Light and Life

Oh Agni! May you become alike the Sun and bless us with food grains.

Samaveda
1500-1000 BC
- Photomedicine
- Lithography
- Industrial Synthesis of Chemicals
- Photography, Xerography and Holography
- TiO₂: Environmental Cleanup
- Solar Energy Conversion
- Sunscreen, Photochromic Glass
- Photostabilization
- Photocuring
Biological Applications of Photochemistry
Photomedicine

- Phototherapy - Jaundice Treatment
- PUVA therapy - Skin Disorders, Blood Cancer
- Photodynamic therapy - Cancer
- Lasik surgery - Vision Correction
Phototherapy for Neonatal Jaundice Treatment

- Accumulation of the potentially toxic yellow lipophilic bilirubin in human serum leads to Jaundice.

- If the percentage of bilirubin increases to 15-25 mg/100 ml, it will lead to hyperbilirubinemia.

- Severe hyperbilirubinemia cases, sufficient pigment may partition into the brain to cause irreversible damage, even death.

Biosynthesis of bilirubin

Glucuronyl transferase activity in fetal and new born liver is very low.
Why bilirubin is lipophilic (hydrophobic)?
Different ways to cure jaundice

- Wait till liver matures soon enough to clear bilirubin unaided.

- Exchange transfusion: blood along with threatening pigment drained and replaced with clean blood.

- Phototherapy - irradiate the baby with light.

Discovery of phototherapy

The discovery of phototherapy stems from the observations of Sister J. Ward, a nurse in U.K.

Evening walk with hyperbilirubinemia patients - lead to discovery of phototherapy by scientists.
“light converts bilirubin to a less hydrogen bonded (more water soluble) isomer”
Skin Disorders and PUVA therapy

Psoriasis

Polymorphic light eruption

Vitiligo - pigment cells are destroyed.

Acute dermatitis
PuVA- therapy

- Egyptians and Asian Indians practised this therapy centuries ago.

- Boiled extracts of fruits of plants *Ammi majus* in Egypt and *Psoralea Corylifolia* L in India plus sunlight cured vitiligo.

- In 1988, PUVA was the first FDA (Food and Drug Administration) approved selective immunotherapy for skin disorders including cancer.

\[
\text{Psoralen + UVA} = \text{PUVA therapy}
\]
How PUVA therapy is done?

- Methoxsalen capsules are taken two hours before exposure to UVA.

- Bath PUVA: hands and/or feet are soaked in a dilute solution of methoxsalen for 30 minutes, then exposed to UVA.

- A few patients may be treated with topical tripsor PUVA - a lotion is applied on the affected areas 10 minutes before UVA exposure.
Photoadduct representation with DNA

- **Intercalation**

- **Monofunctional adduct (3, 4 with pyrimidine base)**

- **Bifunctional crosslinked adduct (3, 4 and 4’, 5’ with pyrimidine bases)**
PUVA-therapy to treat cancer

Centrifugation.

Separate white blood cells.

Drug in saline + Leukocytes.

Irradiate in the machine.

Collect white blood cells.
How a single treatment can activate the immune system in the protection against a dangerous cancer and suppress T cell activity in autoreactive disorders?

Photodynamic therapy

- Photodynamic therapy first used in 1978.
- There is currently one photodynamic drug available on the market: Photofrin™
- Approved for the treatment of esophageal and lung cancers.

![Chemical structures of Porphyrins, Chlorins, and Phthalocyanines](image-url)
How does photodynamic therapy work?

- PDT requires sensitizer, light and oxygen in the target tissue.
- Light generates reactive oxygen species.
- Reactive oxygen species can kill targeted cells either by necrotic mechanisms or by initiating the apoptotic cascade.

Ideal wavelength 650nm
Many tumours have higher lipid content than normal cells, facilitating the uptake of lipophilic compounds such as photosensitizers.

ALA (5-amino levulinic acid) - PDT

In 1999, FDA approved ALA-PDT for the treatment of actinic keratoses.

**Normal Process**
Controlled synthesis of 5-ALA through feedback inhibition of the enzyme.

- ALA-Synthase
- PBG-Deaminase
- Ferrochelatase

**Levulan Process**
Exogenous 5-ALA bypasses feedback mechanism and results in the accumulation of PpIX

- ALA-Synthase
- PBG-Deaminase
- Ferrochelatase

**Present in lesser amounts in cancer cells**
PHOTODYNAMIC THERAPY - Cell destruction

- necrosis
- ER
- mitochondrion
- DNA cleavage
- caspase activation
- cytochrome c
- protein cleavage
Current PDT applications in dermatology

- Actinic keratoses: Clinical response of 80%-100%.

- Squamous cell carcinoma: Clinical response 67-92%. 100% curable at early stage.

- Basal cell carcinoma: 100% curable even in advanced stages.

- Mycosis fungoides-cutaneous cancer: ALA application was successfully used.
Photoablation and Lasik Surgery

Discovery in 1981
US FDA approval in 1995
Inducted into US Inventors Hall of Fame in 2002
Light must be focused precisely on the retina for one to see an image clearly.

The light is focused by the eye through a process called refraction.

Refractive Errors
Myopia (Nearsighted)
Hyperopia (Farsighted)
Astigmatism
Photoablation with Excimer Lasers

Short wavelengths of light (190 to 300 nm) breaks molecular bonds (ablation)

Photablation with eximer laser (eg: ArF, KrF) can be done with a micron accuracy.

Refractive surgeries

PRK – Photorefractive keratotomy
LASIK – Laser assisted insitu keratomileusis
Photorefractive Keratectomy

- Cornea reshaped precisely with excimer laser, treatment is given on the corneal surface
- PRK works for myopia, hyperopia and astigmatism but not for astigmatism with hyperopia
- Healing time is relatively longer
- Used for people whose cornea epithelium is too thin to create a flap
How LASIK differs from PRK?

- LASER In-situ keratomileusis (LASIK)
  - First step is the lifting of corneal flap and then ablation
  - Treatment is given beneath the flap

- Brief recovery time
- Very low infection risk and low enhancement rate
- Very low risk of scarring and minimal discomfort
Applications of Photolithography

Future Light

Arunkumar Natarajan
Photolithography: First Invention 1949-50

Kodak’s Louis Minsk Invents Negative Photoressist Polyvinylcinnamate

Kalle Company’s (today Celanese) Otto Suess Invents Diazoquinone Based Positive Photoressist

DuPont’s Louis C. Plambeck Invents Photoinitiated, Acrylate-Based Photopolymer Relief Imaging
Photoresist

Undergoes a chemical reaction only upon exposure to light.

Principle

Create a difference between light exposed and unexposed regions.

Types of photoresist

- Positive – unexposed regions are retained
- Negative resist – exposed regions are retained
Two Types of Resists

**Positive Photoresist**

![Chemical structure of positive photoresist]

**Negative Photoresist**

![Chemical structure of negative photoresist]
Applications of the Principles of Photoresists and Lithography

*The Workhorses of Electronics and Printing*

- Printing, Litho, Package, Billboards
- Color Printing
- Printed Circuit Boards (PC)
- Integrated Circuit Chips (IC)
- Photopatterning-DNA and Biochips
- Micromachines
Lithography Principles
*Imagewise Polymerization - Analog or Digital*

- Light Source
- Laser
- Precision Pattern Master
- Photopolymer Layer
- Substrate
Lithographic Printing Is the Backbone of Modern Printing Industry
Gray Shading
Three Color Printing

- Color Printing Requires Color Separation
- Color Printing is Done Through Four Color Processing

Yellow  Magenta  Cyan  Overlay of the three
Printed Circuit Board Making
From Sand to Computer Chips
Photo Patterning-DNA Chip

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Biosensors Based on Photopatterning

Optical micrograph of an array of cells formed using microcontact printing.

Polyethylene glycol polymer arrays formed using mid-UV photolithography.

Applications

- blood glucose measurements for diabetes management
- testing food for the presence of pathogenic microorganisms (**Salmonella** and **E. coli**)
- sensing chemical and biological warfare agents
Photochemical synthesis of Rose oxide

Photochemical synthesis of Vitamin – D

Photooximation - Synthesis of caprolactam

Photochlorination

Light in Industry

J. Sivaguru
Rose oxide

(4r,2s)-(-)-cis-roseoxide
floral green with clean sharp, light, rose green note, diffusive, strong (Matsuda); also has been described as powerful fruity.

Odor Threshold = 0.5 ppb

(4s,2r)-(+)-cis-roseoxide
herbal, green floral, hay green, earthy, heavy (Matsuda); also has been described as sweet, floral

Odor Threshold = 50 ppb
Schenk ‘ene’ - Reaction

\[
\text{Dye}^1 \xrightarrow{\text{fl.}} \text{Dye}^3 \xrightarrow{\text{hv}} \text{Dye} \xrightarrow{\text{Ph.}} \text{Energy Transfer} \xrightarrow{\text{ISC}} \text{Dye}^3
\]

\[
\text{1}^1\text{O}_2 \xrightarrow{\text{PPh}_3 \text{ or Na}_2\text{SO}_3} \text{OH} + \text{OOH} + \text{OH}
\]
1) \( \text{hv, Rose bengal, O}_2 \)

Citronellol is separated from citronella oil by fractional distillation.

\[ \text{-H} \rightarrow \text{Rearrangement} \]

\[ \text{Na}_2\text{SO}_3 \]

\[ \text{rose oxide} \]
Photograph of the cylindrical immersion type reactors used by Dragoco for the production of (-)-rose oxide

The reactor is about 3m tall, and is equipped with a 5 kW light source.
Exactly how vitamin D controls our mineral metabolism is unknown.

However, there are three classical target tissues for its biological actions:

a) intestine
b) bone
c) kidney

http://www.vitamind.com/whyimportant.htm
Vitamin D crystals
Commercially synthesized by Roche-Vitamins

Commercial production of vitamin D₃:

a) 7-dehydrocholesterol
   Extracted from animal skins (cow, pig or sheep) followed by an extensive purification.

b) cholesterol.
   Extracted from the lanolin of sheep wool and can be converted to 7-dehydrocholesterol.

At the present time almost all milk sold commercially in the United States has 400 IU of chemically synthesized vitamin D₃ added per quart.
The ring opening take place from the first excited singlet state

**R = C_{9}H_{17}**\hspace{1cm}**Ergosterol**

**R = C_{8}H_{17}**\hspace{1cm}**7-dehydrocholesterol**

**Ergosterol** \hspace{1cm} **7-dehydrocholesterol** \hspace{1cm} **Pre-vitamin-D_{2}**

**Ergosterol** \hspace{1cm} **7-dehydrocholesterol** \hspace{1cm} **Pre-vitamin-D_{3}**

Heat, moderate temperature \hspace{1cm} Vitamin D
Hydrogen migration

Pre-vitamin - D

Vitamin - D

7-dehydrocholesterol

R = C₉H₁₇  Ergosterol
R = C₈H₁₇  7-dehydrocholesterol within parenthesis

R  =  C
H
Ergosterol

Pre-vitamin - D

Tachysterol

R  =  C
H
OH
Sensitizer

**Benzopheonone**

- $E_T = 286.3$ KJ mol$^{-1}$
- (P-D/Tch) = 2.6

**Anthraquinone**

- $E_T = 260.8$ KJ mol$^{-1}$
- (P-D/Tch) = 2.1

**2-Naphthylphenylketone**

- $E_T = 247.8$ KJ mol$^{-1}$
- (P-D/Tch) = 1.5

**Benzil**

- $E_T = 22.5$ KJ mol$^{-1}$
- (P-D/Tch) = 1.8

**9-Fluorenone**

- $E_T = 222.8$ KJ mol$^{-1}$
- (P-D/Tch) = 4.4

**Benzanthrone**

- $E_T = 196.5$ KJ mol$^{-1}$
- (P-D/Tch) = 5.6

**7,12-Dimethylbenzanthrone**

- $E_T = 185.2$ KJ mol$^{-1}$
- (P-D/Tch) = 16.3

Initial ratio (P-D/Tch) = 0.5; solvent = ethyl ether.
Photo-oximation

- Photo-oximation is a special case of photo-nitrosylation.
- Accidentally discovered by Lynn in 1919.
- Important use in industrial application.
Photo-oxidation of cyclohexane - industrial synthesis of caprolactam

The first unit for the photo-chemical manufacture of cyclohexaneoxime was installed in Japan in 1963 by the Toyo Rayon Company.

\[ \text{Cyclohexane} \xrightarrow{\text{hv}} \text{Cyclohexaneoxime} \xrightarrow{\text{H}_2\text{SO}_4} \text{Caprolactam} \xrightarrow{} \text{Nylon 6} \]
Photo-oximation of cyclododecane – industrial synthesis of lauryllactam

ATO Chimie, a french company
Employed an analogous process for the industrial photo-chemical production of lauryllactam

Photochemical technology, Braun, A. M., Maurette, M-. T., Oliveros, E.
The new photochlorination plant will also produce

a) 15,000 tonnes of benzyl chloride and benzylidene chloride.

b) 7,000 tonnes of benzaldehyde.

These are some new addition to its range of synthetic organic products.

Investment, totals ~ FRF 170 million

New chlorinated toluene derivatives production unit, Capacity > 60,000 tonnes a year

Photomedicine

Lithography

Industrial Synthesis of Chemicals

Photography, Xeorography and Holography

TiO$_2$: Environmental Cleanup

Solar Energy Conversion

Sunscreen, Photochromic Glass

Photostabilization

Photocuring
“The rising sun is the giver of energy, heat, all powers, happiness and prosperity.”

Rigveda
2000-1500 BC