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**WINTER COLLEGE ON BIOPHOTONICS:**
**Optical Imaging and Manipulation of Molecules and Cells**
**(10 - 21 February 2003)**

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# *Sources for Biomedical Optics*

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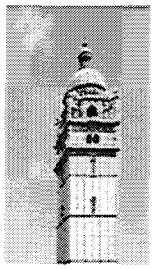
*These are preliminary lecture notes, intended only for distribution to participants.*

## Sources for Biomedical Optics

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## Sources for Biomedical Optics

- Spectral coverage?
  - *ultraviolet – visible – near IR - mid-IR*
- Temporal profile?
  - *c.w or pulsed?*
  - *Spectral profile?*
- Spectral profile?
  - *Broadband or narrow linewidth?*
- Convenience
  - *Lamp or laser?*
  - *portable (LED, diode or diode-pumped-solid-state)?*

## Narrowband/tunable light sources

*Low spatial coherence*

**Thermal Sources (Lamps) with filters**

***Filament lamps (Quartz-Tungsten Halogen)***

***Arc lamps (Hg, Xe, Hg-Xe)***

**LEDs**

*High spatial coherence*

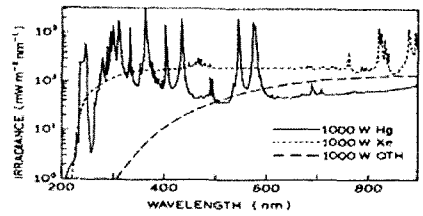
**Lasers**

***c.w. lasers, Q-switched & mode-locked lasers***

***Gas, dye, solid-state and semiconductor lasers)***

## Broadband thermal light sources

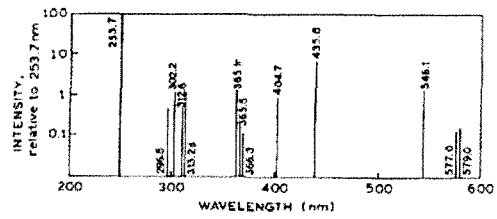
***High pressure Arc lamps (Hg, Xe) and Quartz-Tungsten Halogen lamp )***




*Low spatial coherence (source size down to ~ mm)*
*Very broad spectra (> 50 nm)*
*High average powers (up to 100's W) but low brightness*
*Low cost ($100's)*

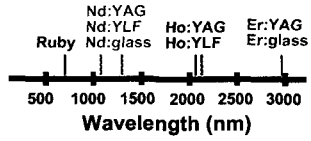
http://cc.joensuu.fi/photobio/lamps.html

## Spectral standards: Low pressure Hg lamp



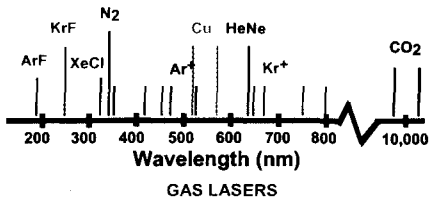

*Low spatial coherence (source size down to ~ mm)*
*Very narrow spectra (high temporal coherence)*
*Moderate average powers (up to ~ W) but low brightness*
*Low cost ($100's)*

## Spectral coverage of lasers: 1960's – 80's



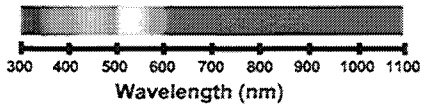

SOLID-STATE LASERS

## Spectral coverage of lasers: 1960's – 80's



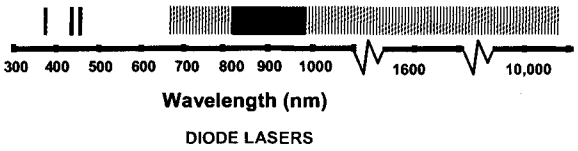

GAS LASERS

## Spectral coverage of lasers: 1960's – 80's



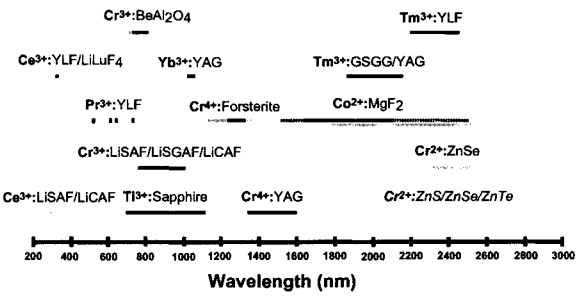

DYE LASERS

## Spectral coverage of lasers: semiconductors




DIODE LASERS

## Tunable solid-state lasers




## Broadband light sources

*Low spatial coherence*

**Thermal Sources (Lamps)**

***Filament lamps (Quartz-Tungsten Halogen)***

***Arc lamps (Hg, Xe, Hg-Xe)***

**LEDs**

*High spatial coherence*

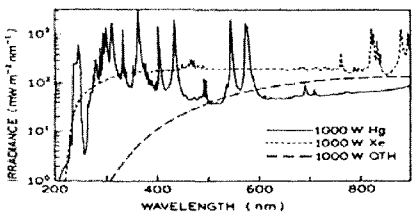
**Lasers & laser amplifiers**

***Mode-locked lasers***

***ASE sources (fibre and diode amplifiers)***

## Broadband thermal light sources

***High pressure Arc lamps (Hg, Xe) and Quartz-Tungsten Halogen lamp )***

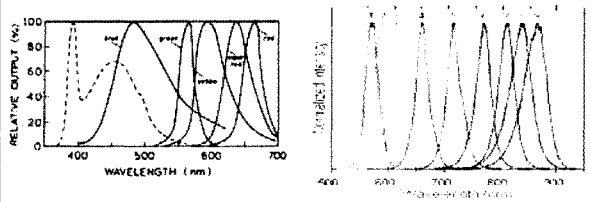



*Low spatial coherence (source size down to ~ mm)*
*Very broad spectra (> 50 nm) ⇔ low temporal coherence (< 1 μm)*
*High average powers (up to 100's W) but low brightness*
*Low cost ($100's)*

http://cc.joensuu.fi/photobio/lamps.html

## Broadband LEDs

***Materials systems ranging from GaN to PbS*** *(cryogenic, mid-IR)*



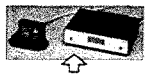

*Moderate spatial coherence (source size down to ~ 10's μm)*
*Moderately broad spectra (> 50 nm) ⇔ low temporal coherence (< 10 μm)*
*High average powers (up to 100's mW)*
*Low cost ($100's)*

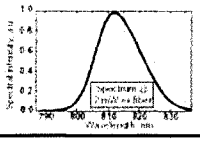
## ASE sources: high spatial coherence

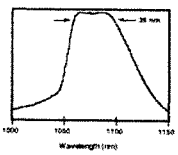
***ASE sources: fibre amplifiers and superluminescent diodes)***

*High spatial coherence (source size down to ~ 1 μm)*
*Moderately broad spectra (> 20 nm) ⇔ low temporal coherence (< 20 μm)*
*Moderate average powers (up to ~ 10 mW) and high brightness*
*Moderate cost ($10,000's)*
*Limited spectral coverage*
*(800 – 900 nm, 1100nm, 1300 nm 1500-1600 nm)*

**SLD**



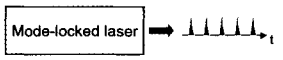




Nd:glass fibre ASE source (7 mW)

## *Mode-locked (ultrafast) lasers*

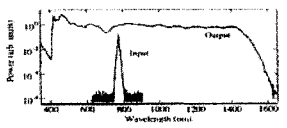
*High spatial coherence High spatial coherence (source size down to ~ 1 μm)*
*Moderate to high broad spectra (~20-300 nm) ⇔ low temporal coherence (<1 - >10 μm)*
*Moderate average powers (up to ~ 100's mW) and high brightness*
*High cost (~ $100.000)*




### *Ultra*broadband sources:

***Femtosecond laser pulse + spectral continuum generation in micro-structured fibre***

***Complex, expensive, but very broadband (>1000 nm)/short coherence length (< 1 μm)***




## Biomedical applications of ultrafast lasers?

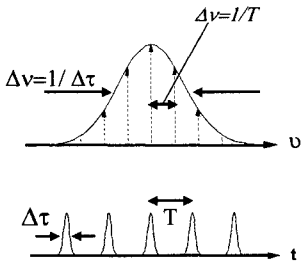
**High peak power applications**
- *Multi-photon microscopy*
- *Ultrafast laser ablation*

**Low coherence applications**
- *Optical coherence tomography*
- *Holographic imaging*
- *whole-field 3-D microscopy*

**Time-resolved applications**
- *Imaging with scattered light*
- *Fluorescence lifetime imaging*
- *Dynamic microscopy*
- *STED*

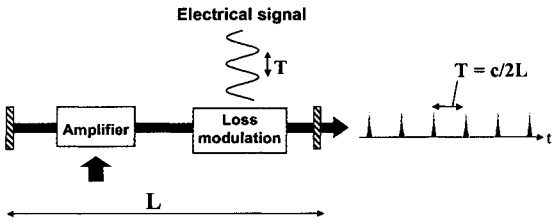
## How do ultrafast lasers work?

Ultrashort pulses may be generated by periodically modulating the loss of a laser cavity *at the cavity round trip frequency – called "mode-locking"*



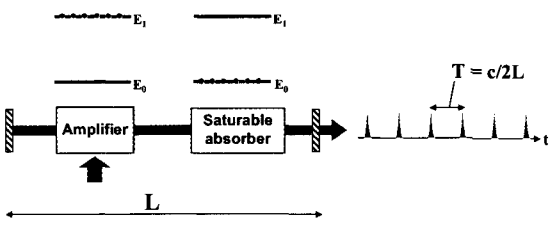

This can be realised by
***Active mode-locking***
***Passive mode-locking***

## Active mode-locking




- Repetition rate = 1/cavity round trip time
- Produces pulses > 10's picoseconds *(1 ps = $10^{-12}$ s)*
- Electrical modulation must ***exactly*** match cavity period

## Passive mode-locking



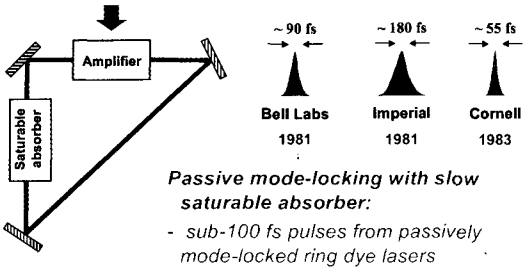

- Repetition rate = cavity round trip time
- Produces pulses > 4 femtoseconds *(1 fs = 0.001 ps = $10^{-15}$ s)*

## How to generate the shortest possible pulses?

- Active mode-locking limited to ~ 10's ps
  ⇒ use passive mode-locking
- Try to find a saturable absorber (*i.e. an **intensity-dependent loss***) with a *response time* $\tau$ *as short as possible*
- We also need broad gain profiles

## Ultrafast dye lasers: 1970's – 80's

Continuous wave dye lasers pumped by argon ion lasers:

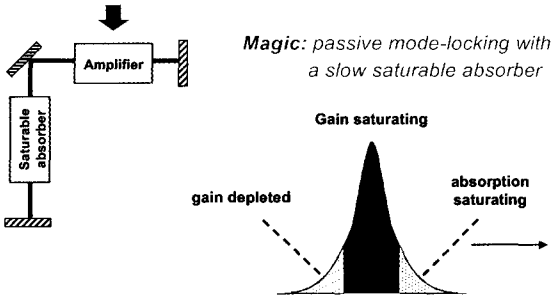



*Passive mode-locking with slow saturable absorber:*

- *sub-100 fs pulses from passively mode-locked ring dye lasers*
- *pulses much shorter than* $\tau$

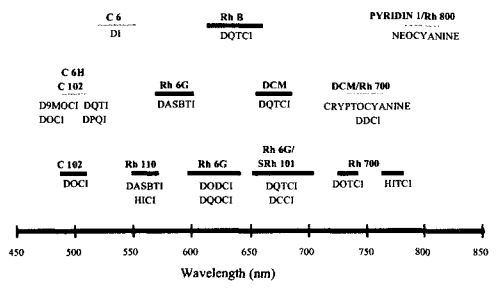
## Mode-locking with a *slow* saturable absorber

Continuous wave dye lasers pumped by argon ion lasers:




***Magic:*** *passive mode-locking with a slow saturable absorber*

## Passively mode-locked femtosecond dye lasers



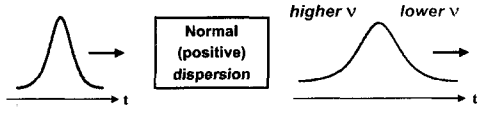

## Dispersion in femtosecond lasers

Uncertainty principle: $\Delta\nu.\Delta\tau \leq 1$

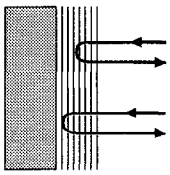
⇒ *ultrashort pulses have broad linewidths*

⇒ *ultrashort pulses consist of a range of different frequency (wavelength) components*

**Dispersion**: different frequency components travel at different speeds



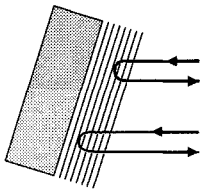
## Dispersion in femtosecond lasers



Multi-layer
dielectric mirror

Shorter wavelengths experience less delay upon reflection at dielectric mirrors

## Dispersion in femtosecond lasers

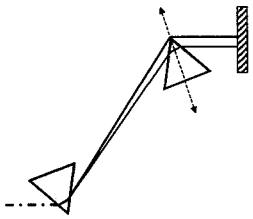


Multi-layer
dielectric mirror

Dispersion and reflectivity are modified when mirrors are used at large angles of incidence

*Accident: - optimisation of negative group velocity dispersion*

## Adjustable dispersion in femtosecond lasers



Different wavelengths experience different path lengths

- can provide positive or negative group velocity dispersion

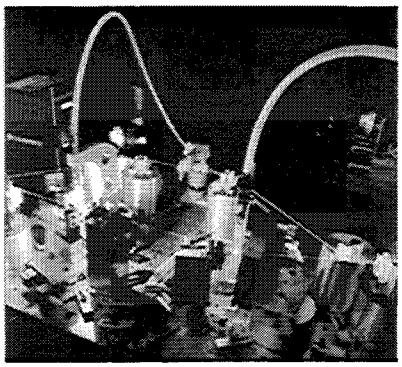
## Passively mode-locked dye lasers: 1987

First c.w. blue
femtosecond laser

***90 fs at 497 nm***

***Pretty*** **but:**

- ***inconvenient***
- ***difficult***
- ***toxic***



## Tunable (vibronic) c.w. solid-state lasers:

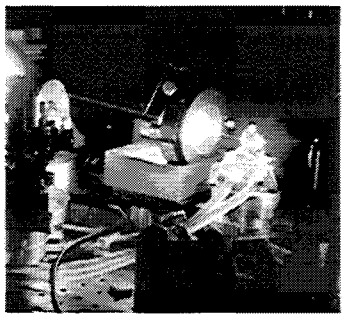
**Ti:Sapphire**

Superb thermal &
mechanical properties

Long upper-state lifetime $\tau$

***- not possible to get femtosecond pulses by passive mode-locking***

***Myth!***



## Femtosecond pulse generation from c.w. solid-state lasers?

Active mode-locking only yields picosecond pulses

With passive mode-locking, pulse duration is limited by recovery time $\tau$ of saturable absorber

Need absorber with femtosecond recovery time

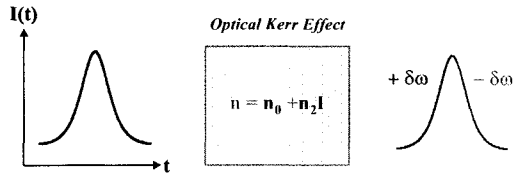
- *use GaAs/AlGaAs MQW saturable absorbers ($\tau$ > ~ 300 fs)*

Use optical Kerr effect to simulate an *infinitely fast saturable absorber* via intensity dependent refractive index

- *use self-phase modulation and interferometry* ***(CCM, APM)***
- *use self-focussing* ***(Self-Mode-locking, Kerr Lens Mode-locking)***

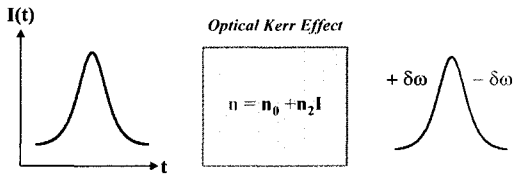
## Nonlinearity in femtosecond lasers

*Nonlinear refractive index: new frequencies generated*




## Nonlinearity in femtosecond lasers

*Nonlinear refractive index: new frequencies generated*

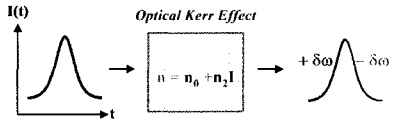



$E(t) = A(t)e^{i\phi(t)}$ $\qquad A(t)e^{i(\phi_0(t)+\Delta\phi(t))}$

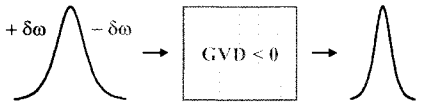
*Frequency chirp:* $\delta\omega = \frac{d}{dt}\phi(t) \propto -\frac{d}{dt}I(t)$

## "Soliton-shaping" in femtosecond lasers

*Nonlinear refractive index:* ***new frequencies generated***




*Negative dispersion:* ***high frequencies travel faster***




*Shorter pulse*

## Soliton-shaping as bunching of high intensity light

*Photons interact with their nonlinear medium:*
*- leads to bunching (pulse compression)*

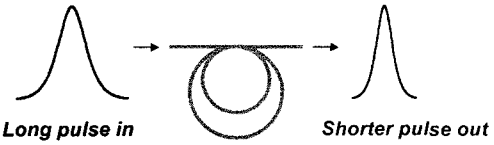
**SOLITONS: The high intensity light pulse creates a moving "valley" of higher refractive index**

**RUNNING ON A MATTRESS; The moving valley pulls along slower runners and retards the faster ones**

## Pulse compression by soliton-shaping in optical fibres:

*Nonlinear refractive index:* ***new frequencies generated***

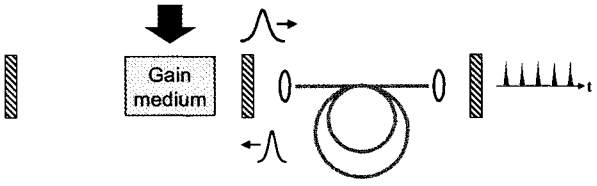
*Negative dispersion:* ***high frequencies travel faster***



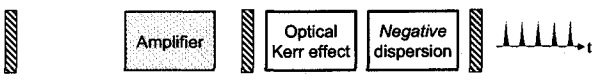
***Long pulse in*** ***Shorter pulse out***

***Magic!***

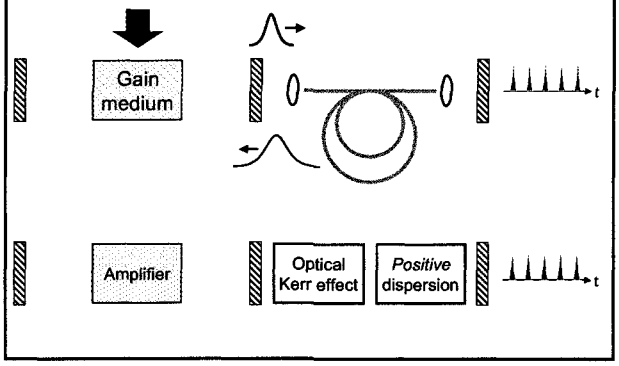
## Soliton laser



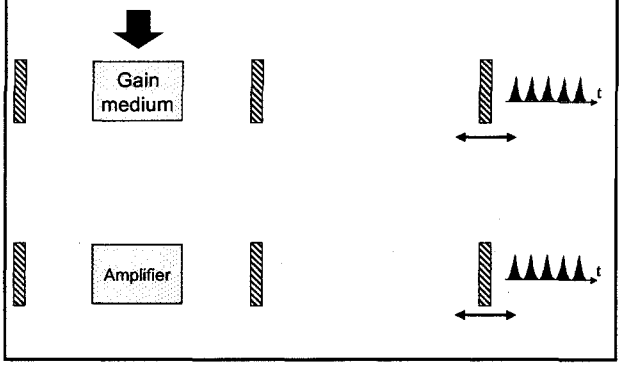

**Theoretical model**



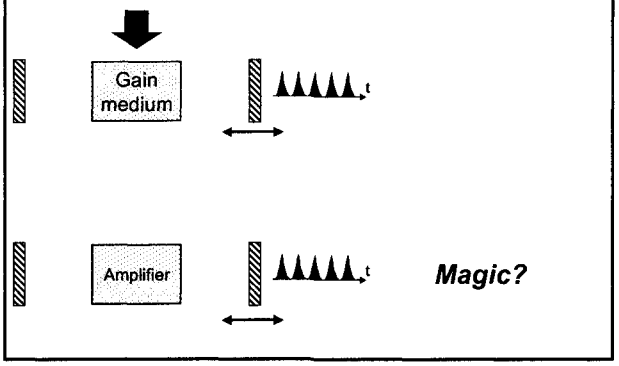
## First Femtosecond Ti:sapphire laser – *mode-locked with nonlinear external cavity feedback*




## Moving mirror mode-locking: *discovered by accident:*

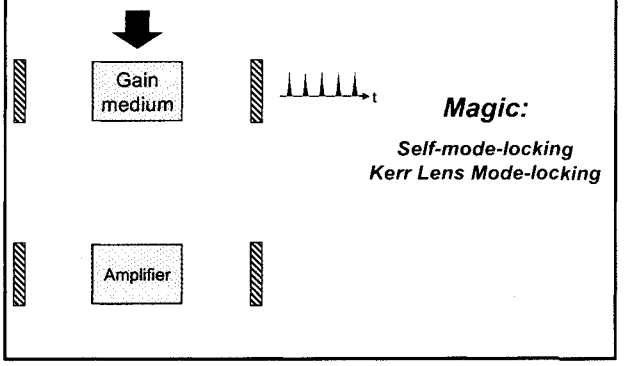



## Moving mirror mode-locking




***Magic?***

## First "self-mode-locked" laser

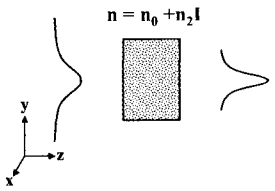



***Magic:***

***Self-mode-locking***
***Kerr Lens Mode-locking***

## Intensity-dependent refractive index in laser rod

**Spatial profile of laser beam**

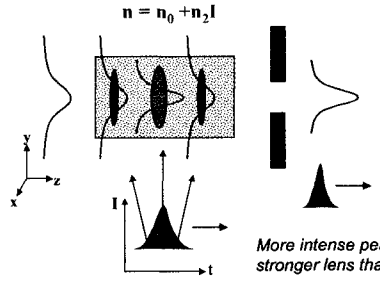



**Laser beam is most intense at centre**

**⇒ laser rod act as a lens – "self-focussing"**

## Kerr Lens Mode-locking: *passive mode-locking with infinitely fast saturable absorber*

**Strength of self-focussing depends on intensity**




*More intense peak of pulse experiences stronger lens than less intense wings*

***⇒ intensity-dependent loss at aperture***

## Kerr Lens Mode-locked lasers

- Initially developed in Titanium-doped sapphire lasers, pumped by argon ion gas lasers
- Now pumped by diode-pumped solid-state lasers
- First user-friendly ultrafast lasers
  - suitable for medical applications
- Pulses as short as 4.5 fs (argument continues over how to measure such a short pulse)
- Commercial products: ~100 fs for ~ £100,000

## Tunable ultrafast solid-state lasers

: $Ti^{3+}$:Sapphire

200 400 600 800 1000 1200 1400 1600 1800 2000 2200 2400 2600 2800 3000

**Wavelength (nm)**

## Tunable solid-state lasers

$Cr^{3+}$:$BeAl_2O_4$ $Tm^{3+}$:YLF

$Ce^{3+}$:YLF/$LiLuF_4$ $Yb^{3+}$:YAG $Tm^{3+}$:GSGG/YAG

$Pr^{3+}$:YLF $Cr^{4+}$:Forsterite $Co^{2+}$:$MgF_2$

$Cr^{3+}$:LiSAF/LiSGAF/LiCAF $Cr^{2+}$:ZnSe

$Ce^{3+}$:LiSAF/LiCAF $Ti^{3+}$:Sapphire $Cr^{4+}$:YAG *$Cr^{2+}$:ZnS/ZnSe/ZnTe*

200 400 600 800 1000 1200 1400 1600 1800 2000 2200 2400 2600 2800 3000

**Wavelength (nm)**

## Evolution of femtosecond lasers

Argon ion laser ➡ Dye laser — *large, highly complex and toxic* — *Not for sale*

Argon ion laser ➡ Ti:Sapphire laser — *large, less complex and easier to use* — *~ £100,000*

Diode laser ➡ Nd:$YVO_4$ laser | SHG ➡ Ti:Sapphire laser — *Compact, robust and user-friendly* — *~ £100,000*

Diode laser ➡ Cr:LiSAF laser — *More compact, robust and user friendly* — *~ £10,000 ?*

⇒ ***many more real-world applications***

## First *diode-pumped* femtosecond vibronic laser

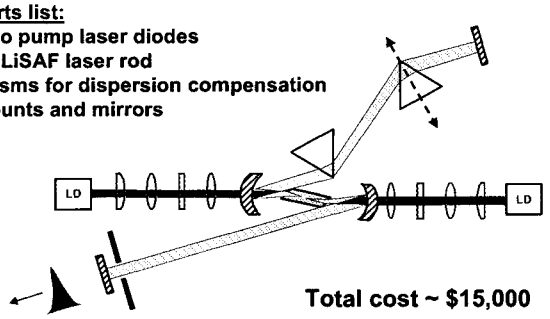
**Diode-pumped Cr:LiSAF laser passively mode-locked with MQW saturable absorber**

LFW "Devil" picture

Two pump diodes at 666 nm

## How to build a diode-pumped KLM femtosecond Cr:LiSAF laser:

**Parts list:**
**Two pump laser diodes**
**Cr:LiSAF laser rod**
**Prisms for dispersion compensation**
**Mounts and mirrors**




**Total cost ~ $15,000**
***= ~ £15,000 = ~ €15,000***

## Diode-pumped ultrafast solid-state lasers

**Diode-pumped tunable fs laser** → *> 25 fs, < 1 nJ, 80 MHz, 800-880 nm*

**Diode-pumped tunable ultrafast regenerative amplifier** → *> 200 fs, > 3 μJ, < 25 kHz, 800-880 nm*

***FLOAT***

***Goals:***

- *turnkey operation*
- *portable, compact*
- *~ $ 50,000*

*suitable for e.g.*

- *micromachining*
- *biomedical instrumentation*

## For more information...

**For a review of the development of ultrafast laser technology:**
French, P.M.W., *The Generation of Ultrashort Laser-Pulses.* Reports on Progress in Physics, 1995. 58(2): p. 169-262.

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J Pawley 1995 *Handbook of Biological Confocal Microscopy* 2nd edn (Plenum, New York)

Brett E. Bouma, Guillermo J. Tearney, *Handbook of Optical coherence Tomography* (Marcel Dekker, Inc). 2002.