

Licht und Leben:

Von der Photosynthese

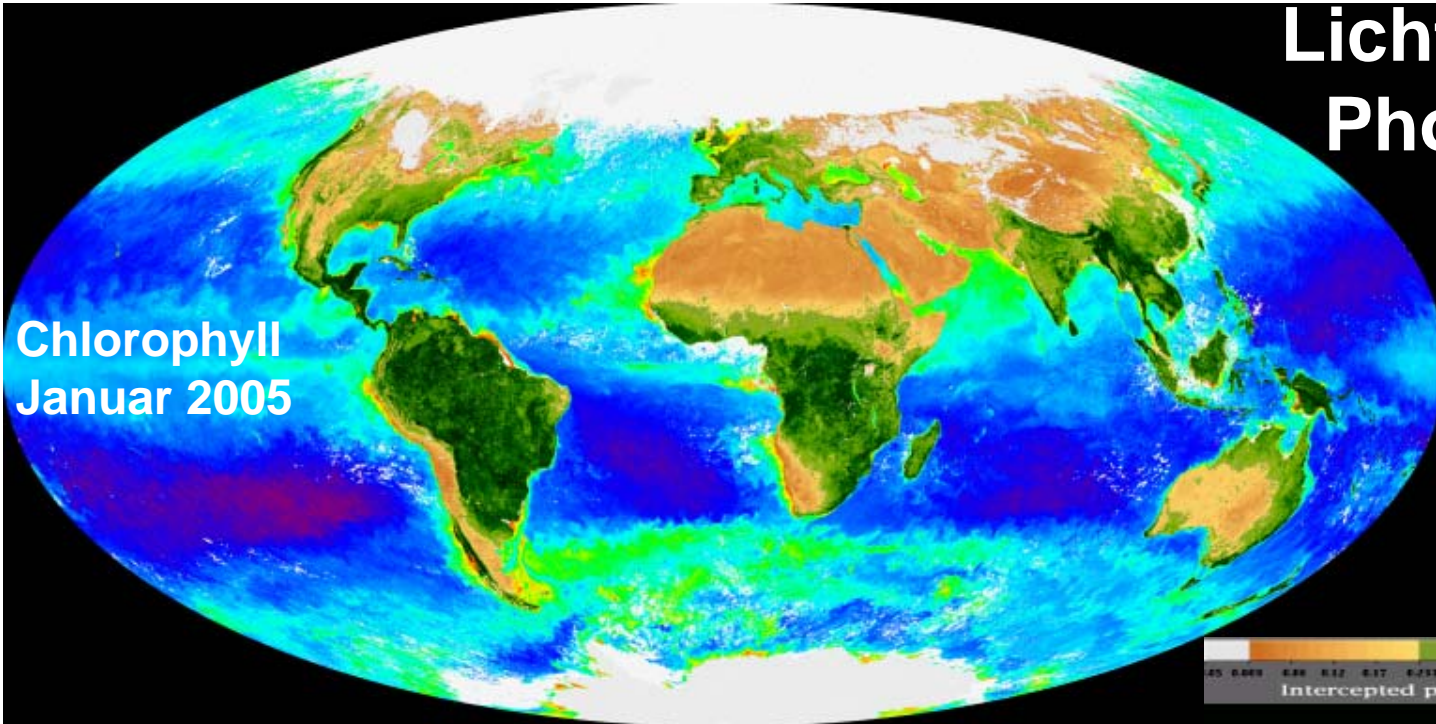
zur

Photodynamischen Therapie:

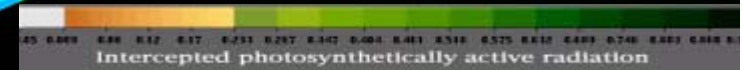
Hugo Scheer

Licht als Energie: Photosynthese

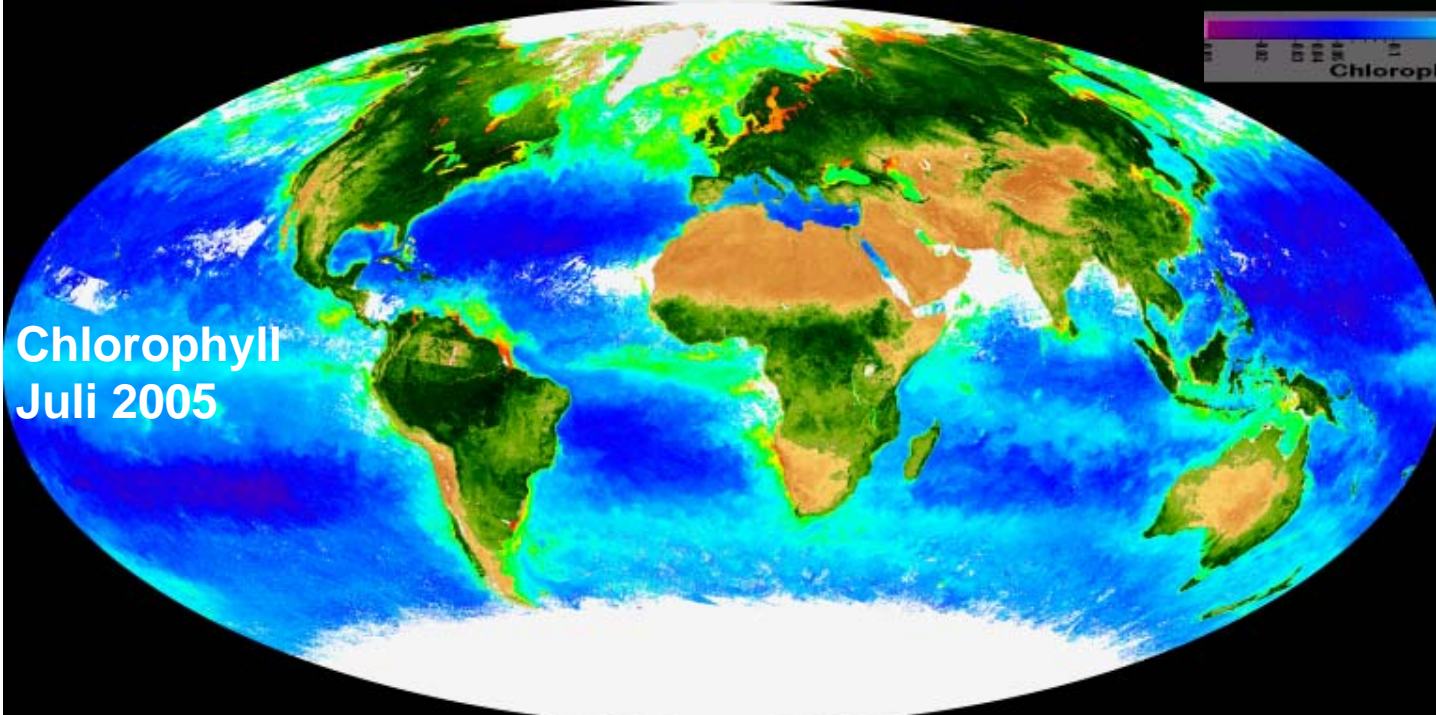
Chlorophyll
Januar 2005



Land



Chlorophyll
Juli 2005



Sea

Scheer, Jan 05
Thanks to Norman Kuring
(norman@seawifs.gsfc.nasa.gov)
and Compton Tucker
(compton@ltpmailx.gsfc.nasa.gov)

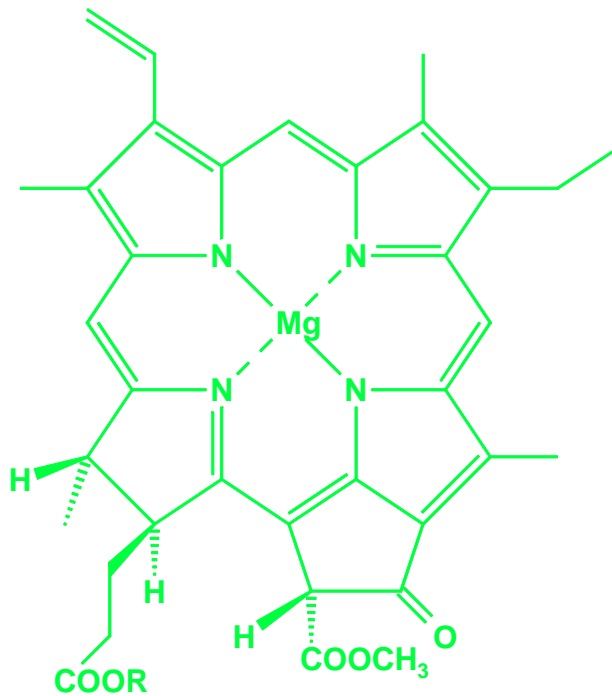
Department Biologie I - Botanik

Ludwig _____
Maximilians _____
Universität _____
München _____

LMU



Lebensdauer angeregter Zustände (1S)

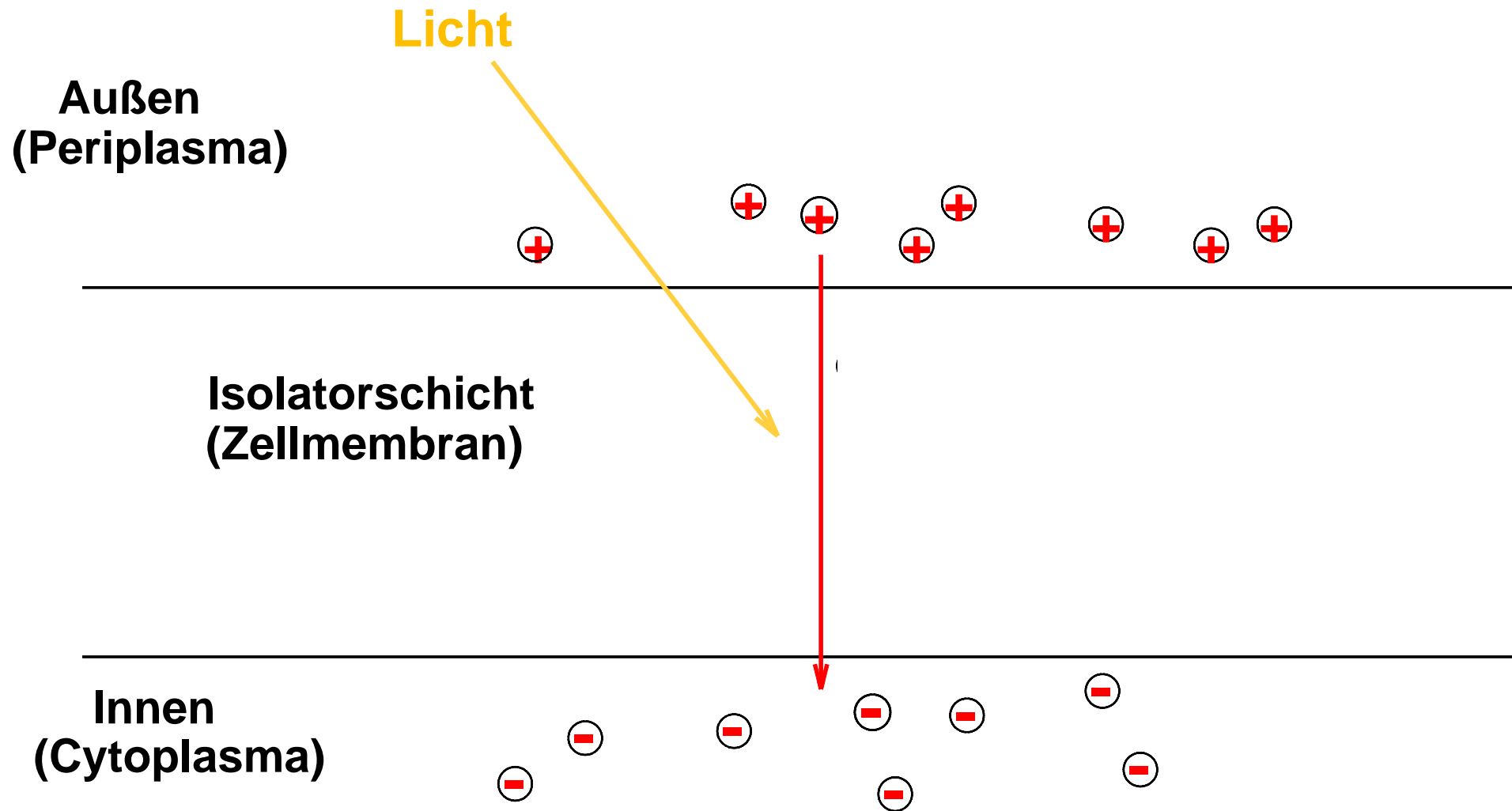


$\tau \approx 5 \text{ ns (0,000.000.005 s)}$

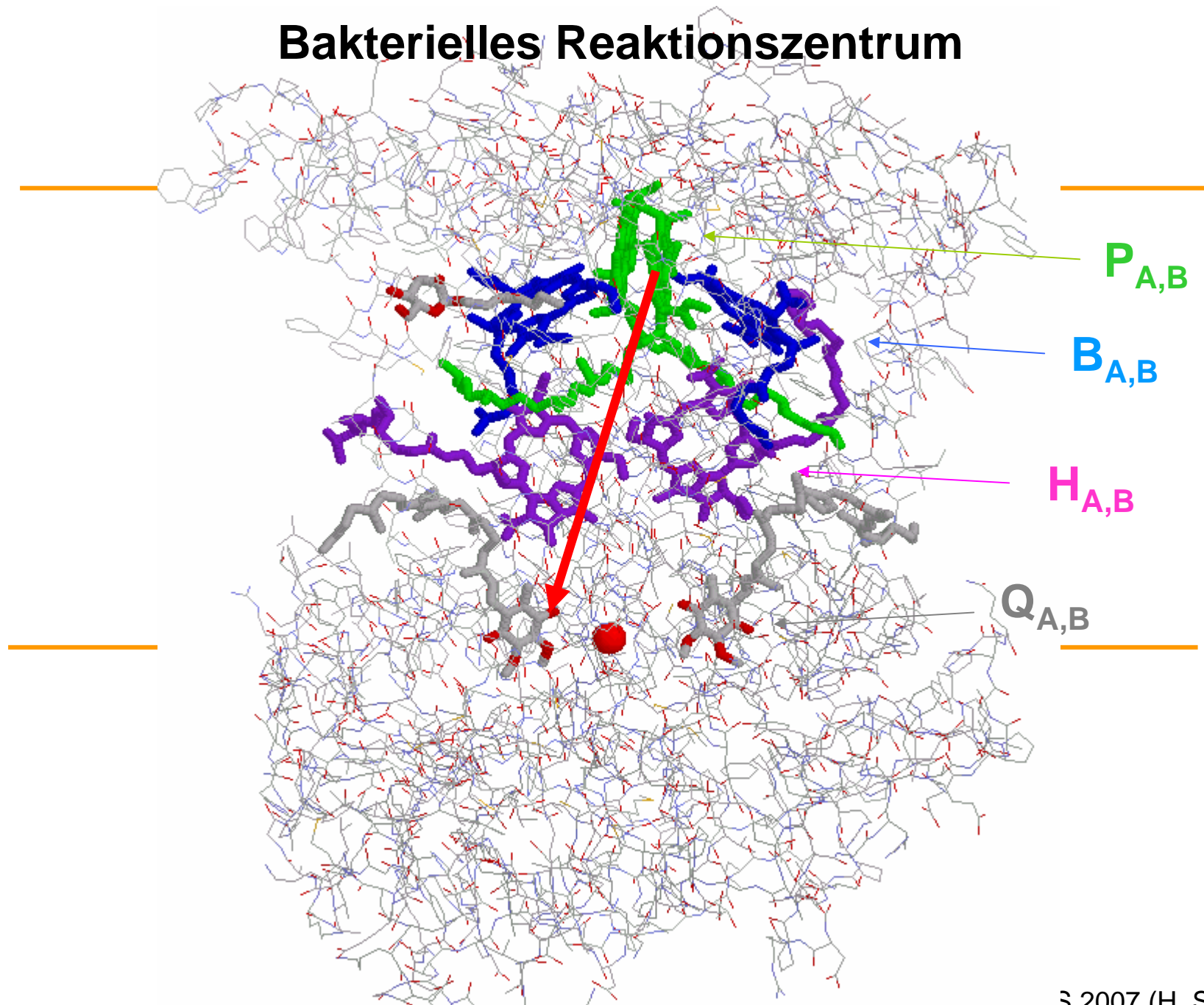


$\tau \approx 0,5 \text{ ps (0,000.000.000.000.5 s)}$

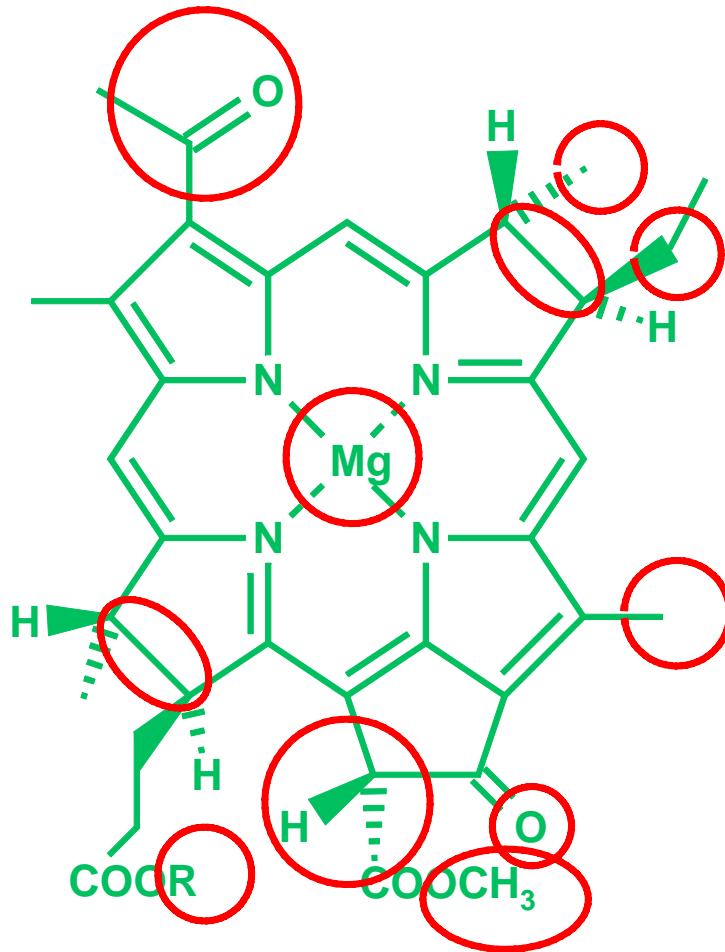
Primärreaktion der Photosynthese



Bakterielles Reaktionszentrum



Variable Strukturelemente in Chlorophyllen



Variable Eigenschaften

Redox Potential

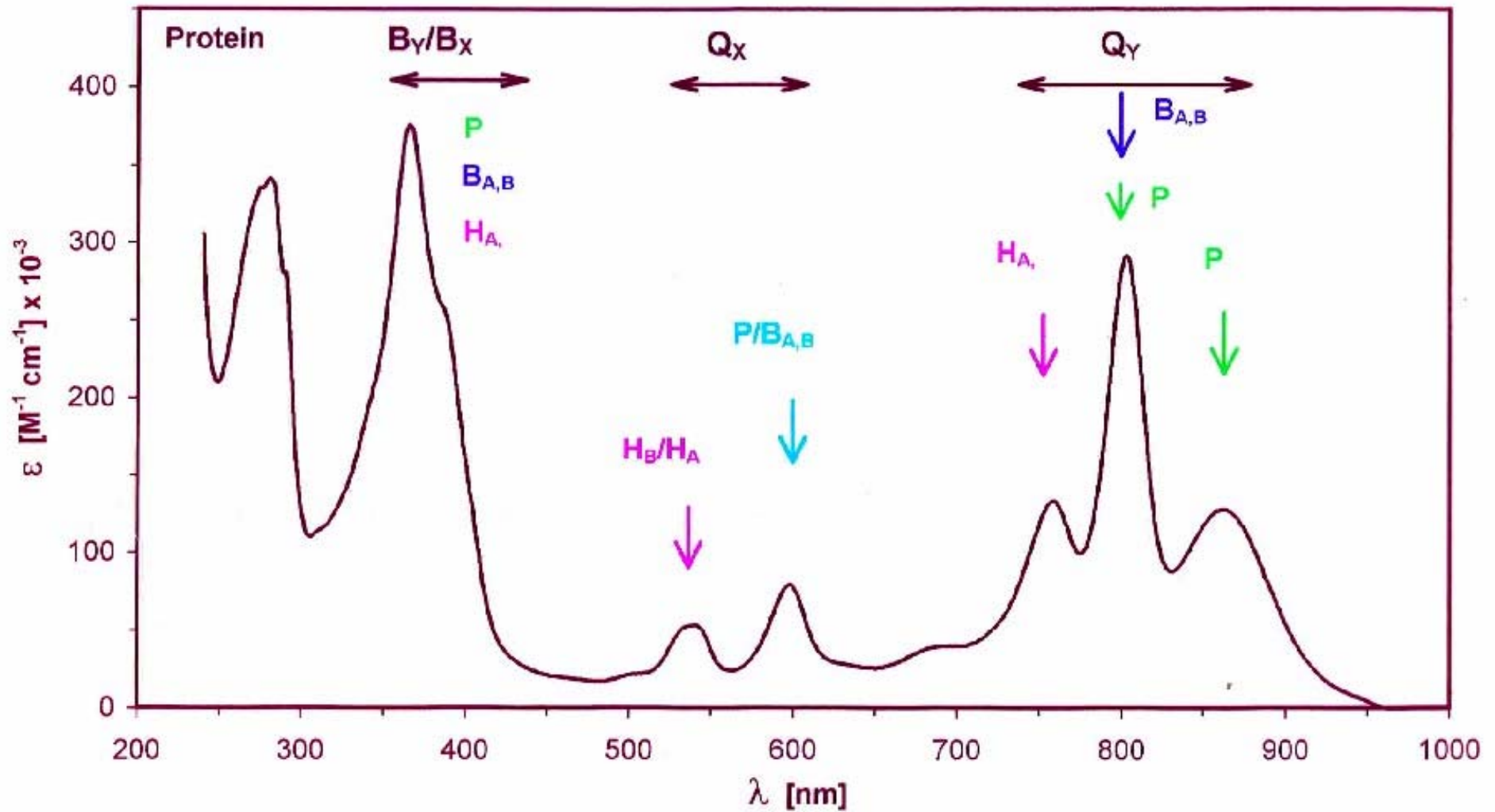
Anregungsenergie

Lebensdauer angeregter
Zustände

Wechselwirkungen mit
Protein

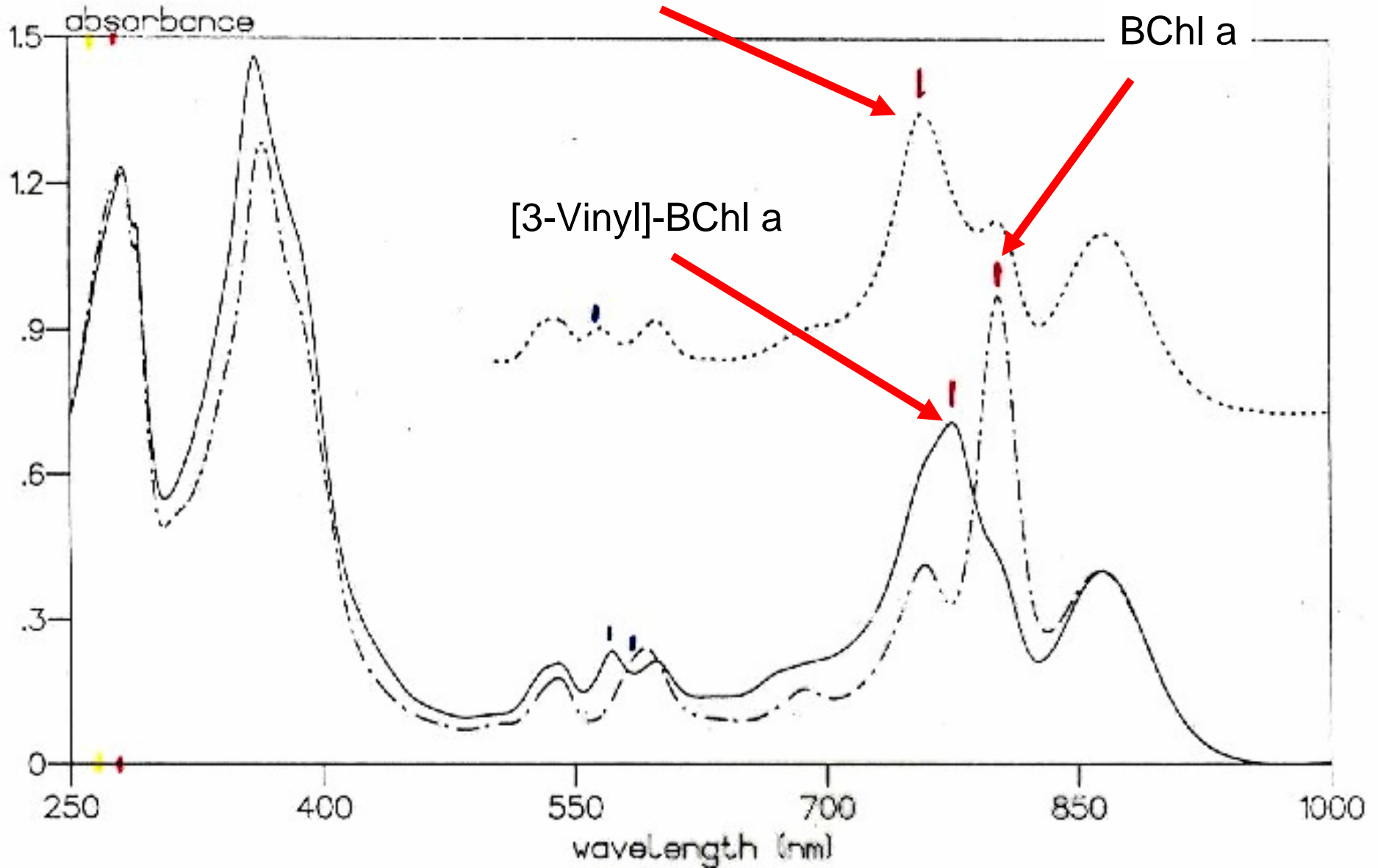
Senioren SS 2007 (H. Scheer)

Absorptionsspektrum des RC



Austausche von BChl – B_{A,B}

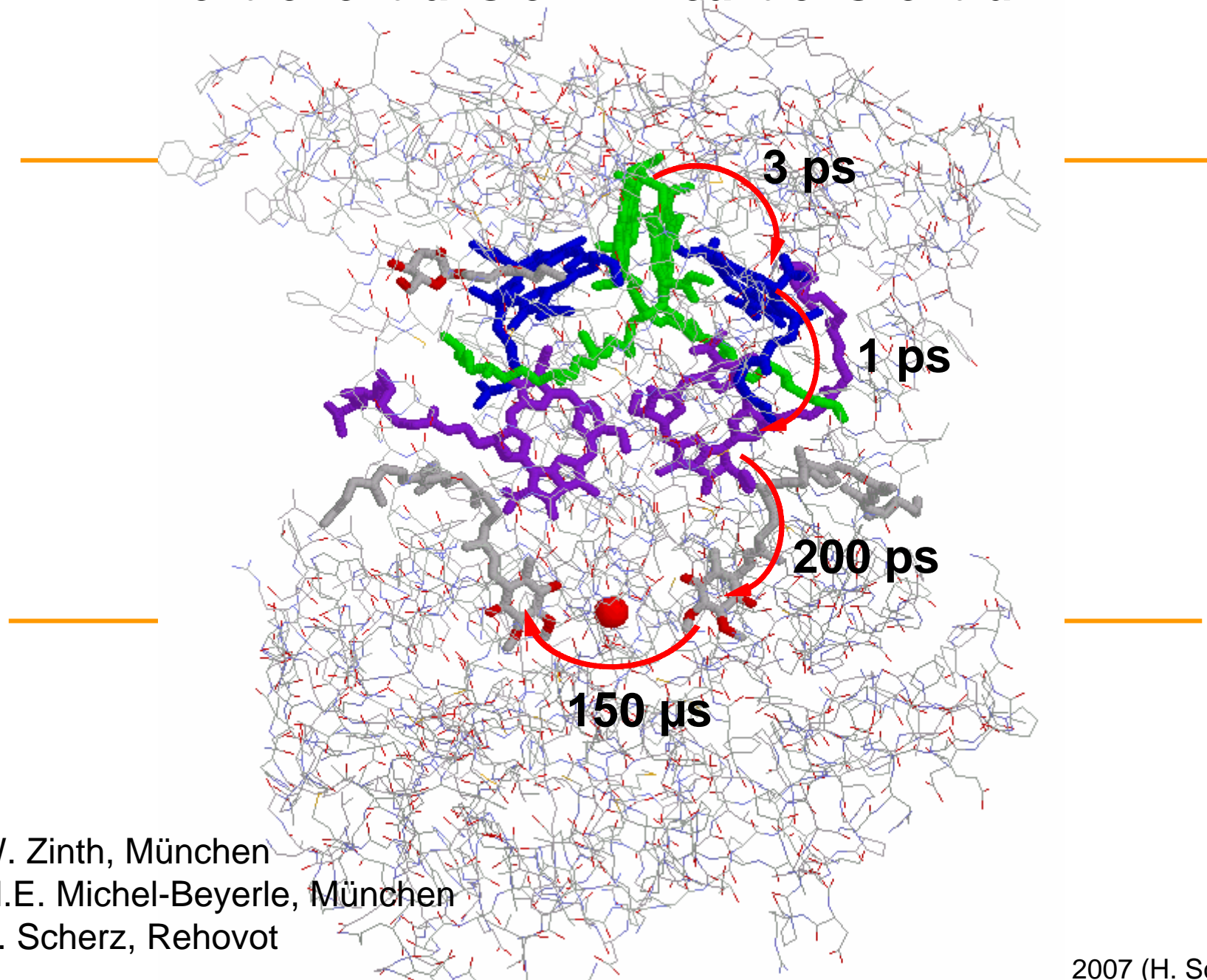
[3-Hydroxyethyl]-BChl a



**Keine starken (excitonischen)
Wechselwirkungen von BChl-B_{A,B}
mit dem „Special pair“ P_{A,B}
oder mit Bphe H_{A,B}**

**Obere Excitonenbande von P870 liegt bei
800 nm**

Elektronentransfer im Reaktionszentrum



W. Zinth, München
M.E. Michel-Beyerle, München
A. Scherz, Rehovot

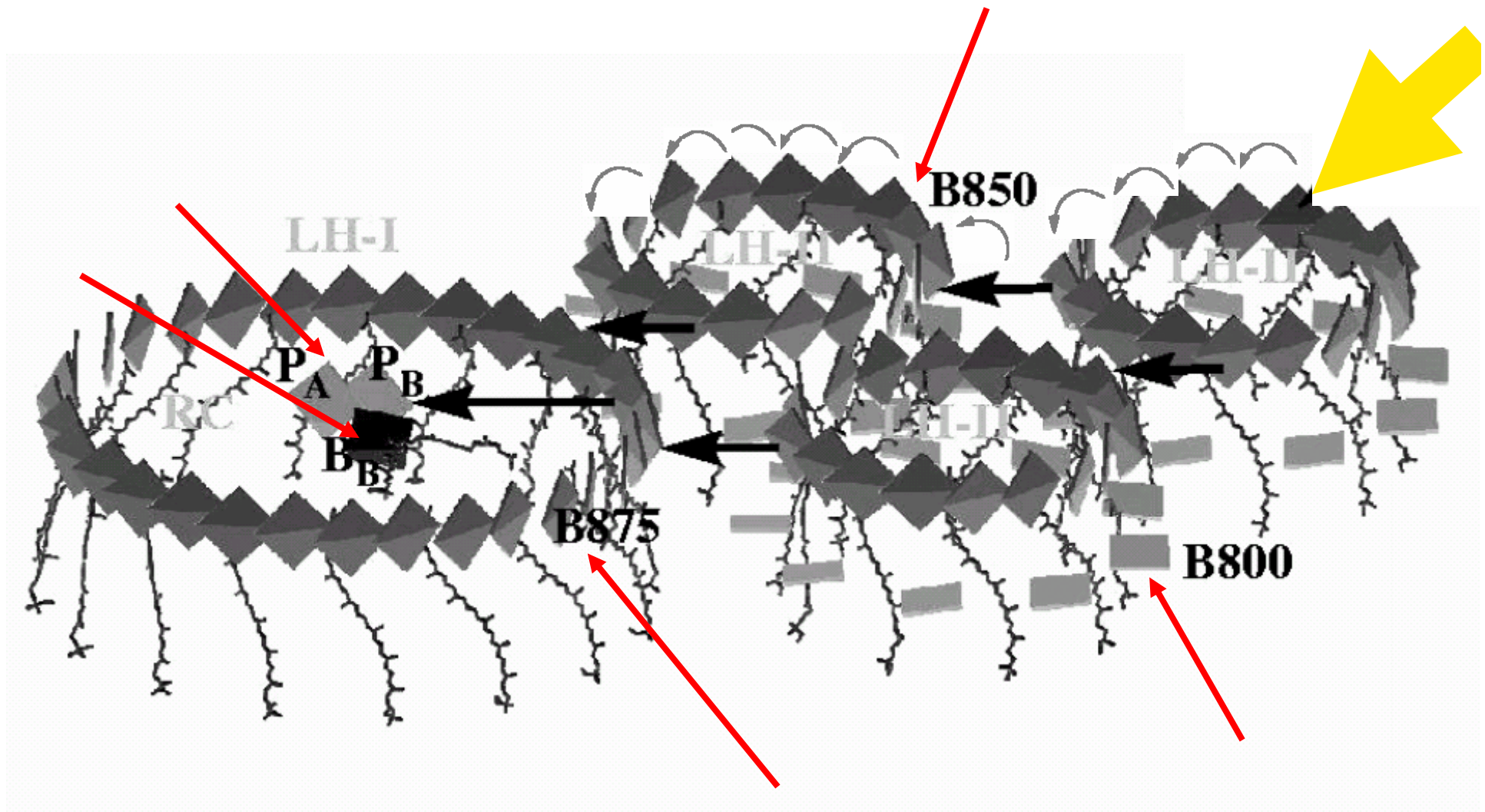
2007 (H. Scheer)

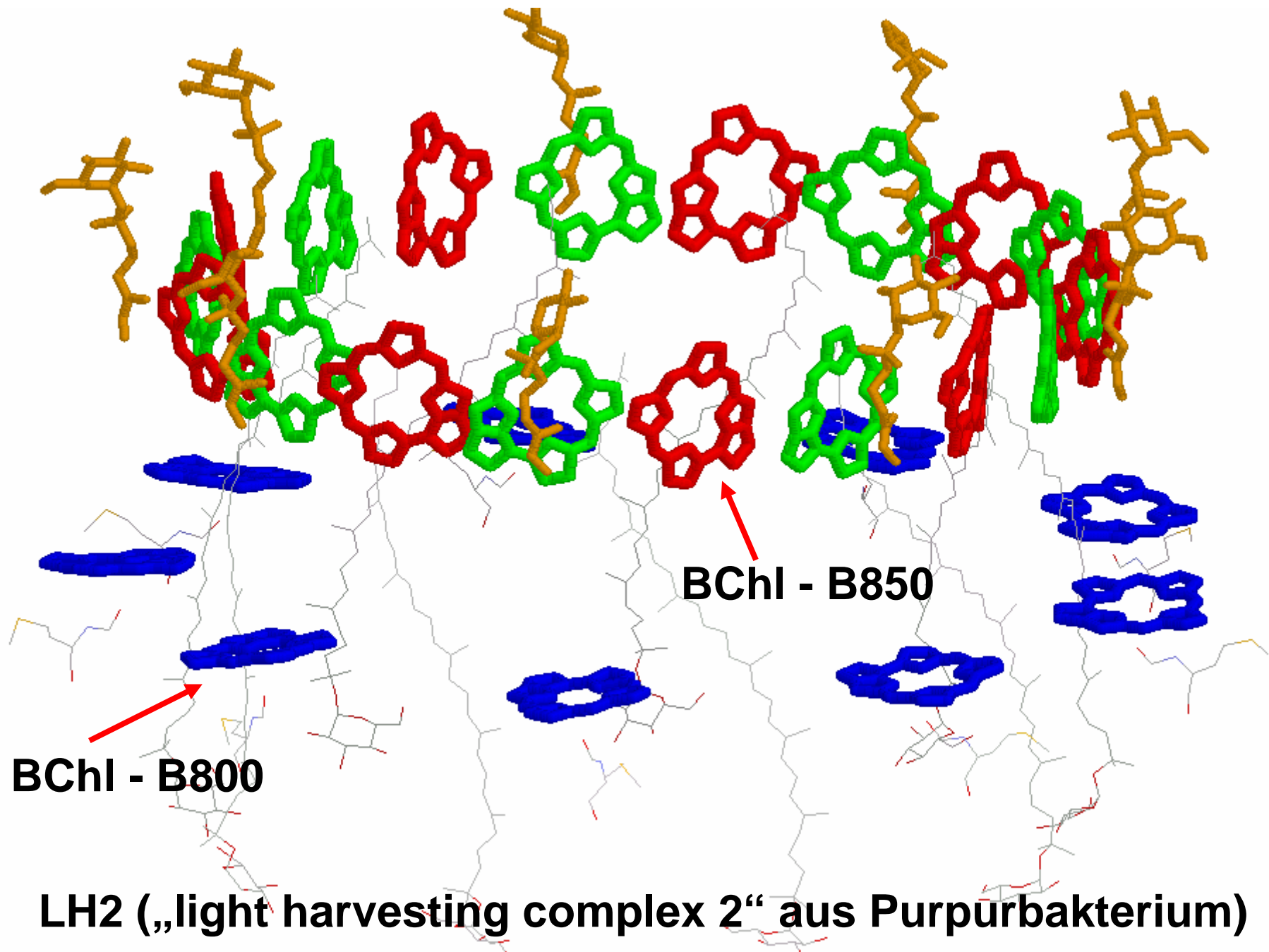
**Monomeres Bakteriochlorophyll B_A ist ein echtes
Intermediat beim Elektronentransfer**

>>>> Viele kleine Schritte verbessern die Effizienz

>>>> Nur der rechte Ast ist „produktiv“

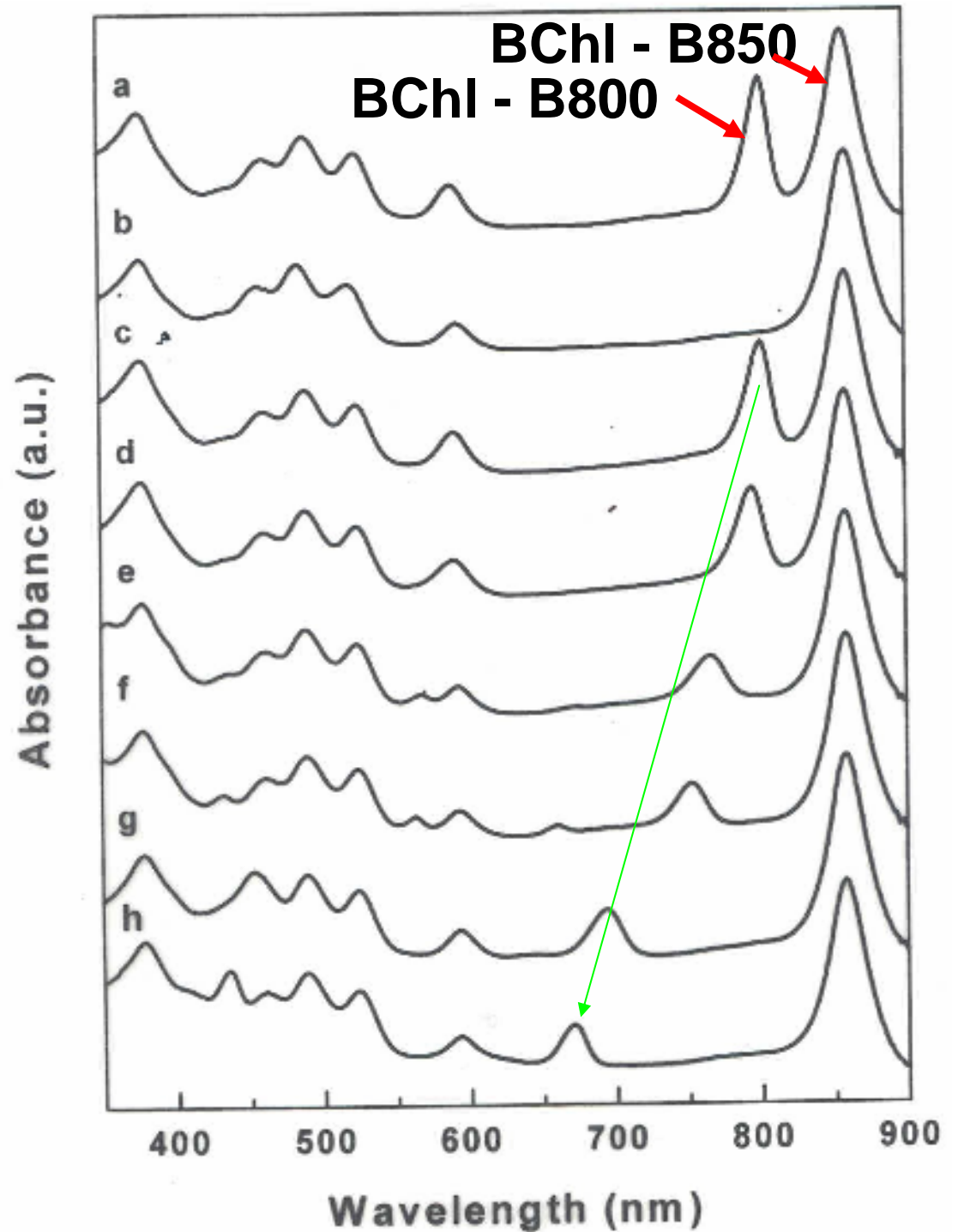
Modell des bakteriellen Photosynthese-Komplexes

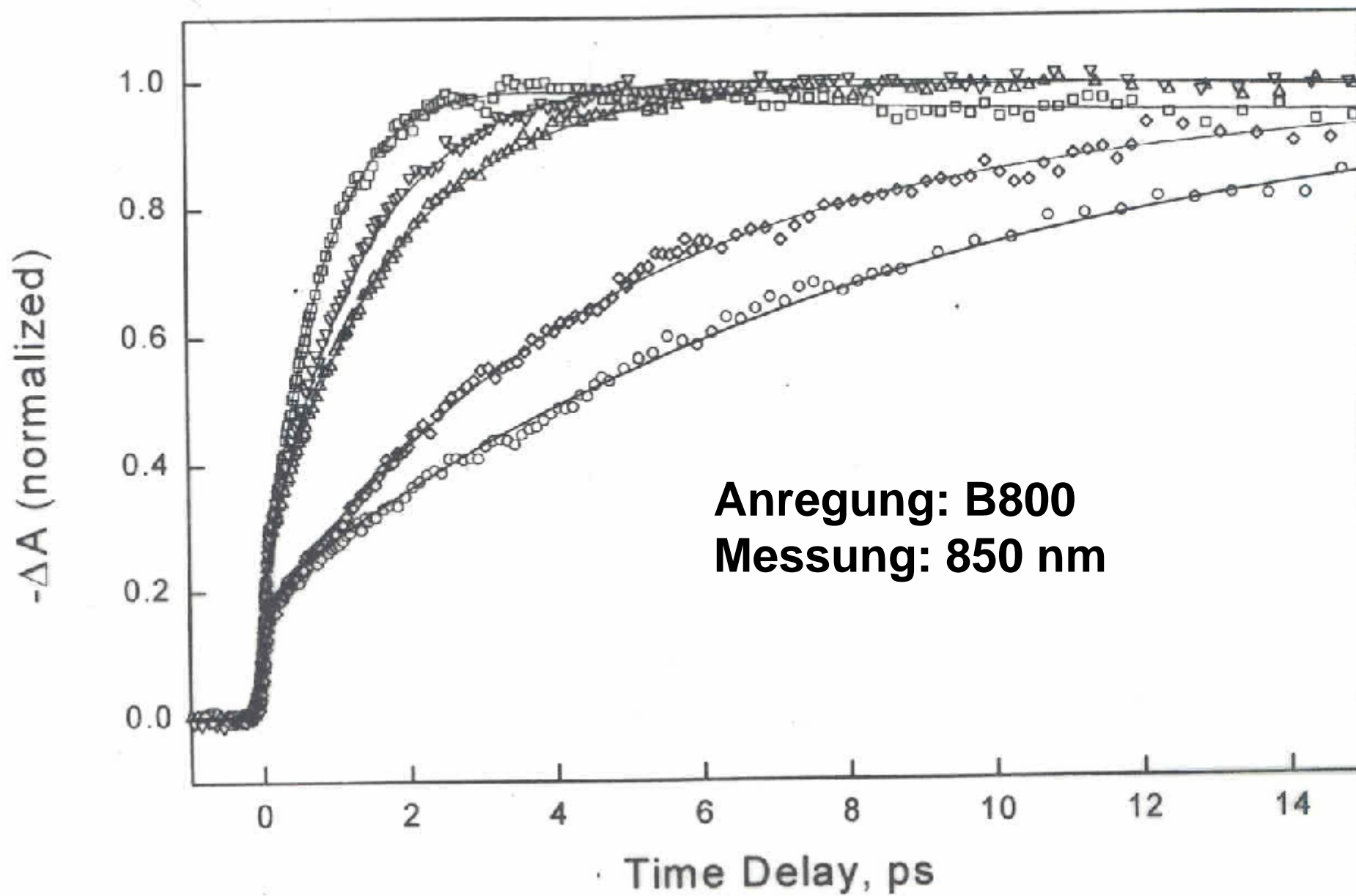


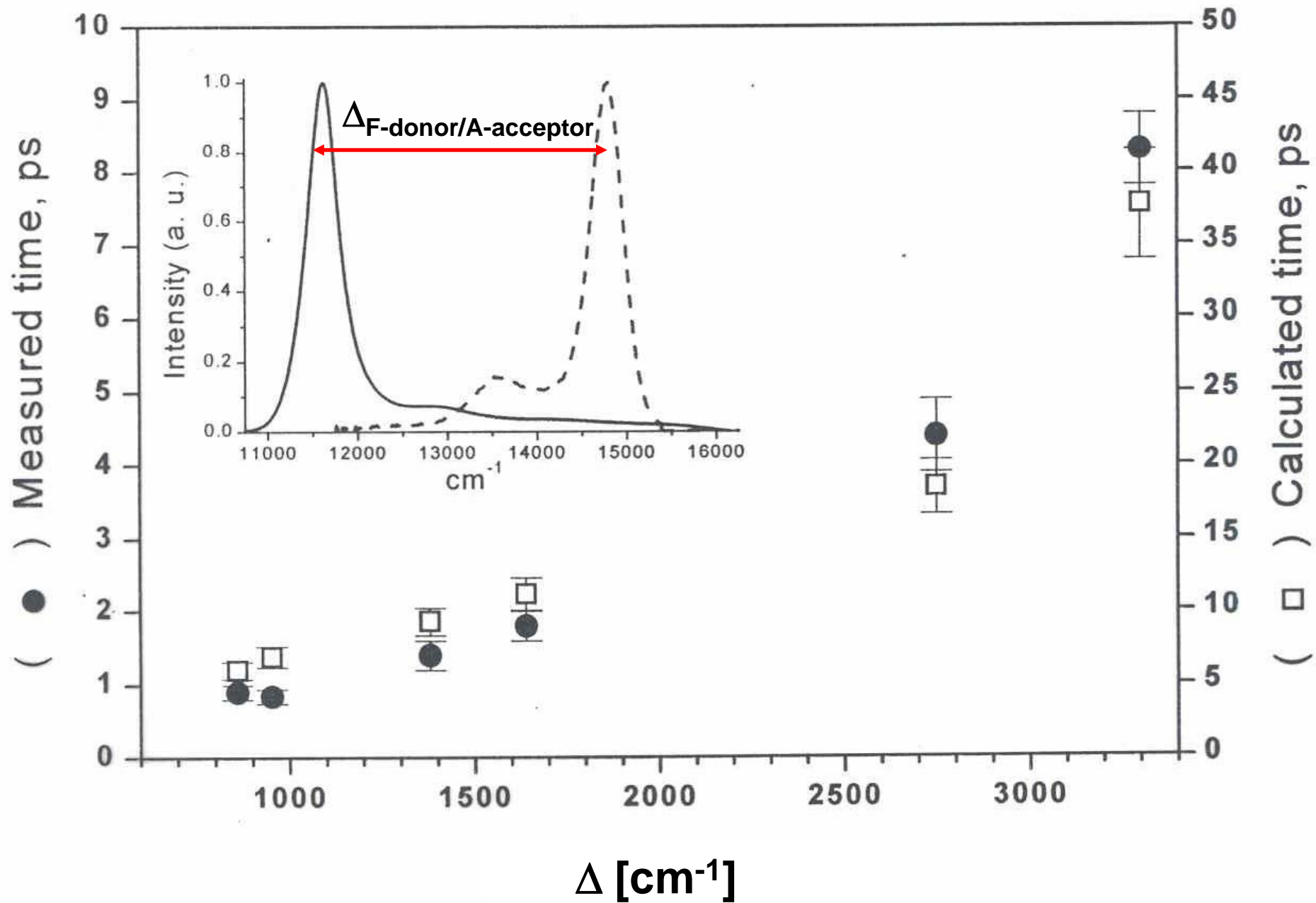


**Einbringen von modifizierten
Pigmenten in die
B800 - Bindungstasche**

R. Cogdell, Glasgow
J. Herek, Lund
D. Leupold, Berlin
L. Fiedor, Cracow







BChl-B800 ist in LH2 selektiv austauschbar

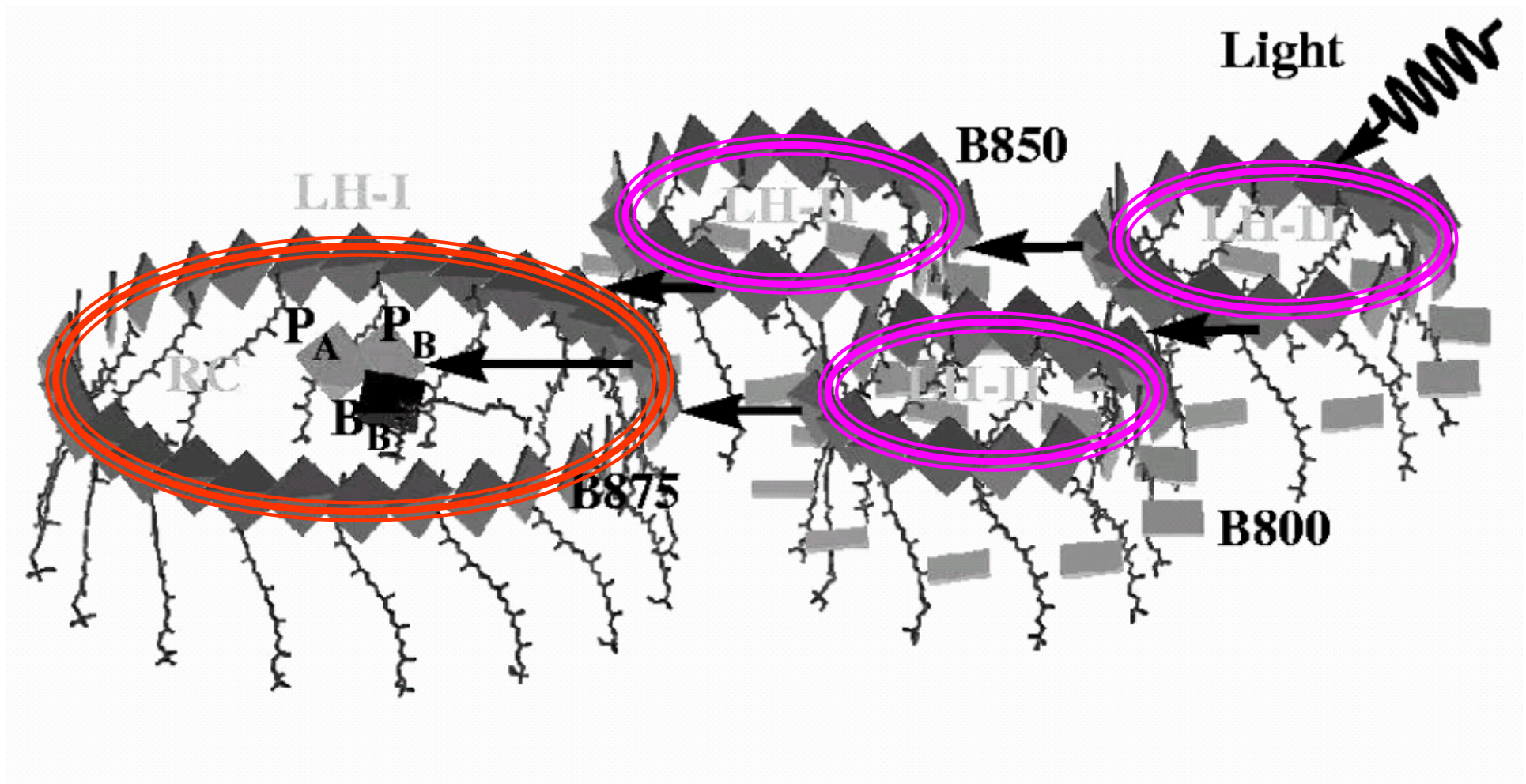
**Energieübertragung verlangsamt sich mit
Vergrößerung der Energielücke**

**Aber: Energieübertragung ist durchgehend um
Faktor 5 schneller als nach Förster berechnet**

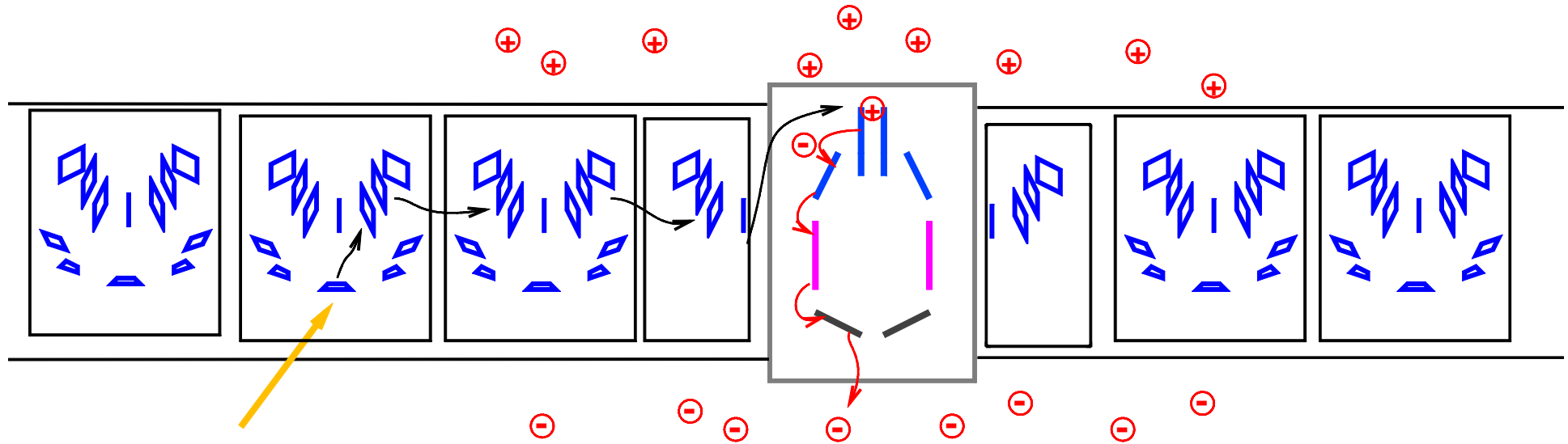
**Akzeptor ist ein „Supermolekül“
(Exciton) aus 16 BChl**

**Auch B870 in LH1 ist ein „Supermolekül“
(exciton) aus ~20 Bacteriochlorophyllen**

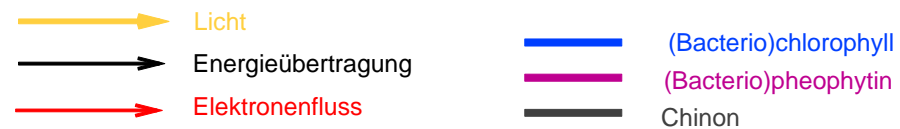
Modell des bakteriellen Photosynthese-Komplexes



Primärprozesse der Photosynthese

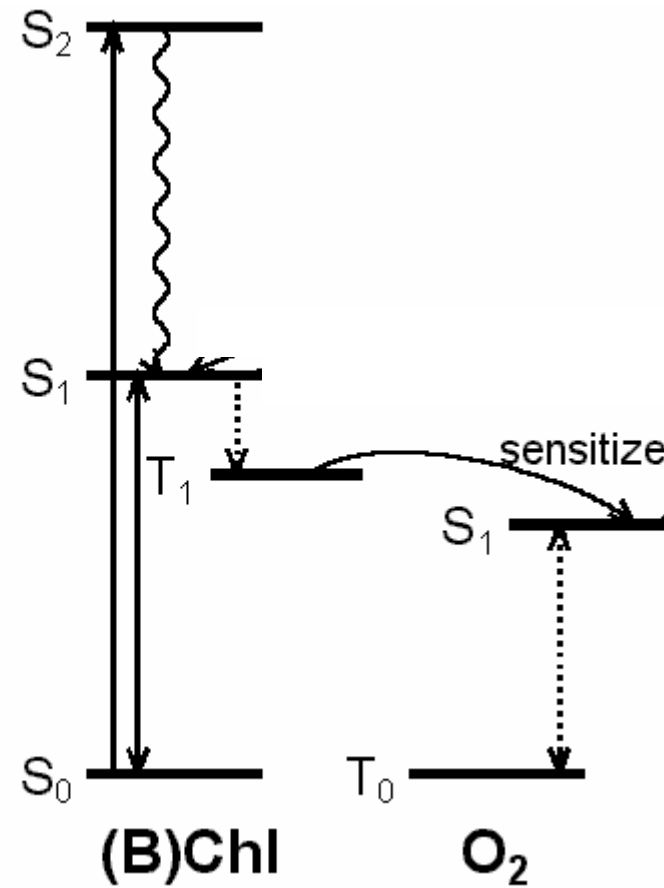


Elektronentransport im Reaktionszentrum



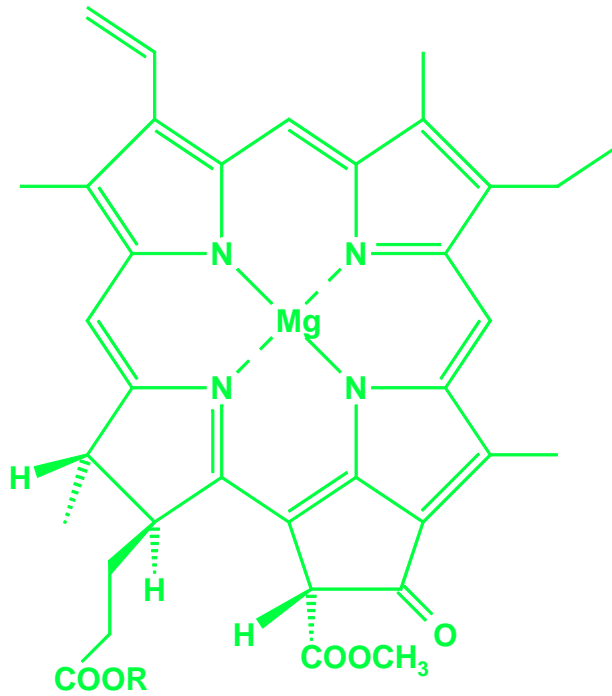
© H. Scheer
ps-membrane-Rc-schematisch.cdw

Jablonski Diagram zur $^1\text{O}_2$ Sensibilisierung



Gefahr

Lebensdauer angeregter Zustände (1S)

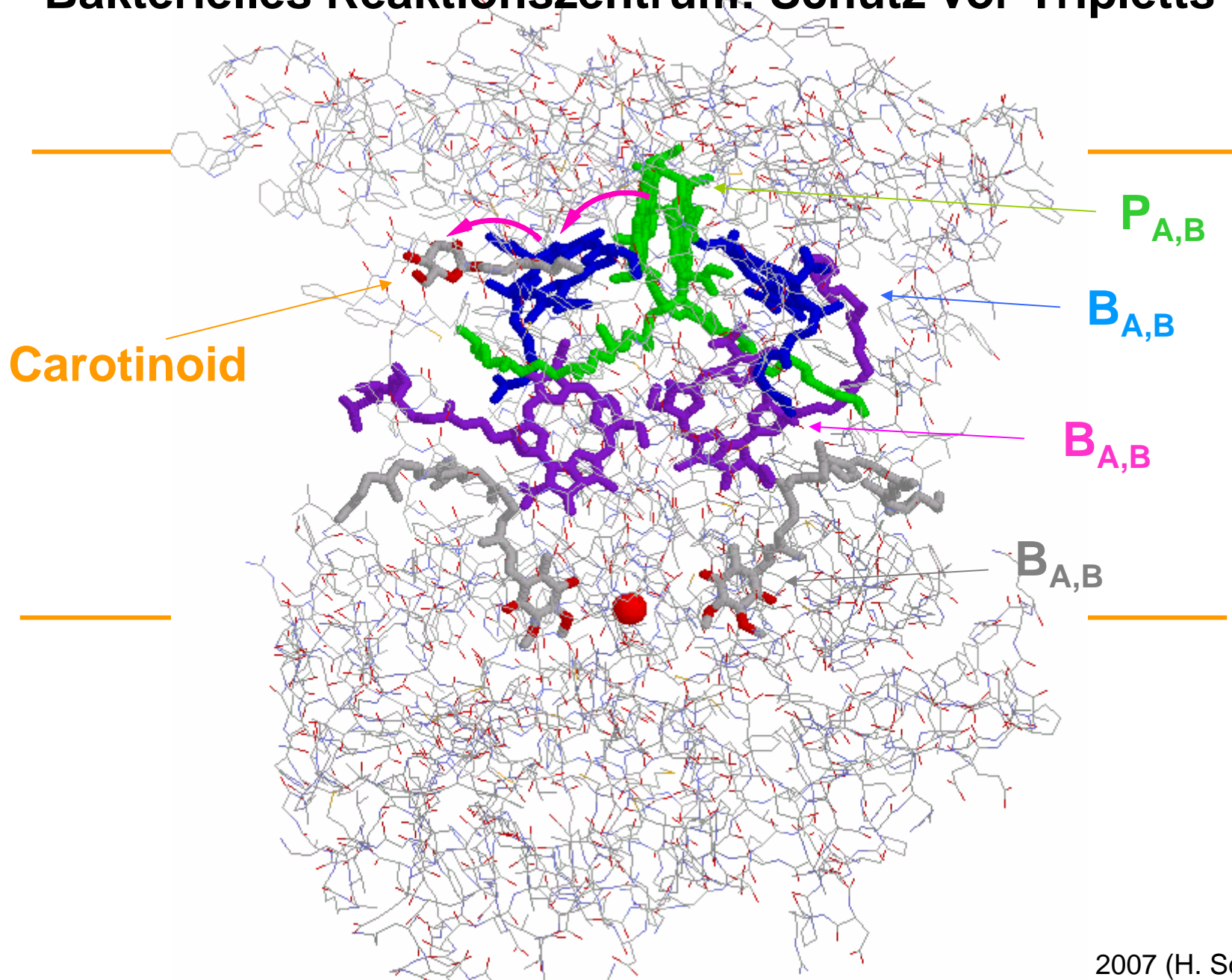


$\tau \approx 5 \text{ ns (0,000.000.005 s)}$



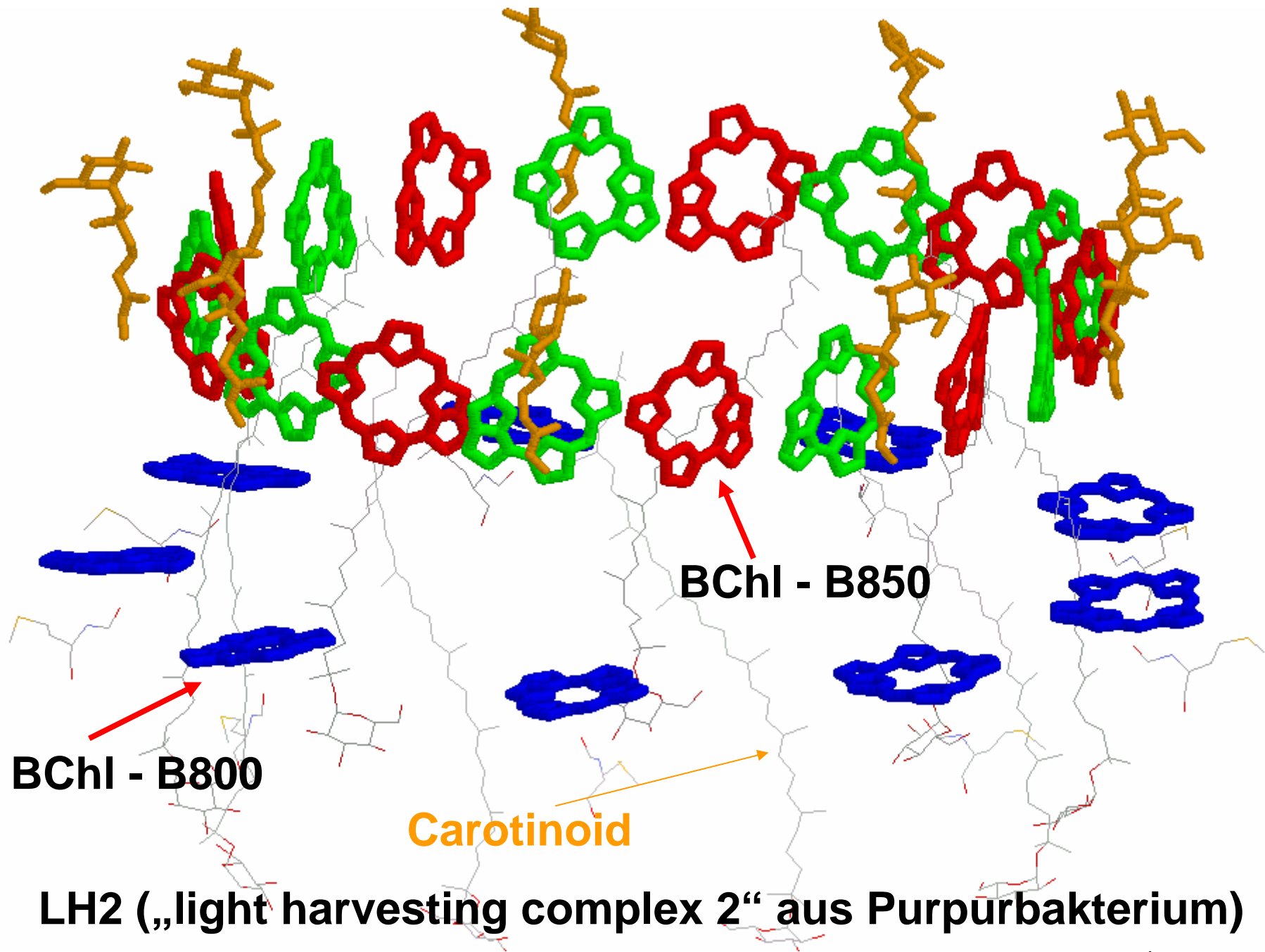
$\tau \approx 0,5 \text{ ps (0,000.000.000.000.5 s)}$

Bakterielles Reaktionszentrum: Schutz vor Triplets

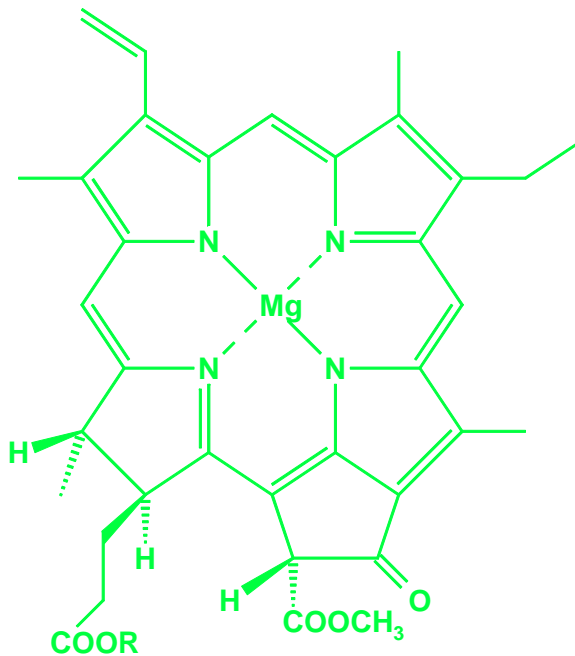


**Das symmetrisch positionierte B_B ist ein Intermediat
beim Triplett Transfer zum Carotinoid**

**>>>>> Rechter Ast ist „produktiv“,
linker Ast ist „Blitzableiter“**

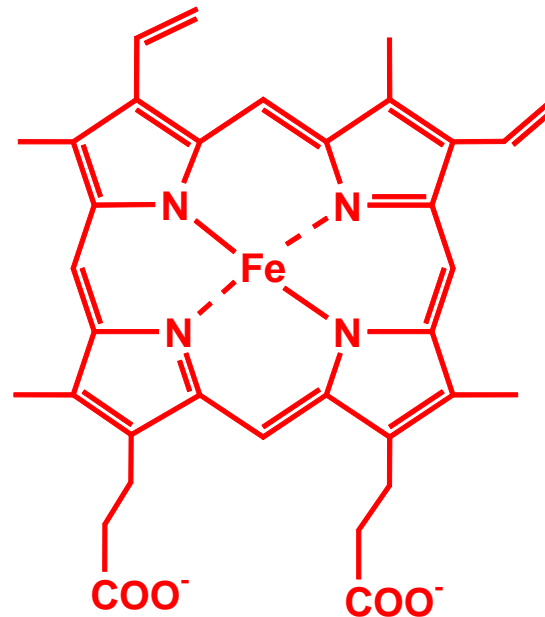


Lebensdauer angeregter Zustände (1S)



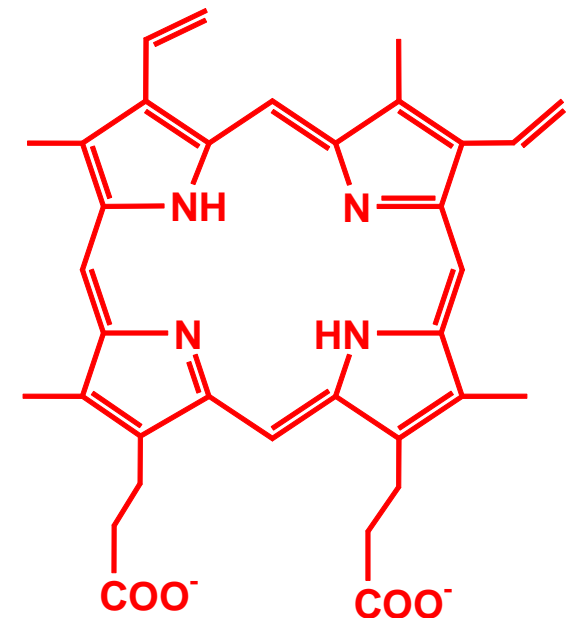
Chlorophyll

$\tau \approx 5 \text{ ns (0,000.000.005 s)}$



Häm

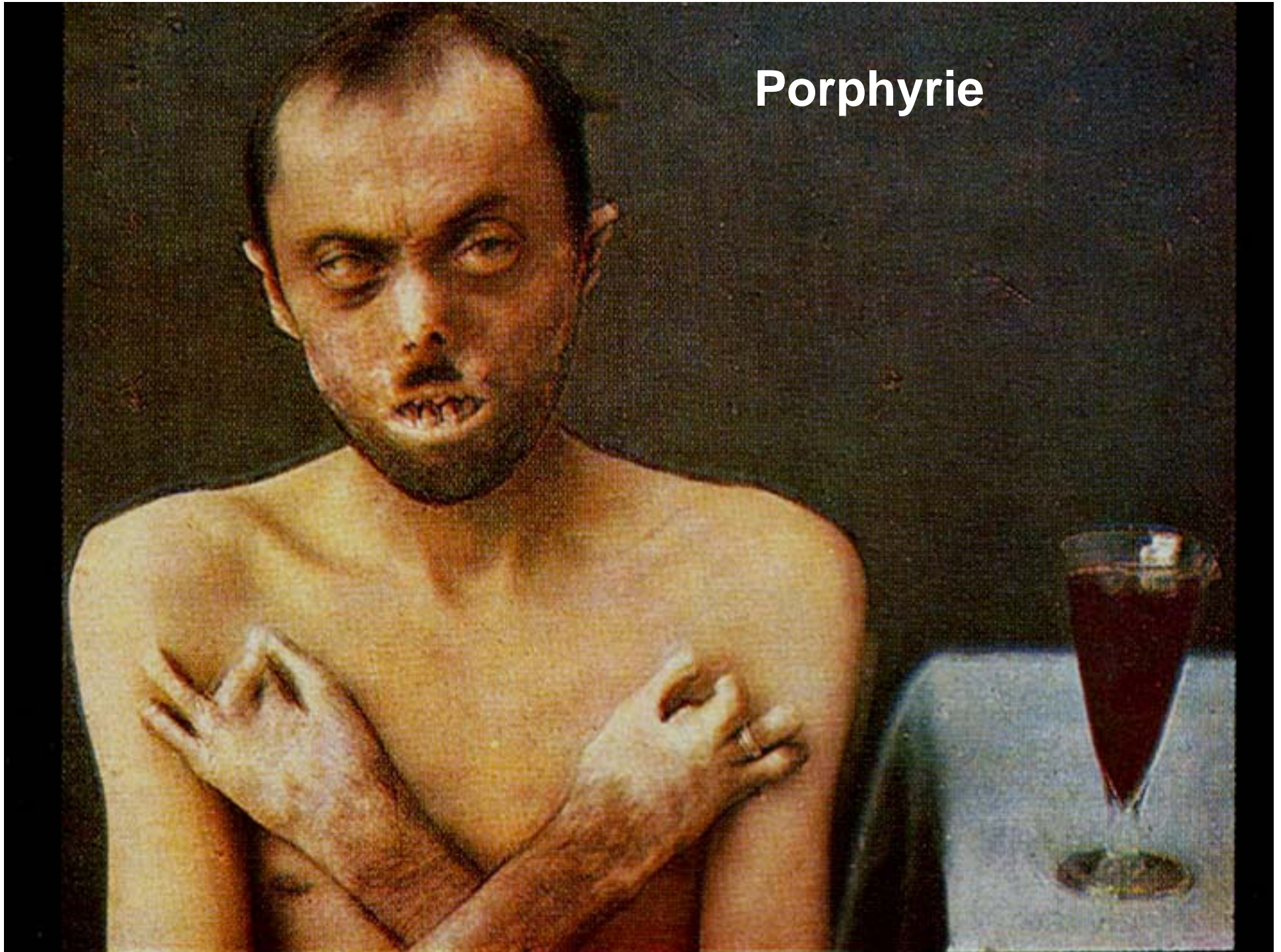
$\tau \approx 0,5 \text{ ps (0,000.000.000.000.5 s)}$



Protoporphyrin

$\tau \approx 5 \text{ ns (0,000.000.005 s)}$

Porphyrie



Photodynamischer Effekt

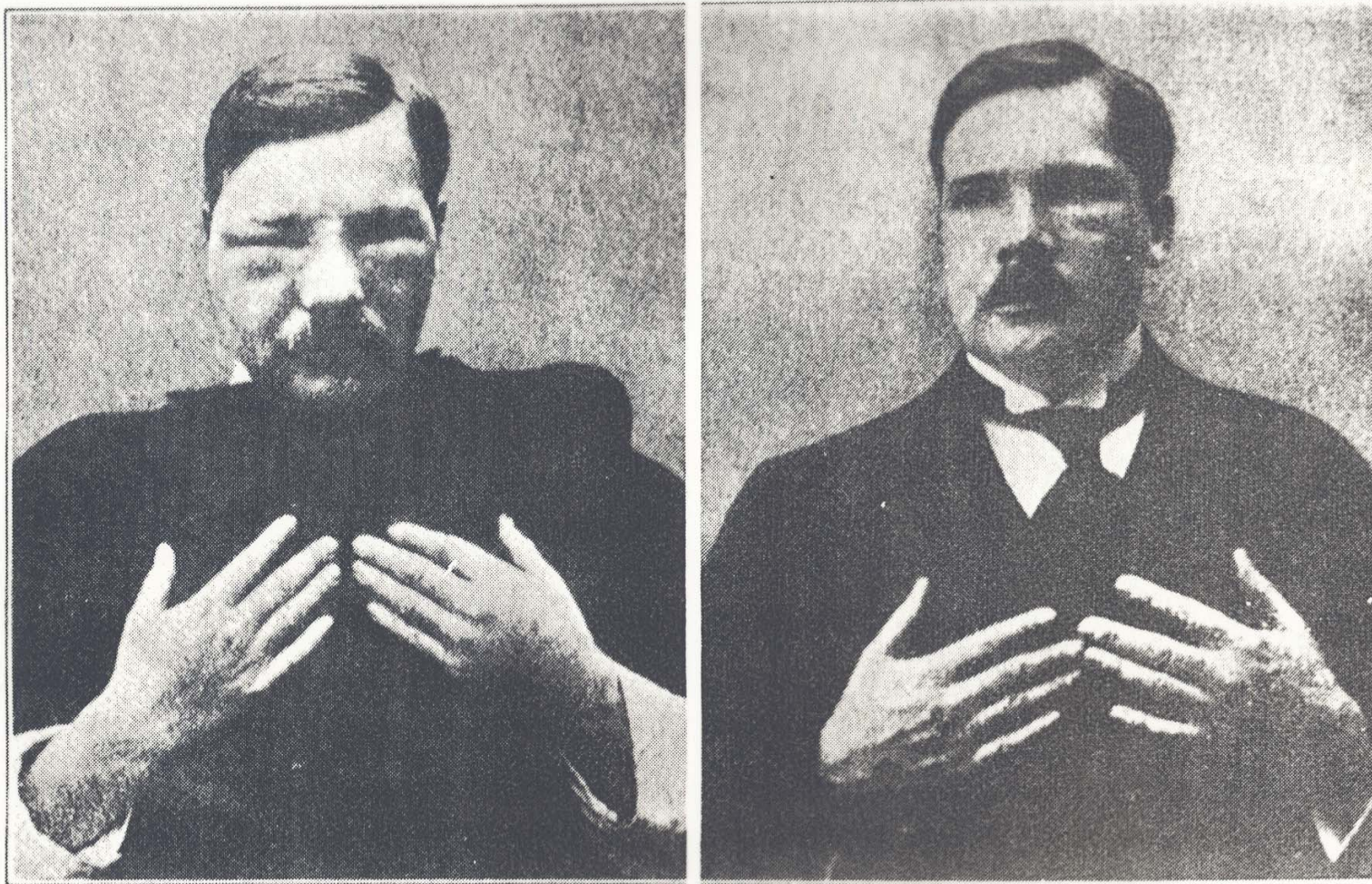
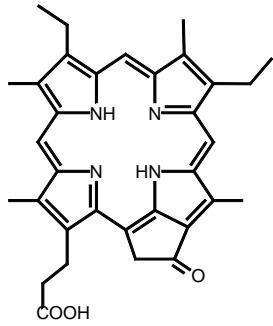
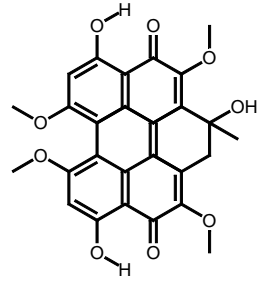


FIG. 10. Swelling observed on exposure to light after intravenous injection of 0.2 gm hematoporphyrin. Meyer-Betz, who performed this "Selbsversuch" on Oct. 14, 1912, was still sensitive to light at the beginning of December. By spring he was completely desensitized. (From Laurens, 1933, p. 496.)

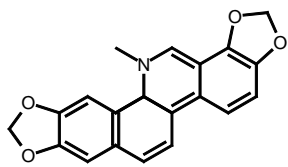
. Scheer)



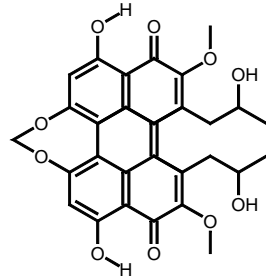
Phylloerythrin



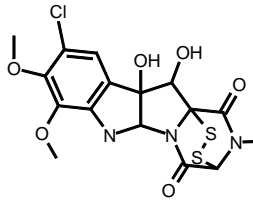
Hypocrellin (Hypocrella bambusae)



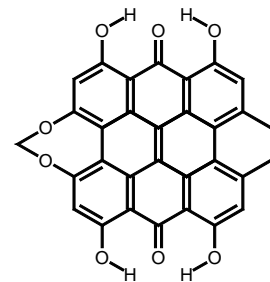
Saguinarin (Saguinaria canadensis)



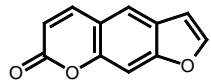
Cercosporin (Pilze)



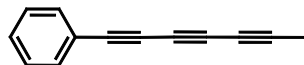
Sporodesmin (Pithomyces chartarum)



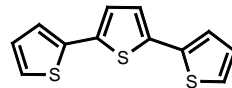
Hypericin (Hypericum perforatum)



Furocoumarine (Umbelliferen)



Polyacetylene (Compositen, Pilze)



Terthienyl (Tagetes)

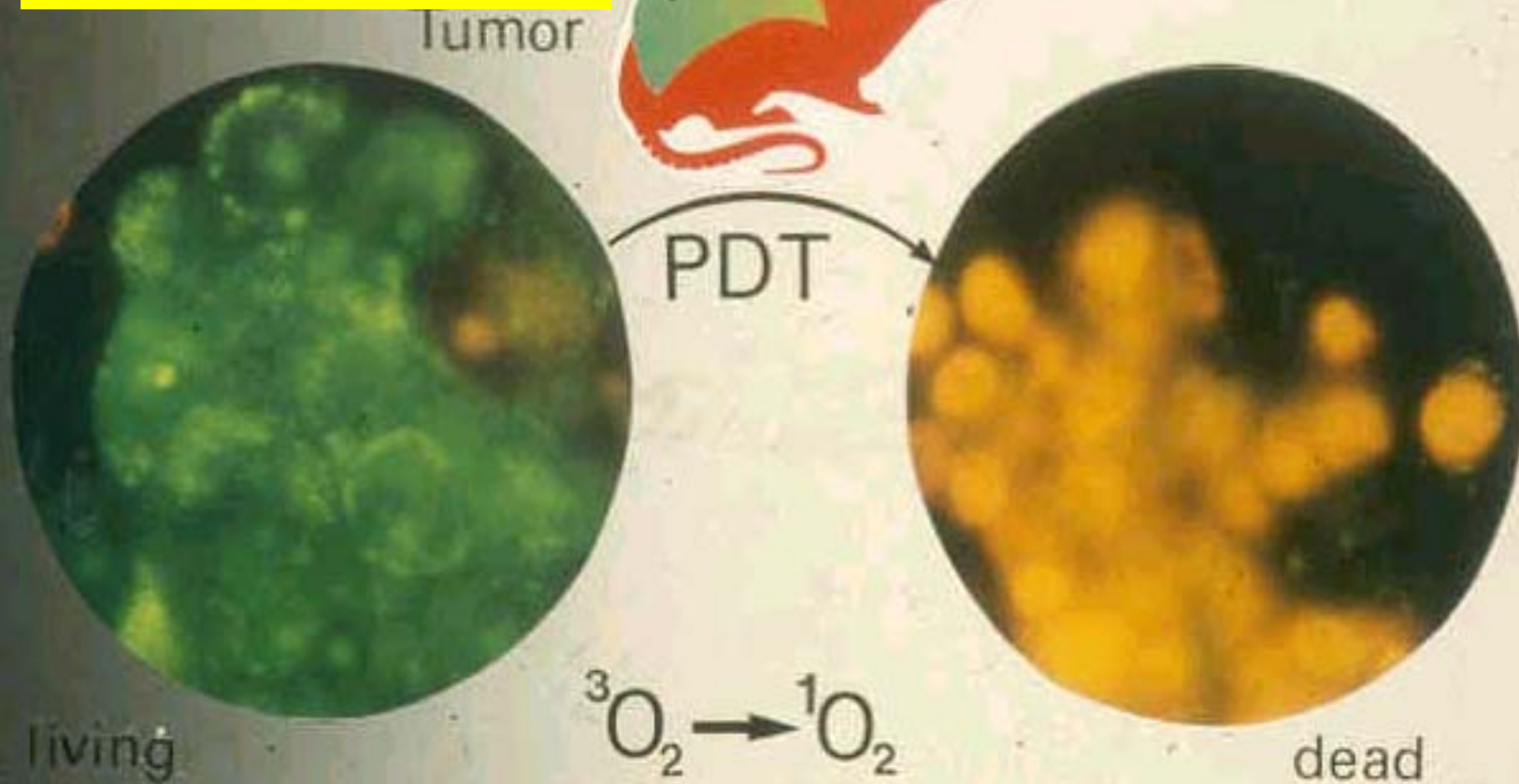
Natürliche Photosensibilisatoren zur Abwehr von Freßfeinden

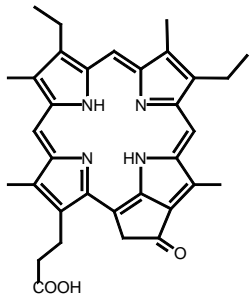
a) Pigmentinjektion

b) Warten bis Pigment Zielzellen erreicht

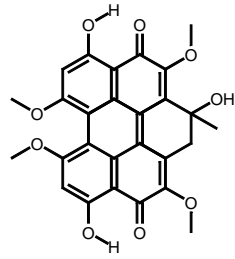
c) Belichtung

d) Warten

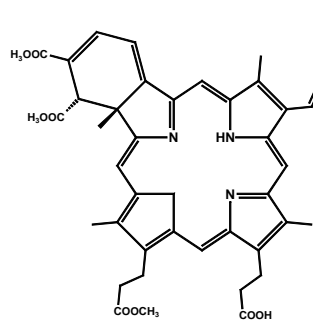




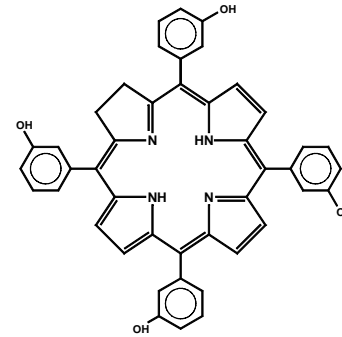
Phylloerythrin



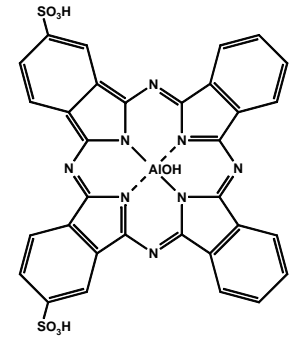
Hypocrellin (Hypocrella bambusae)



Benzoporphyrin-Derivat (Verteporfin, Visudyne® QLT)

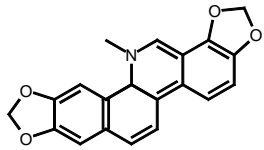


meso-Tetrahydroxyphenyl-Chlorin (m-THPC, Foscan® Scotia)

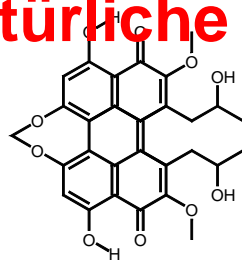


Al-Phthalocyanin-disulfonat (Verteporfin, Visudyne® QLT)

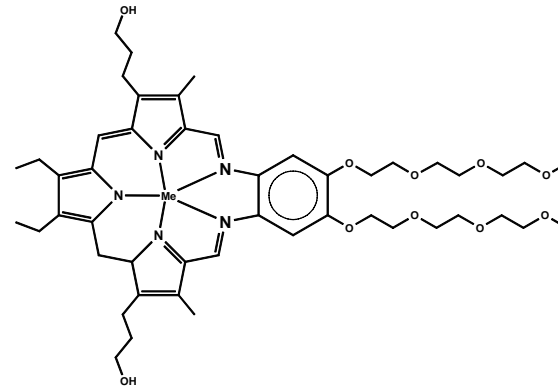
Natürliche und künstliche Photosensibilisatoren



Saguinarin (Saguinaria canadensis)



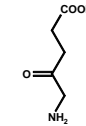
Cercosporin (Pilze)



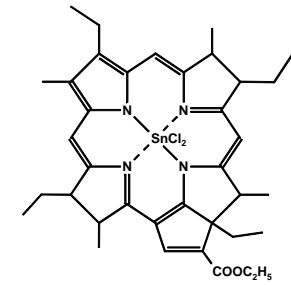
Metallo-Texaphyrin

Me = Lu: Lutrin®, Lutex Pharmaceuticals

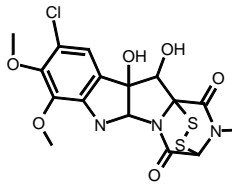
Me = Gs: Xcytrin®, Gadolite® Pharmaceuticals



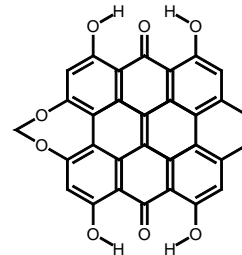
5-Amino-levulinic acid (ALA, Levulan® DUSA)



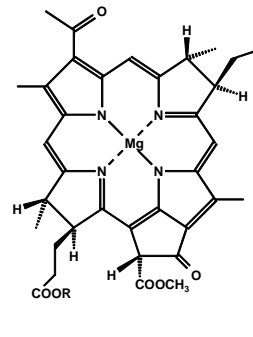
Sn-Etiopurpurin (Purlytin® Miravant)



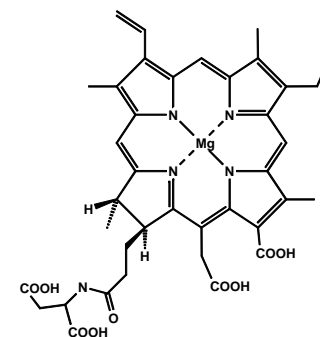
Sporodesmin (Pithomyces chartarum)



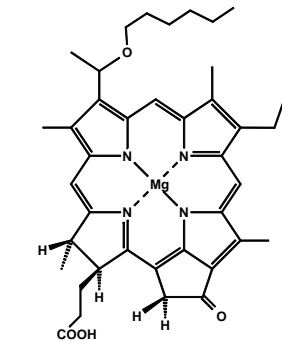
Hypericin (Hypericum perforatum)



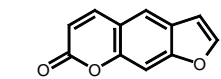
Sn-Etiopurpurin (Purlytin® Miravant)



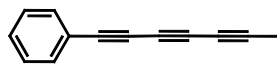
Aspartyl-chlorin e₆ (NPe₆, Nippon Petro)



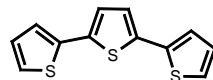
Hexylether of 3-Hydroxyethyl-pyropheophorbide a
(Roswell Park Cancer Inst.)



Furocumarine (Umbelliferen)

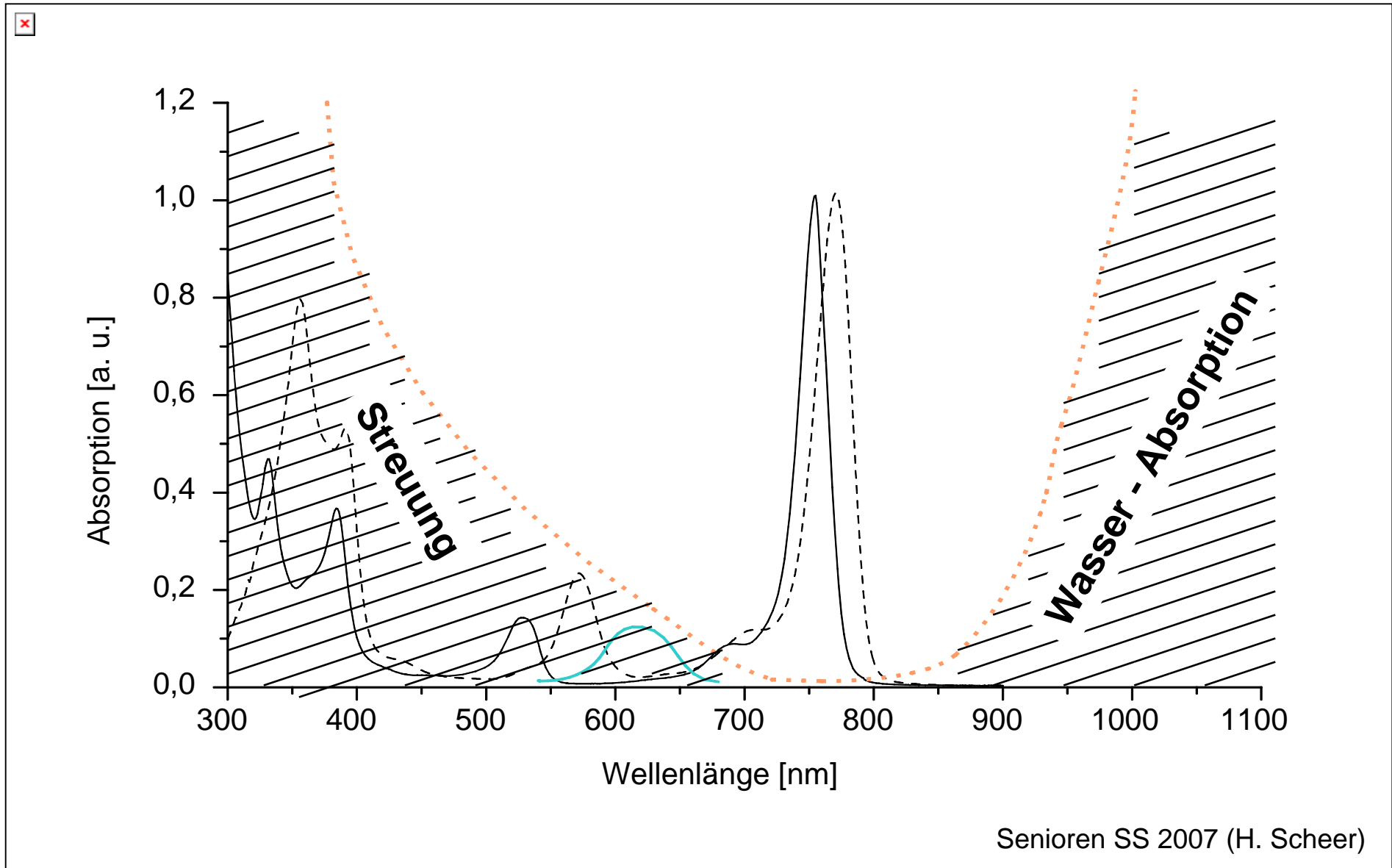


Polyacetylene (Compositen, Pilze)



Terthienyl (Tagetes)

Absorption von **Photofrin**[®] und Bacteriochlorophyllen



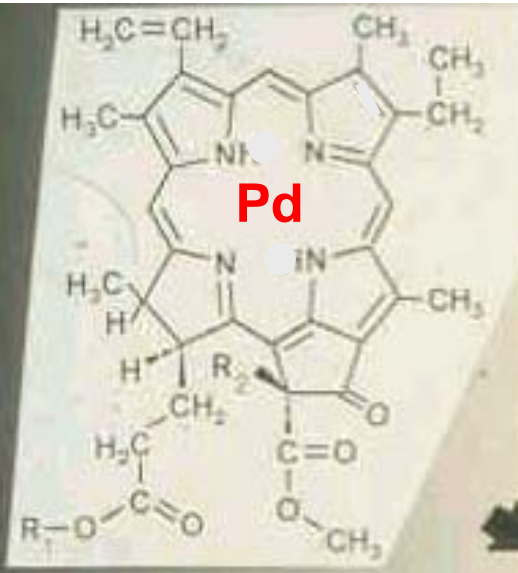
Bakteriochlorophyll im Vergleich zu HPD

Vorteile

- a) Sehr hohe Absorption
- b) Sehr gute spektrale Lage im „therapeutischen Fenster“
- c) Schneller Abbau

Nachteile

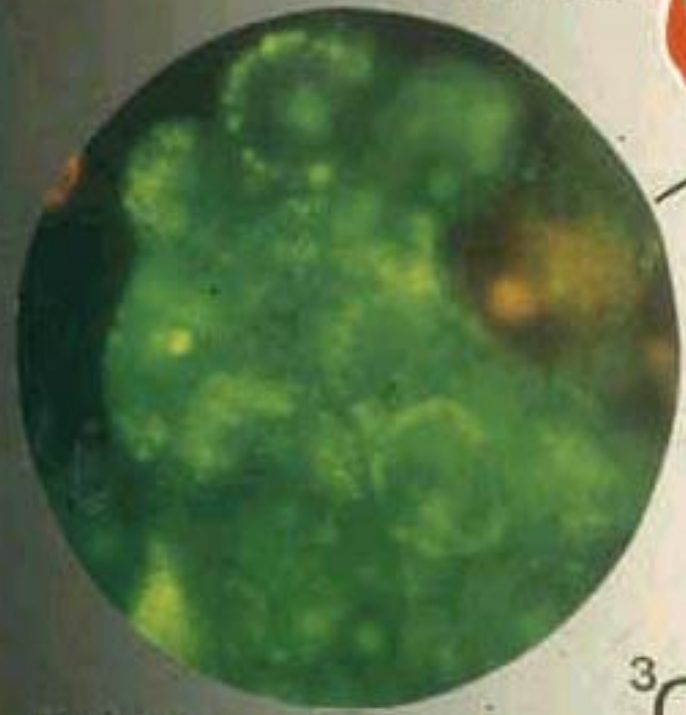
- a) Schlecht zugänglich
- b) Geringe Triplettausbeute
- c) Geringe Wasserlöslichkeit
- d) hemisch und photochemisch sehr empfindlich



O_2

LASER

Tumor

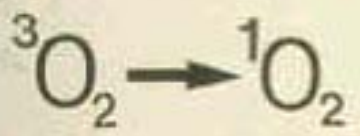


living

PDT



dead



Pd – Bacteriopheophorbid ist sehr guter Sensibilisator

- a) Intensive Absorption im nahen Infrarot
„Therapeutisches Fenster“
- b) Sehr gute Triplettausbeute (>90 %)
- c) Langlebiges Triplett
- d) Anreicherung im High Density Lipoprotein (HDL)
- e) Keine untere Grenzdosis
- f) Schneller Abbau
- g) Angriffsort sind neu gebildete Gefäße,
die den Tumor versorgen

Ich danke:

Meinen Mitarbeitern

Andreas Struck
Gerhard Hartwich
Michael Bandilla
Heike Snigula
Beate Ücker

Nina Kälin
Jörg Dandler
Leenawaty Limantara

Meinen Partnern

Richard Cogdell, Glasgow
Wolfgang Haehnel, Freiburg
Yasushi Koyama, Japan
Avigdor Scherz, Israel
Wolfgang Zinth, München

Unseren Geldgebern

Deutsche Forschungsgemeinschaft
Deutsch-Israelische Stiftung
Hans-Fischer-Gesellschaft
NEDO
Volkswagen Stiftung

Senioren SS 2007 (H. Scheer)

Ende