs.

Supercontinuum generation in microstructure fiber at the advent of femtosecond combs [8940-36]

Author(s): Steven T. Cundiff, JILA (USA)

Abstract: The development of frequency combs based on femtosecond lasers revolutionized optical frequency metrology, enable optical atomic clocks and is essential to the production of atto-second pulses.

Frequency combs are produced by locking the offset frequency of the laser, which in turn is most easily done if the spectrum spans an octave. Supercontinuum generation in microstructure fiber can easily span an octave, even for the nanojoule pulses produced by a mode-locked laser, while preserving coherence, and thus the comb spectrum.

Collapsing light really shines [8940-37]

Author(s): Alexander L. Gaeta, Cornell Univ. (USA)

Abstract: The history of super continuum generation with ultrashort pulses in bulk media will be reviewed. In particular, a description on how the self-focusing dynamics leads to shock formation and the generation of extremely broad spectra when an ultrashort pulse travels through a transparent gas, liquid, or solid.

Cross-phase modulation in optical Kerr media: from early discovery works to recent all-optical applications [8940-38]

Author(s): Patrice L. Baldeck, Univ. Joseph Fourier (France)

Abstract: Kerr cross-phase modulation (XPM) occurs when optical waves co-propagate in instantaneous intensity-dependent media. This all-optical effect leads not only to phase changes, but also to frequency, amplitude and spatial effects. In 1986, the first experiment reported the spectral broadening of a probe pulse by a pump pulse. Subsequent experiments demonstrated optically-induced phenomena, such as frequency shift, amplitude modulation, and spatial focusing that have been investigated in thousands of publications during the last two decades.

SPIE Photonics West Anniversary Session: 45 Years of Supercontinuum Generation

San Francisco, Wednesday 5, February 2014

Thanks for the support of this symposium by companies that market Supercontinuum sources:

Leukos
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Corning
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NKT Photonics Inc.

1

Ultimate ultrafast white light's first observations: early discovery circa 1970

Robert R. Alfano
Distinguished Professor of Science and Engineering
The City College of New York

Wednesday 5, February 2014
SPIE Photonics West Anniversary Session: 45 Years of Supercontinuum Generation
San Francisco

2

Today I will discuss an elegant and most colorful phenomena of generating

The Ultimate White Light

discovered in 1969, about 45 years ago and still going strong for various applications in biology, metrology, condensed matter, chemistry, and now in biomedicine.

This discovery was made from the knowledge from many Giants in science.

3

Peaceful Scene in Nature

RIOT OF ACTIVITY

Need a clock with time scale of the molecular, atomic, electronic world – to probe fundamental processes in nature – laser pulse – (ps, fs, as)

In late 1960's, ultrafast era appeared

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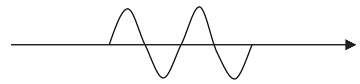
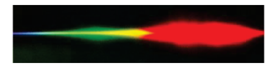
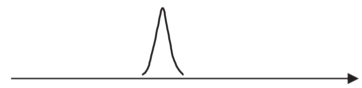
Salient Properties of Light

- **Wavelength (color)**





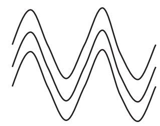
- **Time**



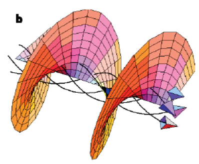
key for clocks

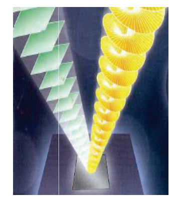
- **Polarization**

- **Coherence**



- **Wave fronts – plane, helical, spiral**





Optical vortex - Helical Phase

Processes

- **Emitted – fluorescence spectroscopy**
- **Absorbed – excitation spectroscopy**
- **Scattered– Raman and elastic**

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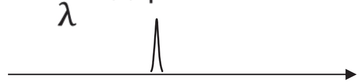
Laser light and Supercontinuum

Typical laser light beam has narrow spectral band:

$$\frac{\Delta\lambda}{\lambda} << 1$$

Red



Spectrum

Supercontinuum light is white light:

$$\frac{\Delta\lambda}{\lambda} \sim 1$$

White **Violet** **Red** **NIR**

Spectrum

arises from nonlinear optical effects from the third (χ_3) and second (χ_2) order susceptibilities (n_2, SRS, 4WM) using short ps and fs laser pulses via polarization (dipole moment/volume):

$$P = \chi_1 E + \underbrace{\chi_2 E^2 + \chi_3 E^3 + \ldots}_{\text{Nonlinear optical processes}}$$

E – electric field

$\chi_3 \rightarrow n_2(t) \rightarrow \Phi(t)$ **– phase**

xv

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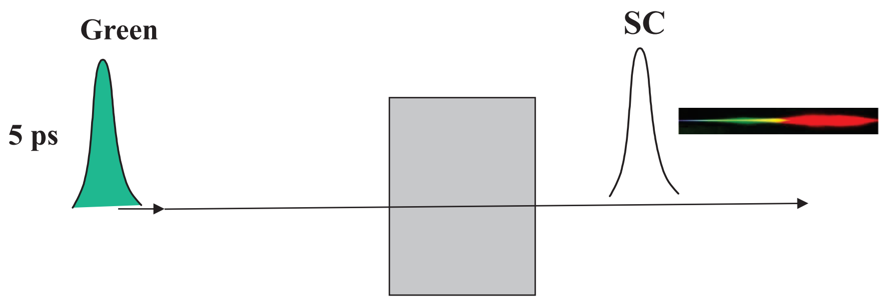
Brief History Behind Supercontinuum



Three seminal PRL Papers in 1970, Vol. 24 (Alfano and Shapiro):
SC in solids (glasses, crystals)
SC in rare gas liquids (Ar, Kr) and solid Kr

- observation of SPM, PRL 24, 592, (1970),
- observation of 4WM, PRL 24, 584, (1970),
- underlying mechanisms due to electronic clouds, PRL 24, 1217 (1970), for n_2

45 years has passed

7

Brief SC history

Early 1969 – Alfano and Shapiro teamed up at GTE Lab, Bayside, NY

GTE ⟶ Verizon

1969 – Alfano and Shapiro observed the light continuum from 400 nm to 7000 nm in glass (optical phonons in solids, daughter vibrations…)

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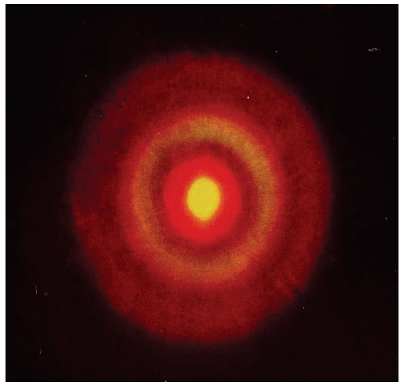
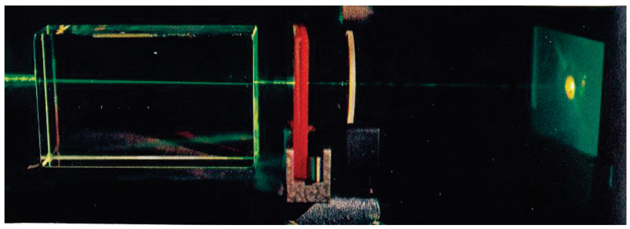
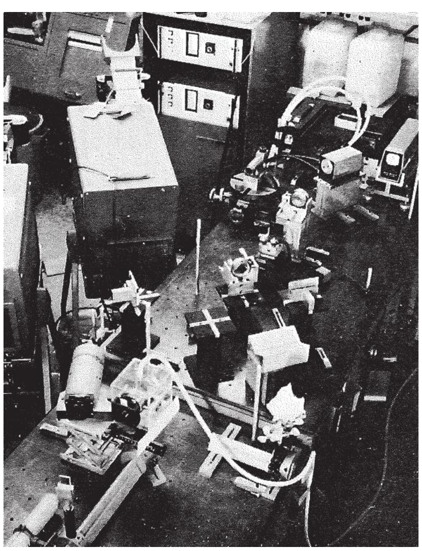
From 1970 Physics Review Letters: Alfano and Shapiro

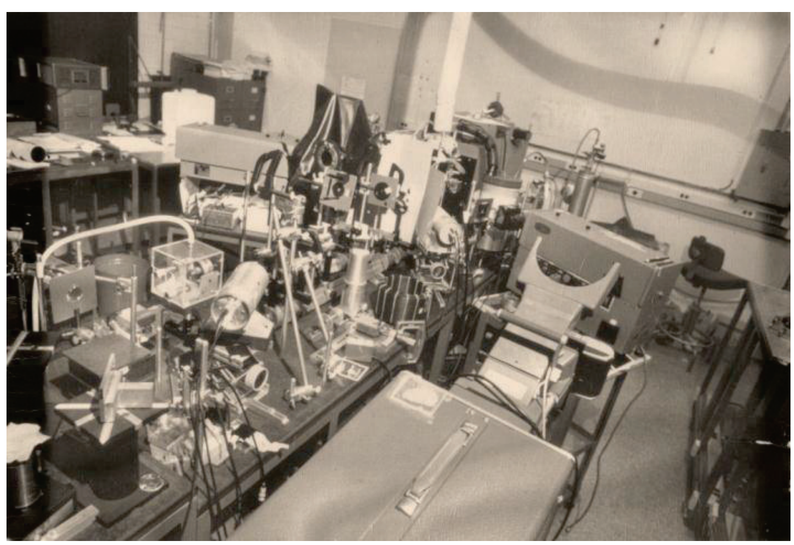


Pattern of 5 ps green light pulse after it passes transparent piece of glass



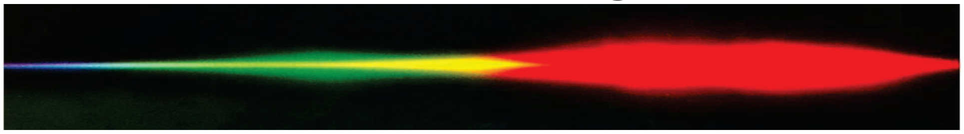
GTE Picosecond Lab Photos (~1969)





Brief History of Supercontinuum

Ultimate White Light



Solids (glasses, crystals)	**1969; PRL 24, 584, 592 (1970), Alfano and Shapiro**
Rare gas liquids (Ar, Kr) and solid Kr	**1970; PRL 24, 1217 (1970), Alfano and Shapiro**
Liquids	**1972; Opt. Commun. 4, 413 (1972), Werncke et. al.**
Semiconductors	**1985; Opt. Lett. 10, 624 (1985), Corkum et. al.**
Gases	**1986; PRL 57, 2268 (1986), Corkum et. al.**
Fibers	**2000; Opt. Lett. 25, 25 (2000), Ranka et. al.**
Optical vortex	**2006; Opt. Lett. 31, 2725-2727 (2006), Sztul et. al.**

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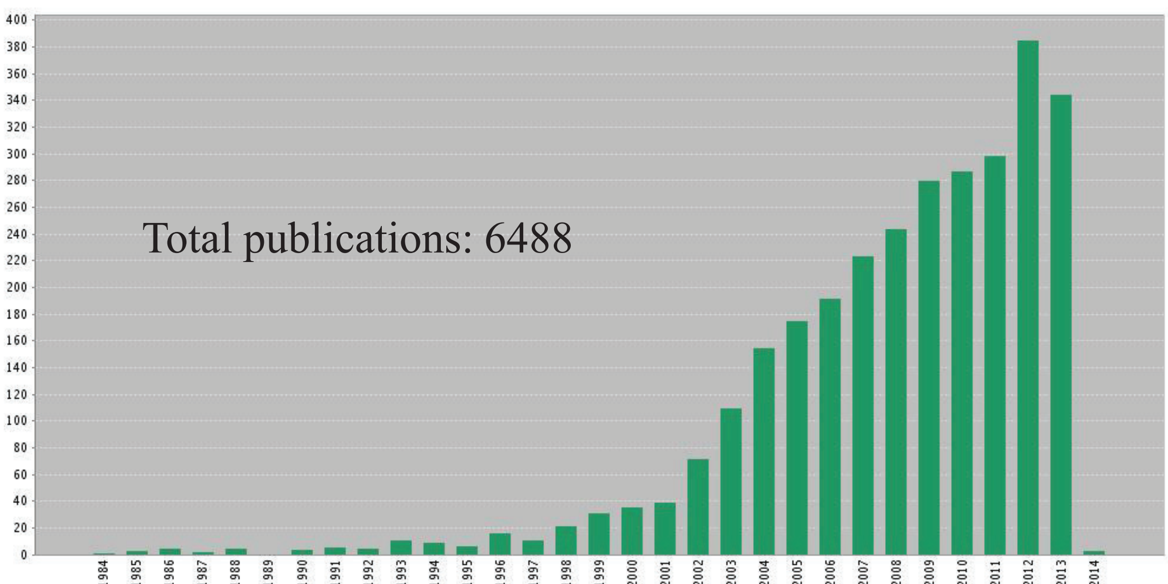
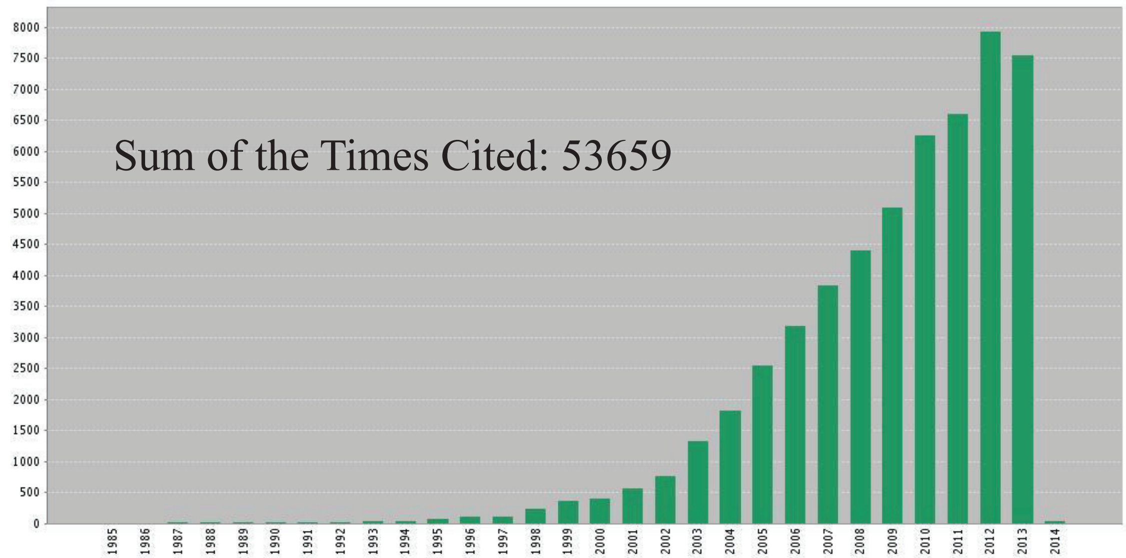
Publications on Supercontinuum in Scientific Literature



Citations of Articles on Supercontinuum



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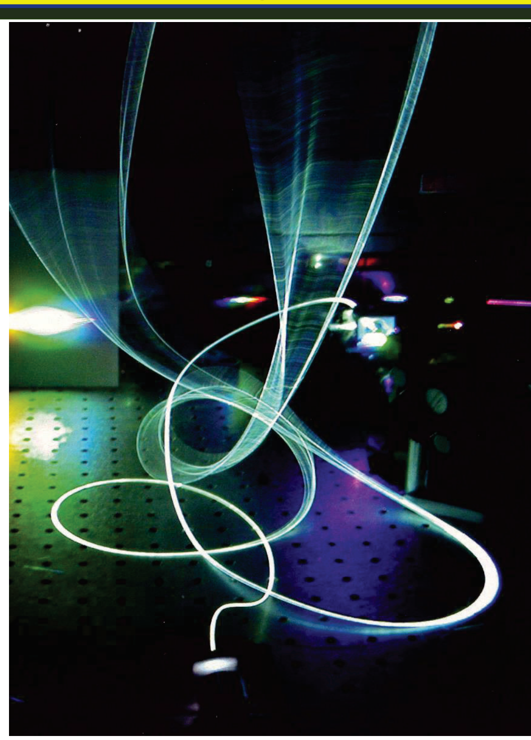
Current day SC from special holey fiber



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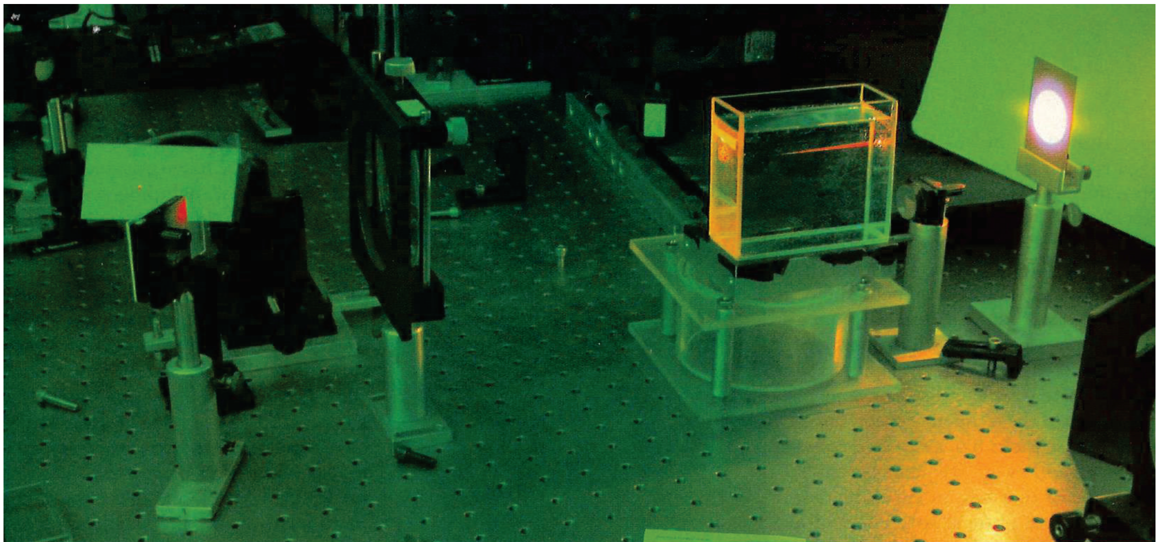
R. R. Alfano, The Ultimate White Light, Sci. Am. 295, 64-71 (2006)

Current day SC from bulk material

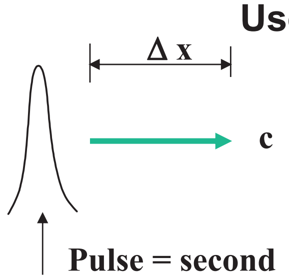


EXPERIMENTAL SETUP to produce supercontinuum light sends high-intensity laser light (*red*) through a suitable optical medium (here a container of liquid) that greatly broadens the light's bandwidth (*white light*).

R. R. Alfano, The Ultimate White Light, Sci. Am. 295, 64-71 (2006)

Ultrafast Optical Clocks

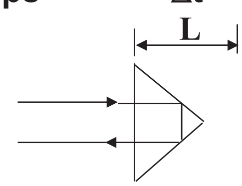
Use space to delay light



Δx = v Δt

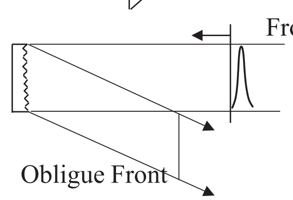
For Δx = 1 mm
Δt = 3 ps

For Δx = 100 μm
Δt = 300 fs



Delay = 2L/c

Mechanisms for optical clocks:
- prism
- grating
- array of mirrors
- streak camera
- NLO gates



xx

Supercontinuum – ultimate light pulse source: - wide spectra (400 – 7500 nm)
- short time (ps/fs)

SC – Supercontinuum – SPM underlying processes

Phase:

$$\phi(\omega,t) = \omega_L t - n\omega z/c$$

Index of refraction:

$$n = n_0 + n_2 E^2(t) + \ldots$$

SPM

$$\phi(\omega,t) = \omega_L t - (n_0 + n_2 E^2(t))\, \omega z/c$$

SC

$$\Omega = \partial\phi/\partial t = \text{new frequencies}$$

$$\Omega = \omega_L - \underbrace{\frac{n_2 \omega z}{c} \frac{\partial E^2(t)}{\partial t}}_{\partial n/\partial t}$$

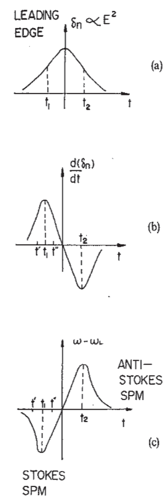


FIGURE 2.1. A simple mechanism for SPM for a non-linear index following the envelope of a symmetrical laser pulse: (a) time-dependent nonlinear index change; (b) time rate of change of index change; (c) time distribution of SPM-shifted frequencies $\omega(t) - \omega_0$.

$$\Delta\Omega \sim \frac{n_2 I z}{\tau_p}$$

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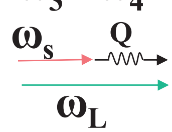
Main Supercontinuum Mechanisms: n_2

SPM – Self Phase Modulation (real χ_3): $\Delta n = n_2 I(t)$

FWM – Four Wave Mixing (real χ_3): $\omega_1 + \omega_2 \rightarrow \omega_3 + \omega_4$

SRS – Stimulated Raman Scattering (imag χ_3)



XPM – Cross Phase Modulation: $\Delta n(\omega_1) = n_2(I_1 + 2I_2)$

SS – Self Steepening

Ionization

Avalanche

Solitons – Fission, Raman shift, Dispersion, Roque waves (interplay between SPM (+) and GVD anomalous (-))

xxi

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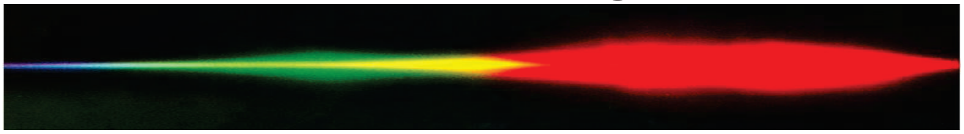
Supercontinuum generation

Ultimate White Light



From: X-rays, UV, Visible, NIR, IR

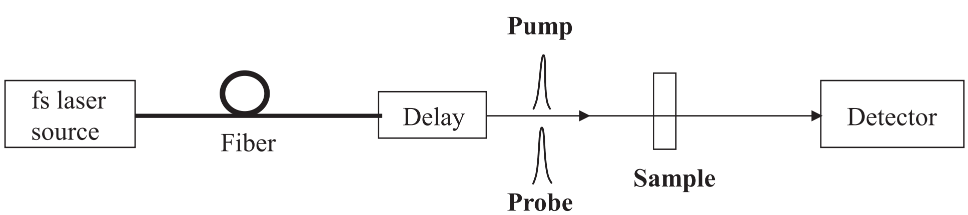
Nonlinear part of index of refraction: n ⟶ n_2

Mechanism: n_2 = electronic, vibration, rocking, orientation, translation

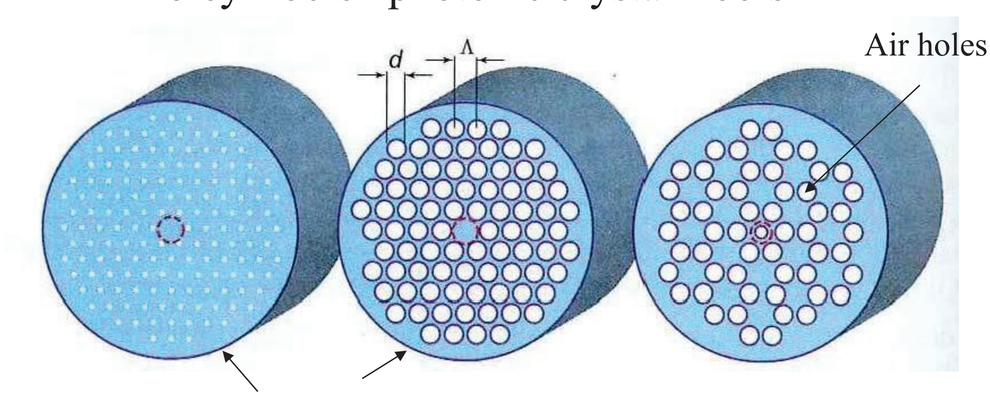
Response Time:	electronic	vibration	rocking	orientation	translation
	10^{-15} sec	10^{-13} sec	10^{-12} sec	10^{-12} sec	10^{-10} sec

n_2 (electronic) ⟶ attosecond pulses

Major advance - fibers for compact SC source



Holey fibers –photonic crystal fibers

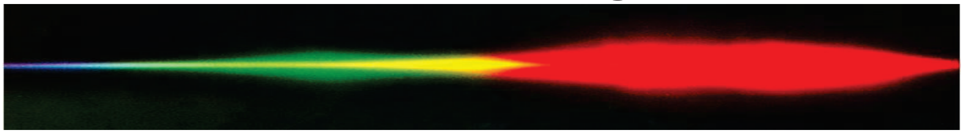


D_ω - dispersion (depends on d/Λ)

Ranka et. al., Opt. Lett. 25, 25 (2000)

Supercontinuum (SC)

Ultimate White Light



Spans: 400 nm to 1400 nm
Energy: 1mJ; pulse < 1 ps
Spectral energy brightness: 1 mJ/1000nm = µJ/nm
Focus to 100 µm gives <u>10 mJ/nmcm^2</u>
Spectral power brightness:
10mJ/nmcm^{2}ps = 10x10^9 W/ nmcm^2 = <u>10 GW/nmcm^2</u>

SC average 100 mW/mm^2 = 10 W/cm^2;
⊙ Sun - 0.14 W/cm^2

	SC	UV using fibers 300 nm (aim)
Now,	SC	200 eV enters x-rays in Argon gas using 16 mJ, 800 nm, 60 fs pulses

Commercially available fs lasers:
1 W, 10nJ, oscillator@100 MHz; 1mJ amplifier@1kHz;
2.5 W, 10 µJ amplifier@250kHz

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Enabling SC Applications

Ultimate White Light

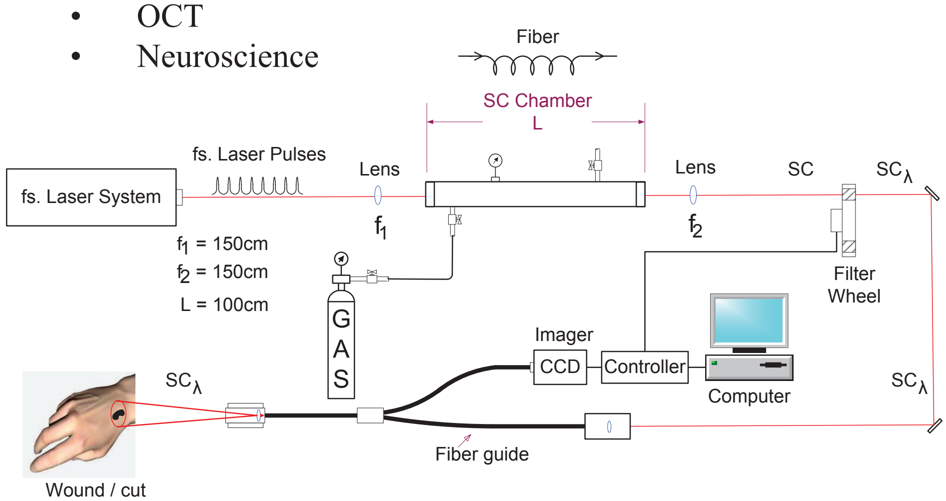
Enabling SC applications:

- accurate clocks ⟶ Nobel prize (2006)
- chemistry/biology ⟶ Nobel prize (1999)
- communication
- NLO
- biological and medical - OCT
- nm microscopy
- as laser pulse
- optical vortex beams

Next Medical Advances – Use of Supercontinuum in Biomedicine

Supercontinuum applications in biomedicine is in its infancy

- Therapy (SC room)
- Wound healing
- NLO in tissue (proteins imaging)
- Ultra microscopes
- OCT
- Neuroscience



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Closing

SC use: - in biomedical optics, biomedicine
- in communication with OAM and spatial modes (pentabits/sec, terabits/sec)

Hyper-photon: SC + OAM + vector beam(polarization) + spatial modes

Zeptosecond pulses