A novel biophysical model for radical pair mechanism in birds' magnetoreception

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Contents

Background

First discovery in magnetoreception

Magnets Interfere with Pigeon Homing

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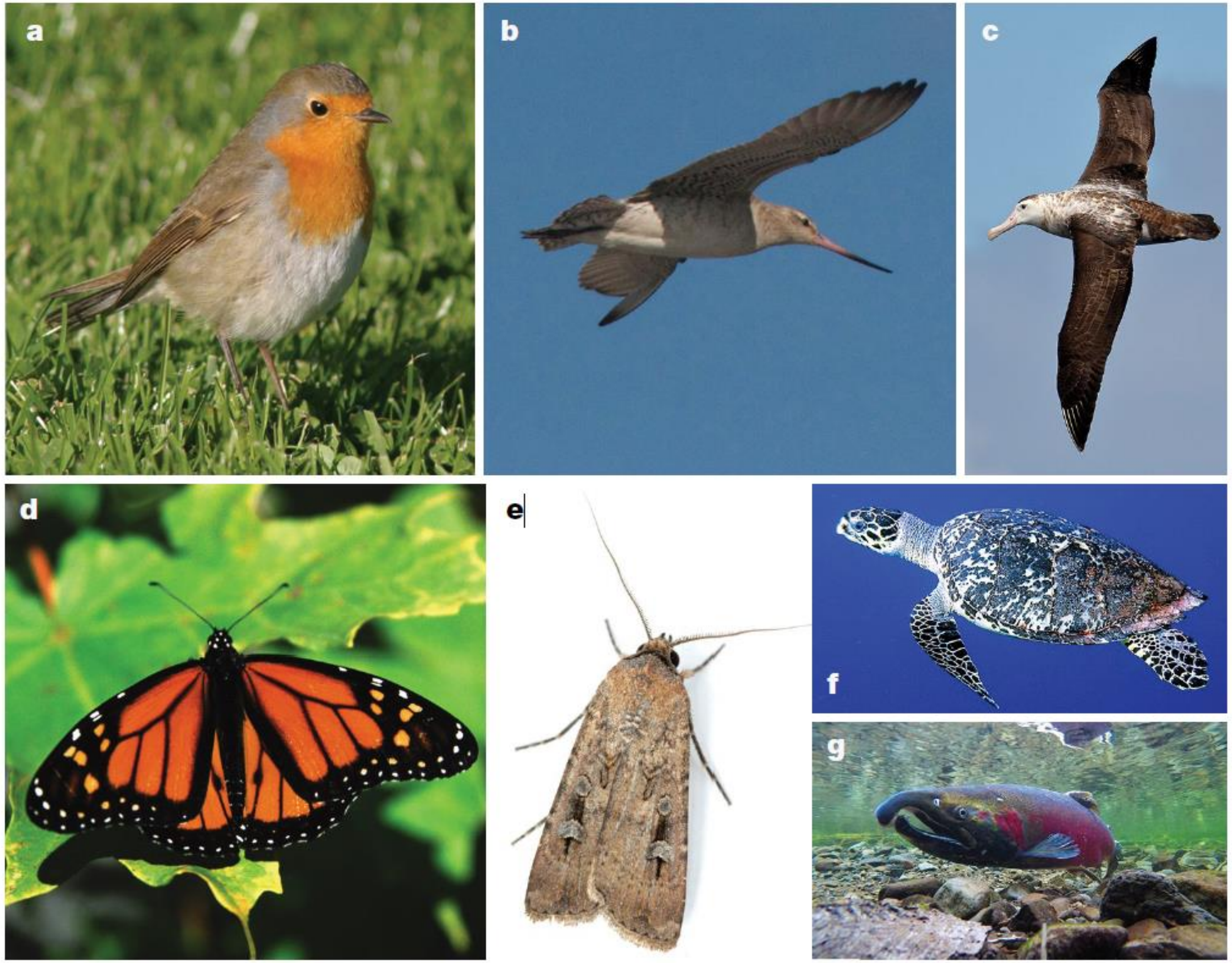
ABSTRACT Magnets glued to the backs of experienced pigeons often resulted in disorientation when the birds were released from distances of 17–31 miles (27–50 km) under total overcast, whereas no such disorientation occurred during similar releases under clear skies. The magnets did, however, often cause disorientation when first-flight birds were released under sun, and there was some indication of disturbance to experienced pigeons released under sun at longer distances.

Modified after Ref.[1]

Magnetic compass is ubiquitous across species

Vertebrates: birds, fishes, amphibians, reptiles, mammals.
Invertebrates: mollusks, crustaceans, insects.

- *Erithacus rubecula*
- *Limosa lapponica*
- *Diomedea exulans*
- *Danaus plexippus*
- *Agrotis infusa*
- *Eretmochelys imbricate*
- *Oncorhynchus kisutch*



Modified after Ref.[2]

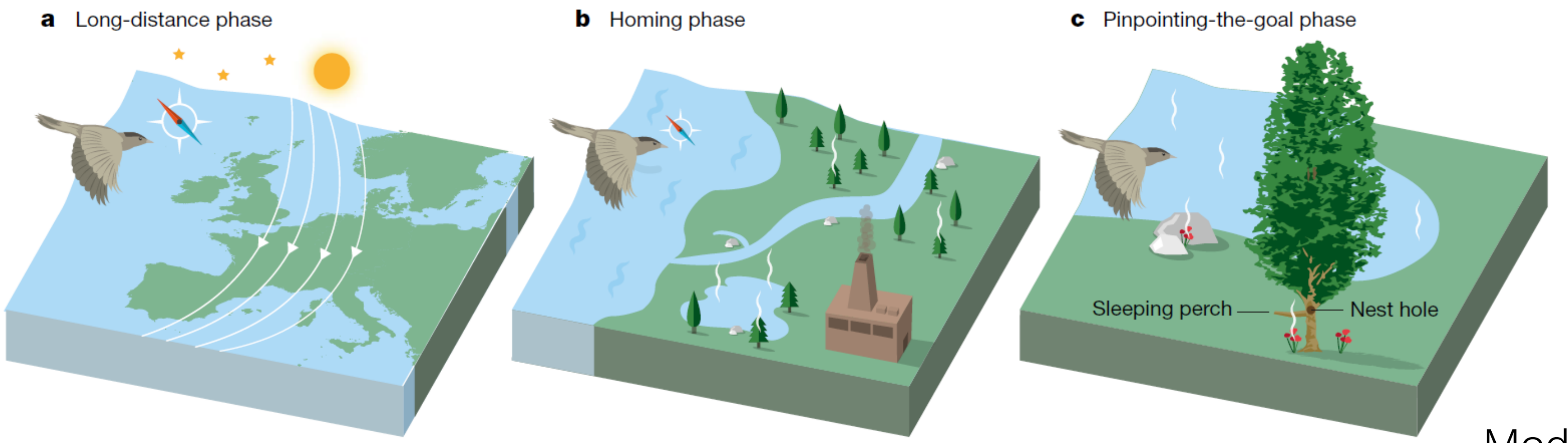
Multisensory cues for bird navigation

- **Long-distance navigation – Migration maps**

  Magnetic compass, sun compass, star compass

- **Homing and pinpointing – Local orientation**

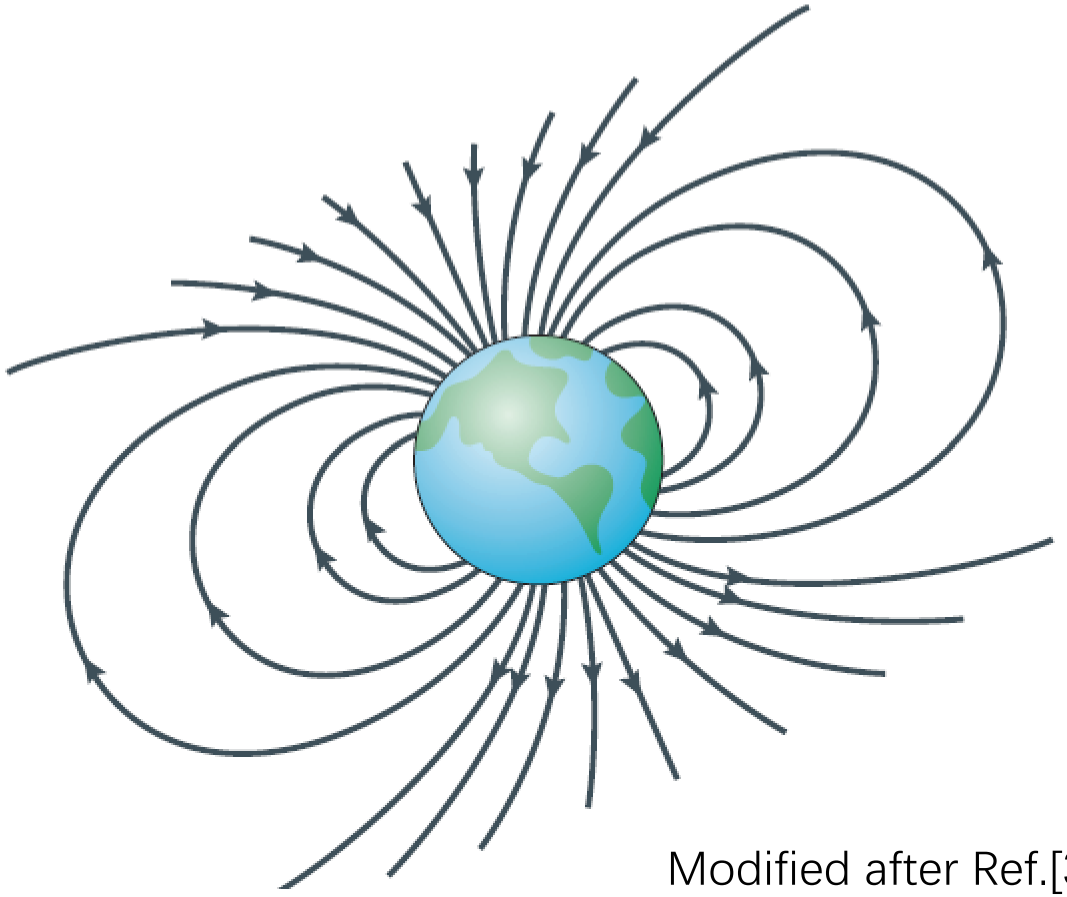
  Odors, borders, coast lines, sound, landmarks such as a tree, a small hill, a specific coral



Modified after Ref.[2]

Earth magnetic fields

- Field strength:25~60uT



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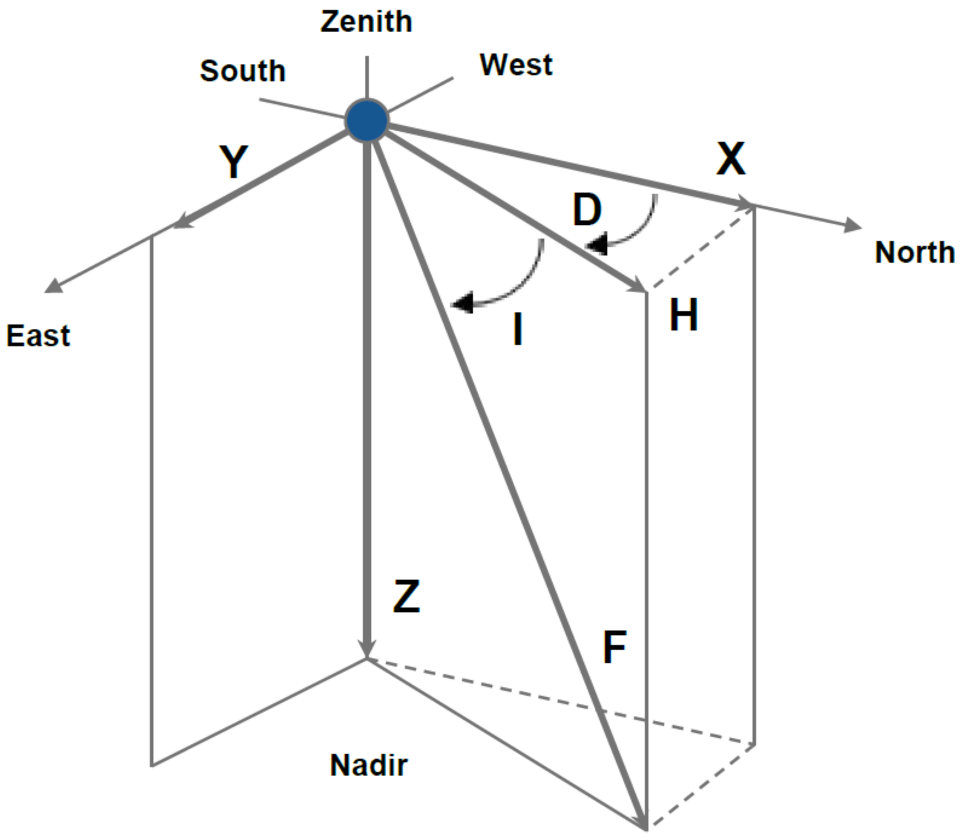


Magnetic field information

Inclination

Polarity/Declination

Intensity

Mechanisms

Three possible mechanisms

- Electromagnetic induction
- Magnetite based magnetoreception
- Radical based magnetoreception

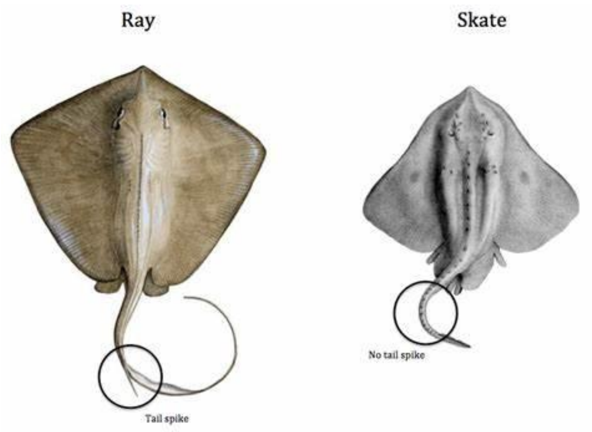
Difficulties for verification

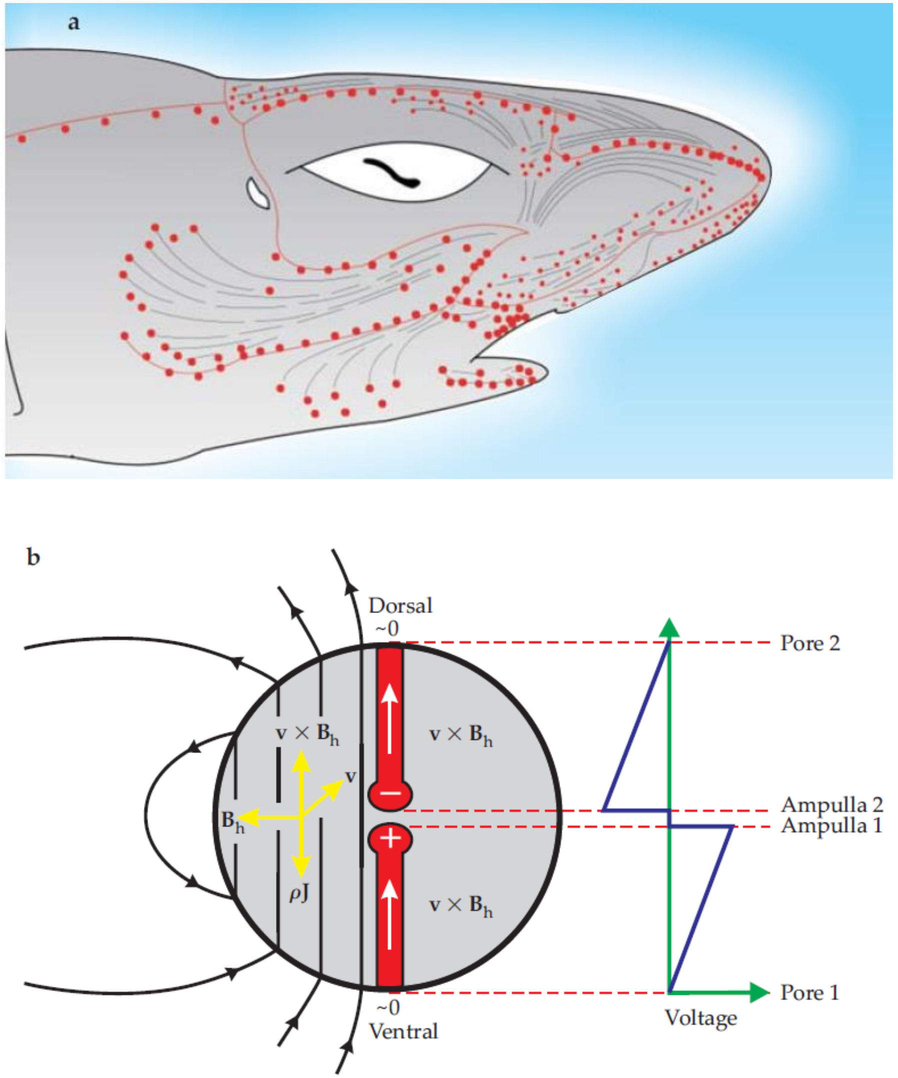
- No specific organ is found
- No unique behavioral phenotype
- Multisensory cues coupling
- Adaptation and acclimation
- Multi origins or single origin?

Electromagnetic induction

Magnetic information -> Electric signal

- A unique organ in cartilaginous fish:
- **Ampullae of Lorenzini**
- Jelly-filled pores with electroreceptors
- Moving magnetic field accumulates electric potential on two ampullas via proton flux, which can be detected by electroreceptor cells.
- Elasmobranch species: **sharks, rays and skates**.



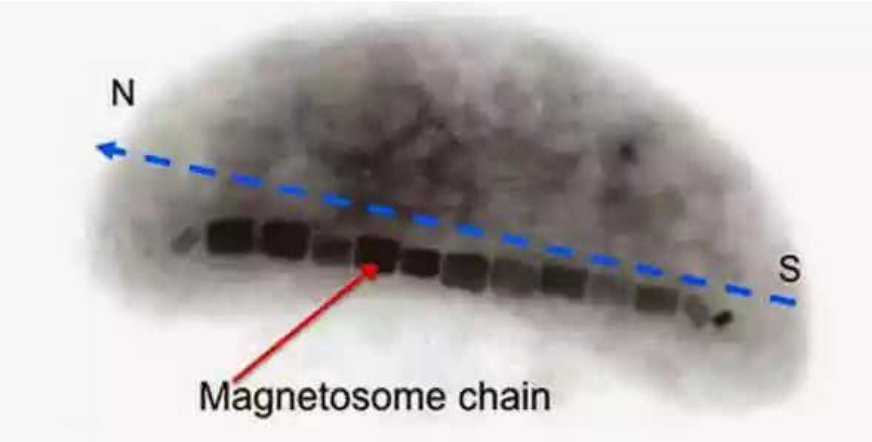


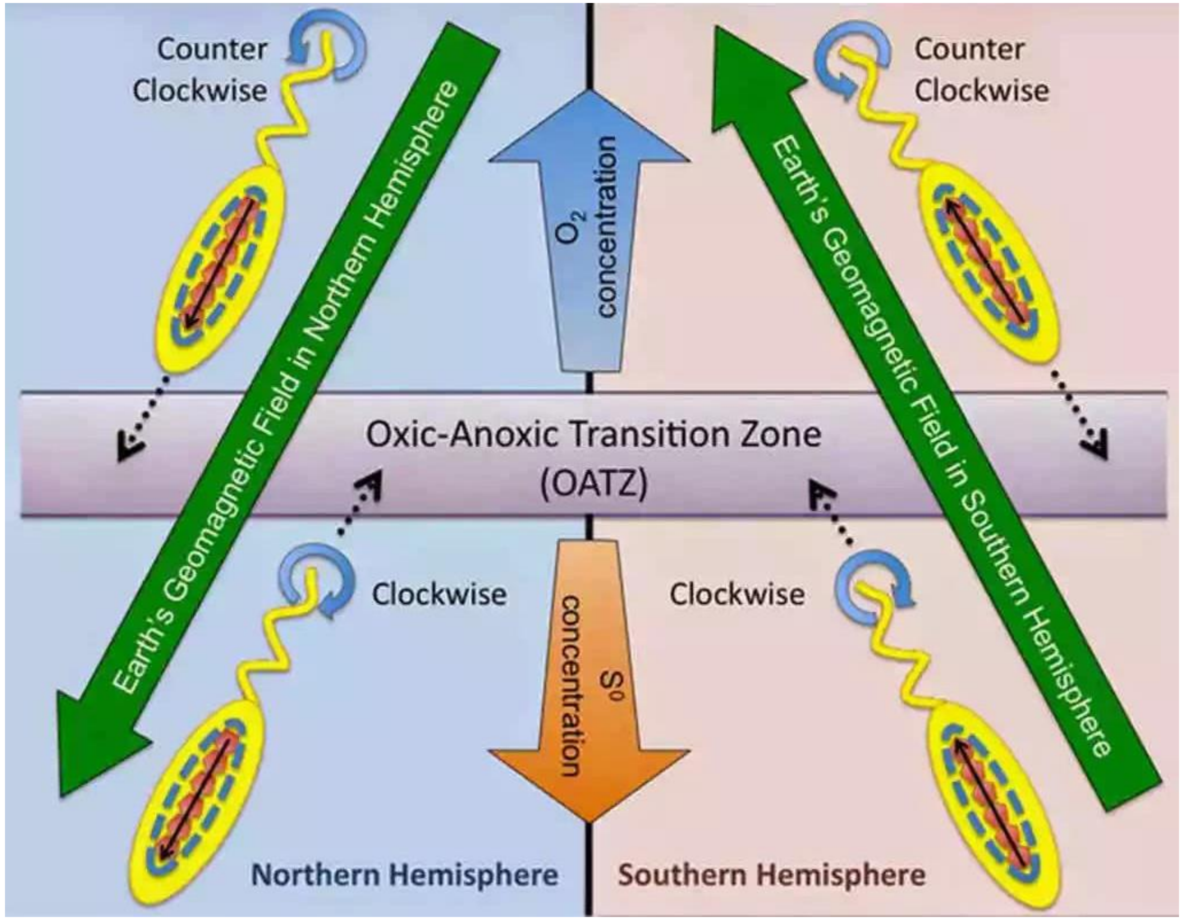
Modified after Ref.[4]

Magnetite based Magnetoreception

Magnetic force -> Physical rotation

- Magnetotactic bacteria
- A magnetosome chain:
- 15-20 Fe_3S_4, Fe_3O_4 crystal
- 30-100nm for each crystal

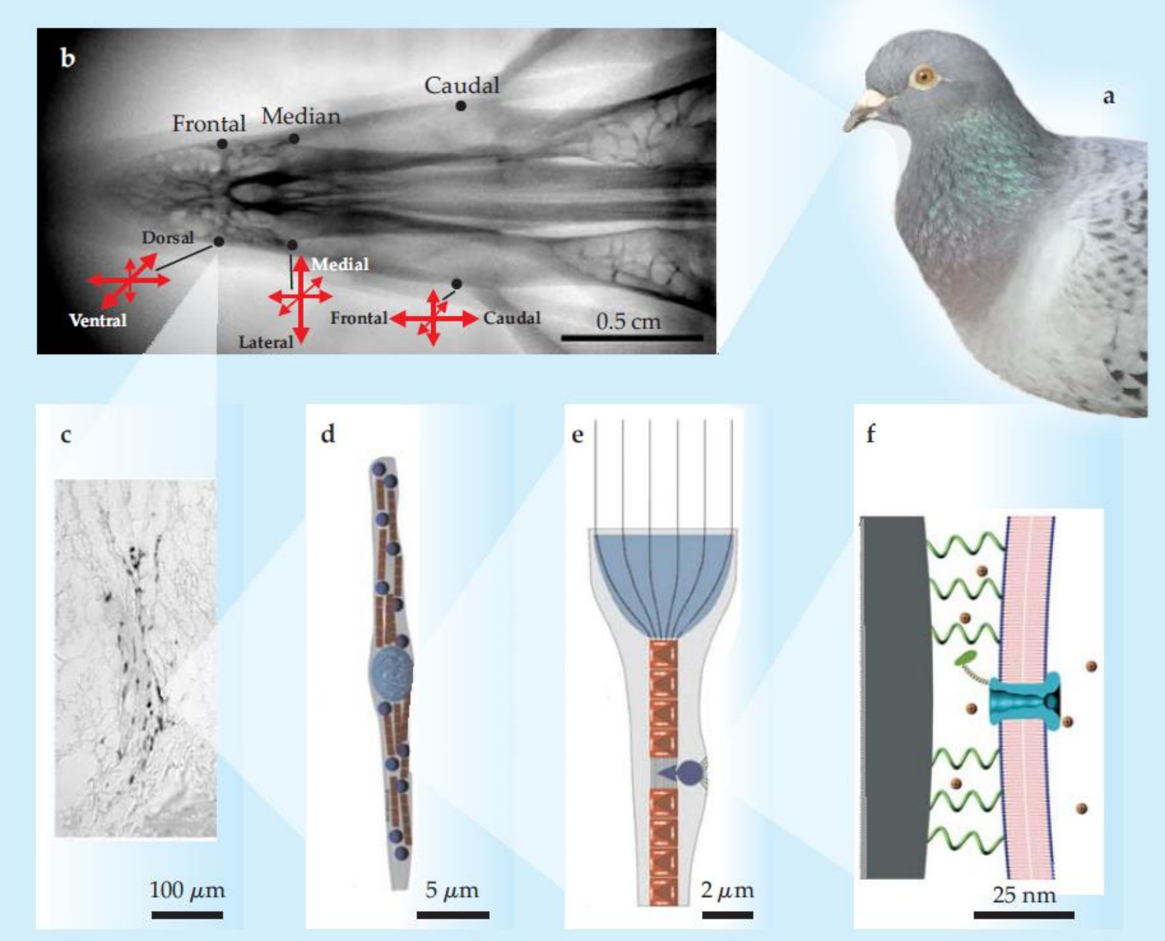




Modified after Ref.[5]

Magnetite based Magnetoreception

Magnetic information -> Pressure signal -> Electric signal



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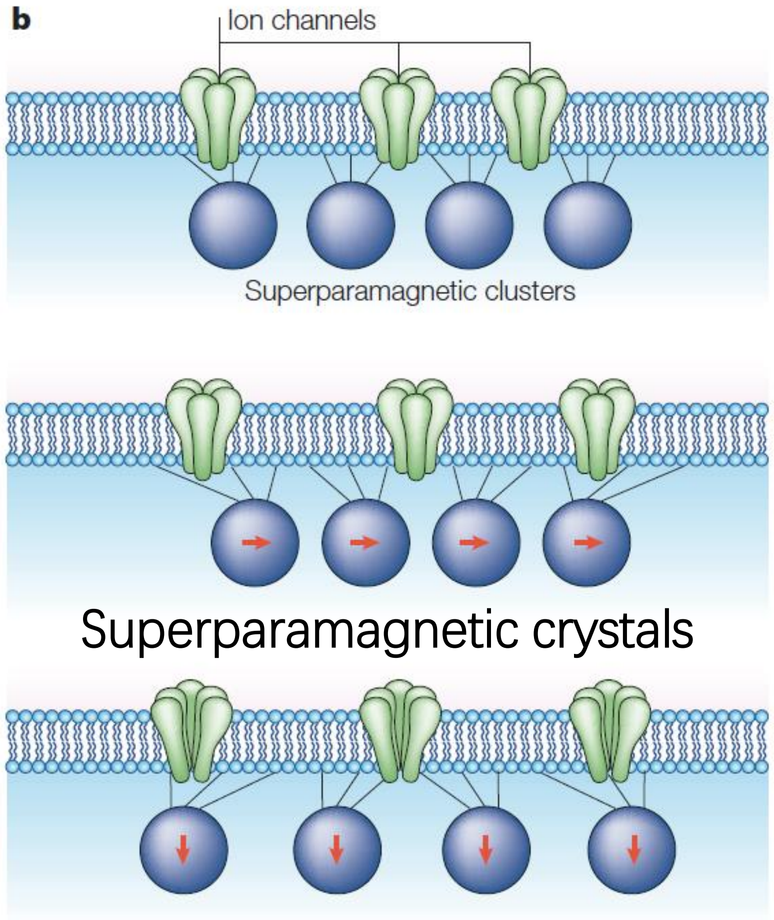
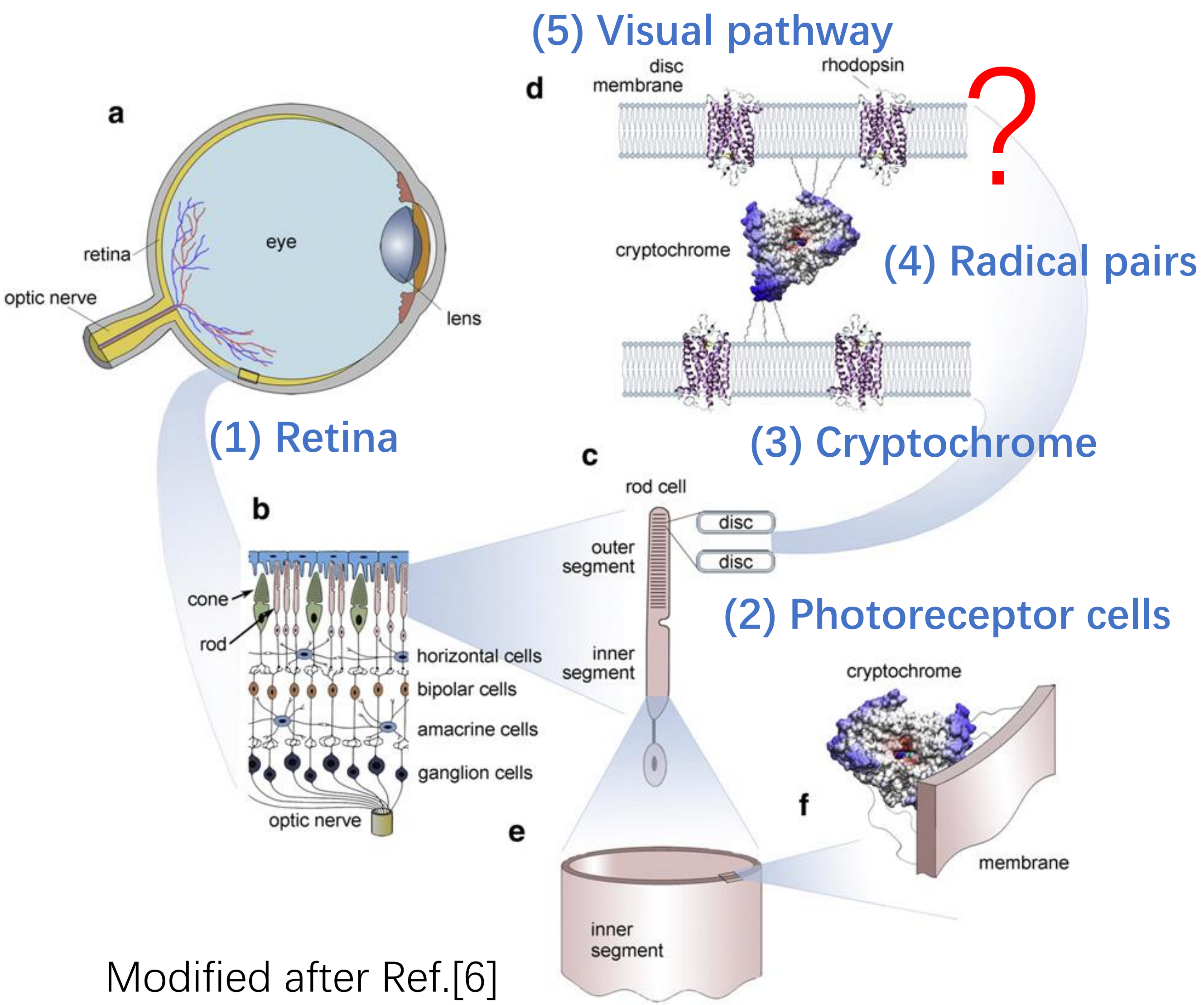


Modified after Ref.[3]

Radical based magnetoreception

Magnetic information -> Chemical signal -> Electric signal



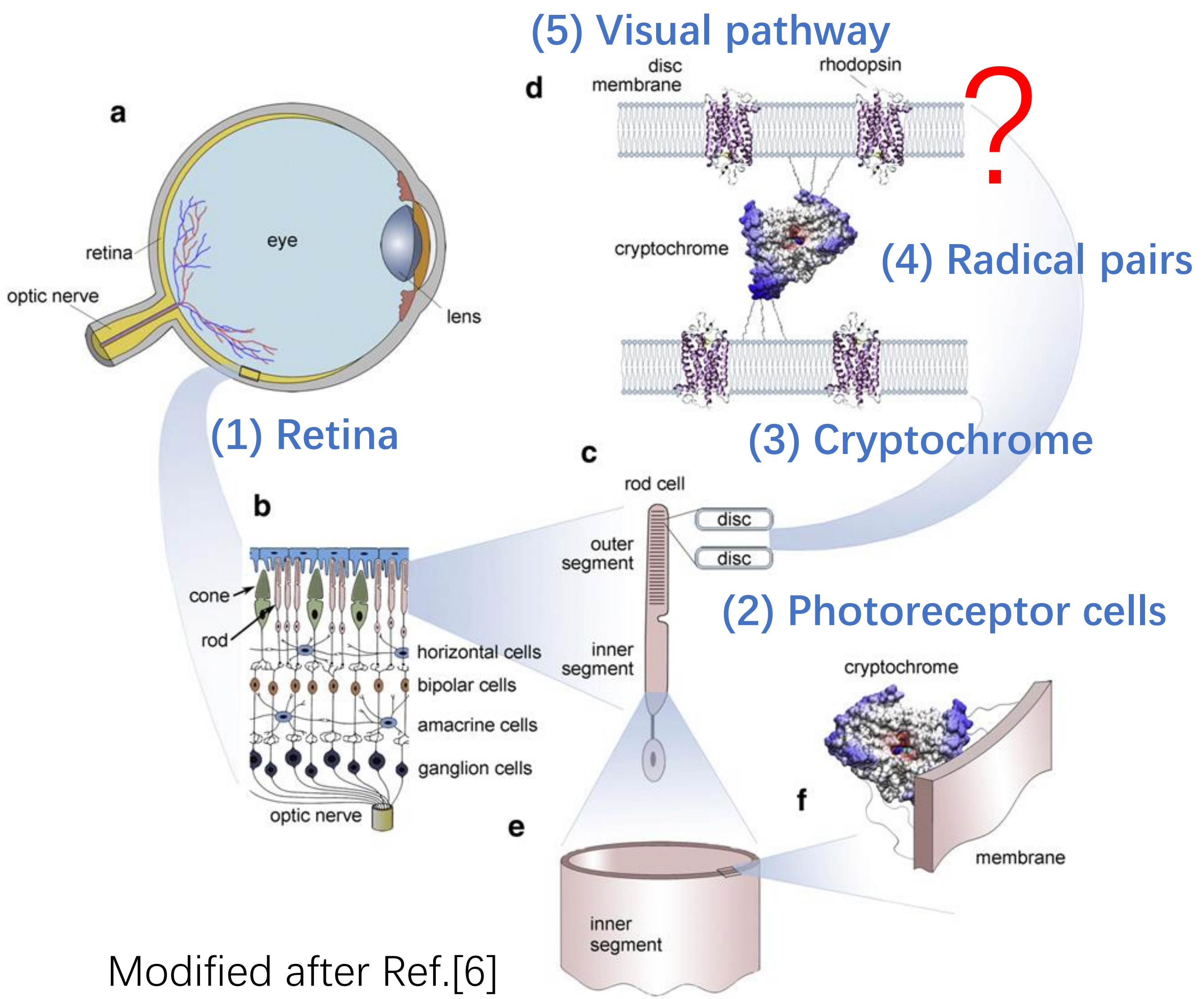
Modified after Ref.[6]

- 1) A **neural connection** between night vision and magnetic sensing in European robin.[12]
- 2) Different wavelength of incident light can **disrupt magnetic orientation** of European robin.[13,14]
- 3) The magnetic compass of European robin is **a inclination compass with <5° precision**, which can be explained by radical pair mechanism instead of any other hypothesis.[15,16]
- 4) Cryptochrome is the **only protein family** that can form **a light-induced radical pair**.

Appendix

Radical based magnetoreception

Magnetic information -> Chemical signal -> Electric signal



Modified after Ref.[6]

- 5) **Cry4 protein**, a member of cryptochrome family, is found recently located on the **outer segment** in cones in birds' retina.[17]
- 6) A popular hypothesis of (4)-(5) is an noncanonical biological pathway of visual system that can modulate night vision. **No such signaling pathway** is found till now.
- 7) We propose that no downstream signaling involved and instead a photon competition plays a key role.

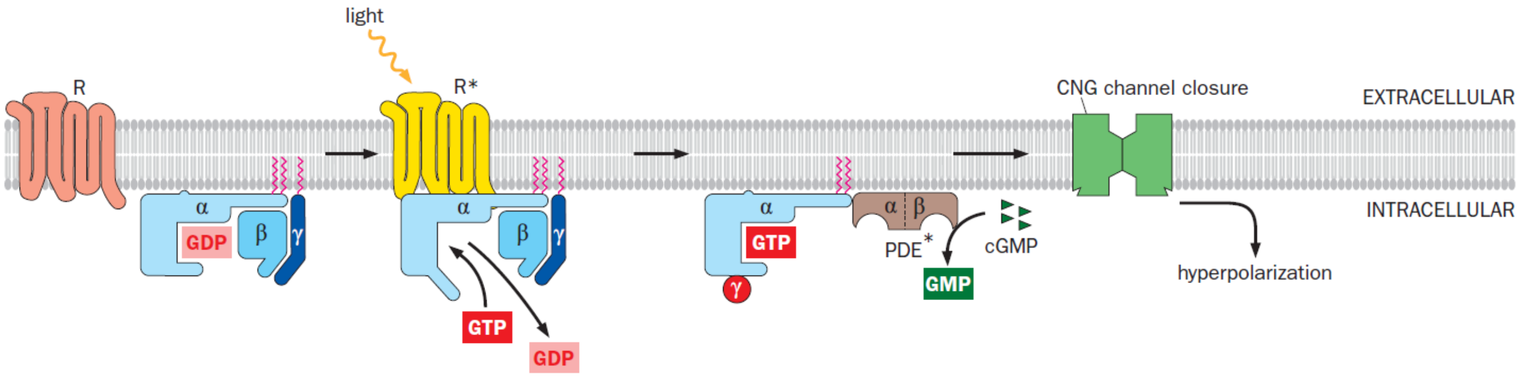
A novel biophysical model:

Opsin-Cryptochrome competition model(OCC model).

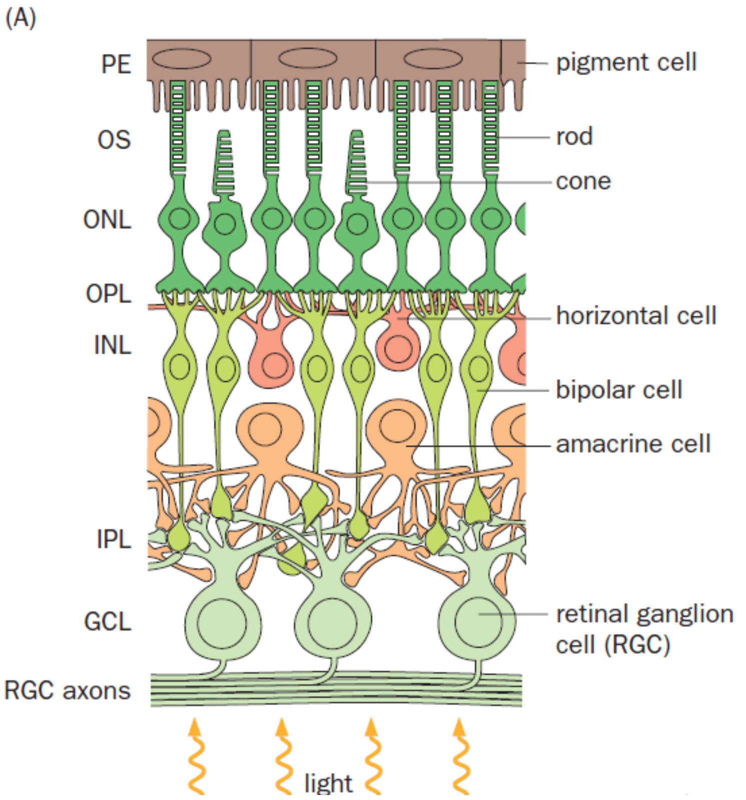
OCC

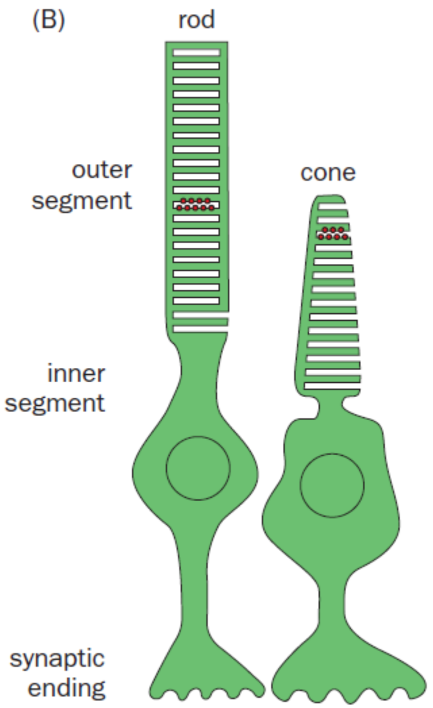
Opsin, Visual system

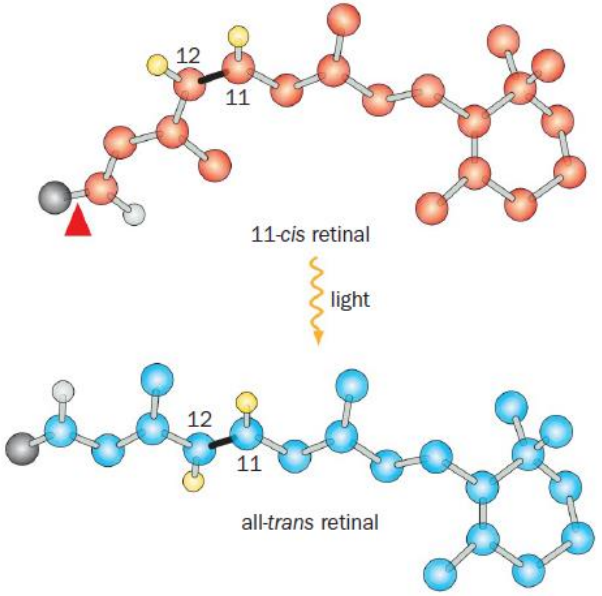
Light perception



Phototransduction cascade

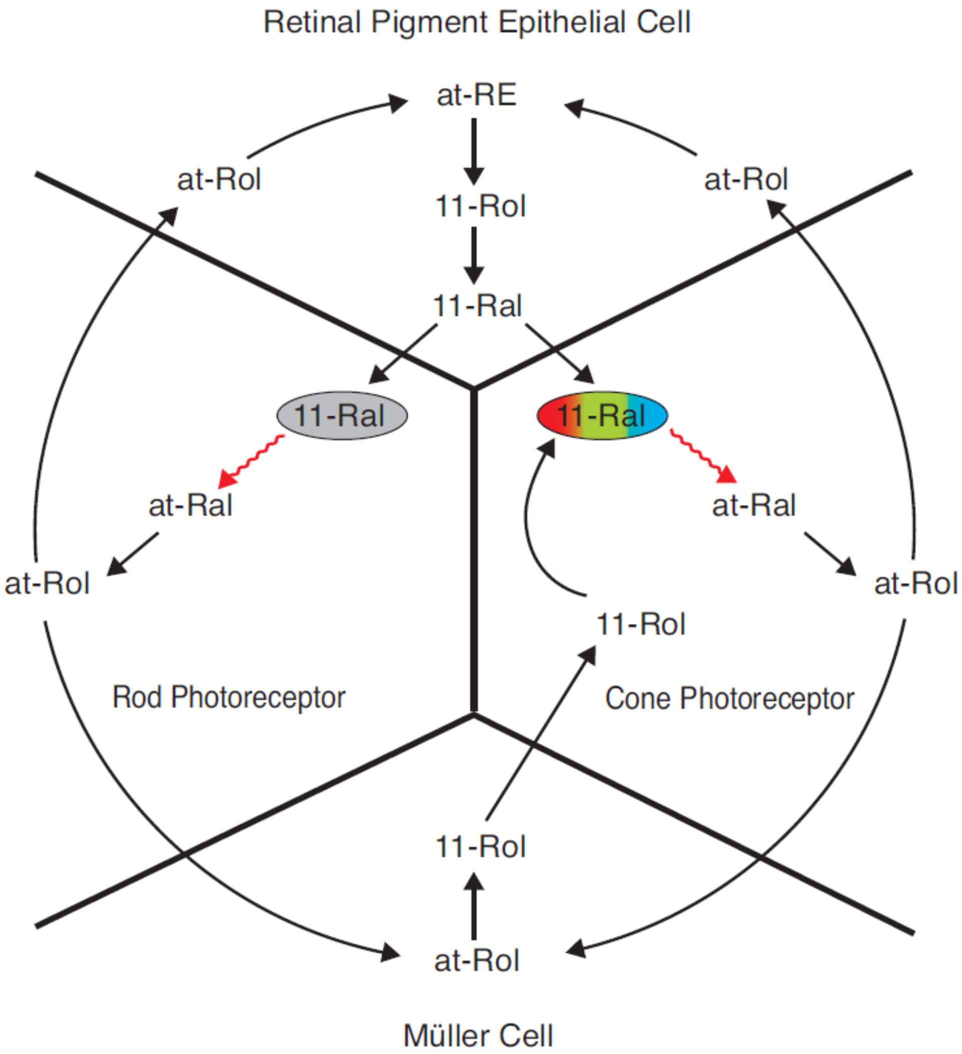


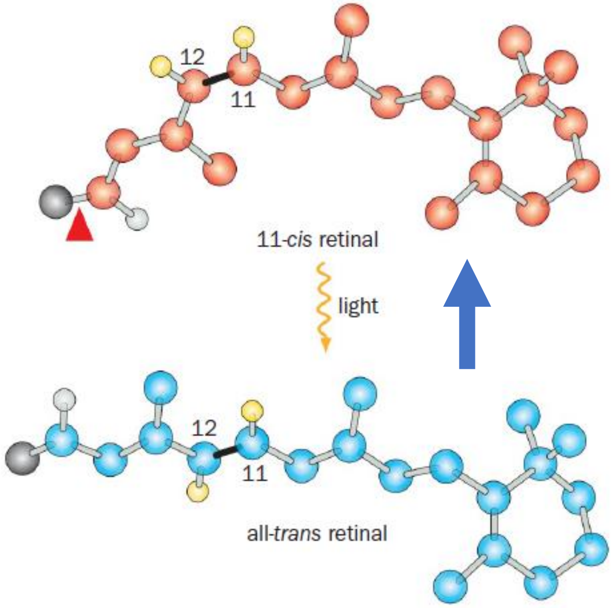




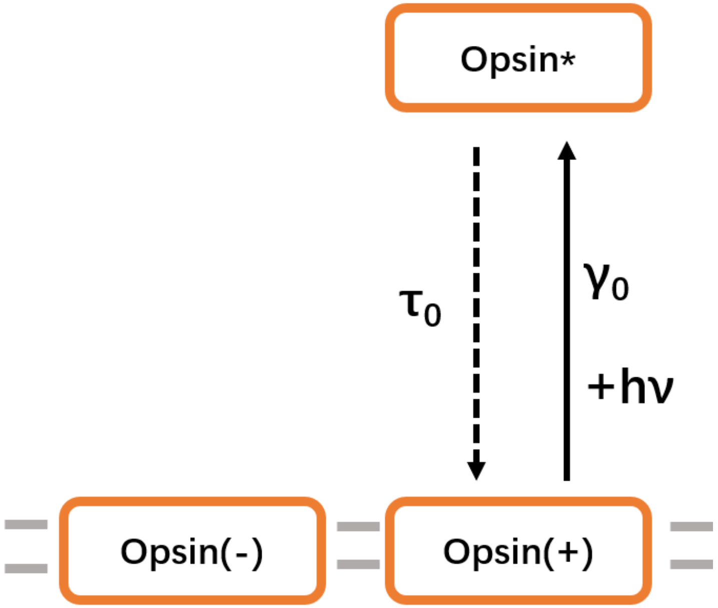
Modified after Ref.[7,8]

A cone visual cycle: cis-retinal <> trans-retinal





Retinal in a rhodopsin



Abbreviations: at-RE, all-*trans*-retinyl esters; at-Ral, all-*trans*-retinal; at-Rol, all-*trans*-retinol; 11-Ral, 11-*cis*-retinal; 11-Rol, 11-*cis*-retinol.

Modified after Ref.[7,8]

Photoreceptor proteins responsible for vision

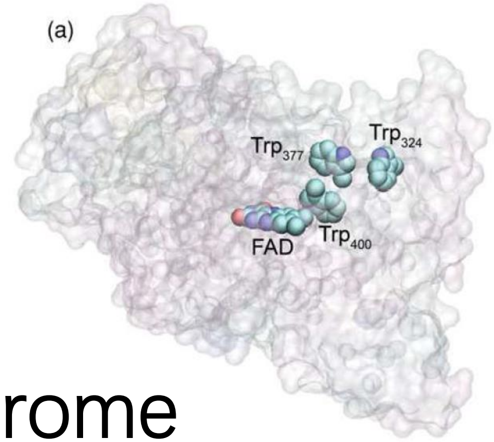
Name	Abbr.	Photo receptor	λ_{max}	Color
Long-wave sensitive	LWS	Cone	500–570 nm	Green, yellow, red
Short-wave sensitive 1	SWS1	Cone	355–445 nm	Ultraviolet, violet
Short-wave sensitive 2	SWS2	Cone	400–470 nm	Violet, blue
Rhodopsin-like 2	Rh2	Cone	480–530 nm	Green
Rhodopsin-like 1 (vertebrate rhodopsin)	Rh1	Rod	~500 nm	Blue–green

Cryptochrome can absorb one photon with wavelength ranging from 400-565nm.

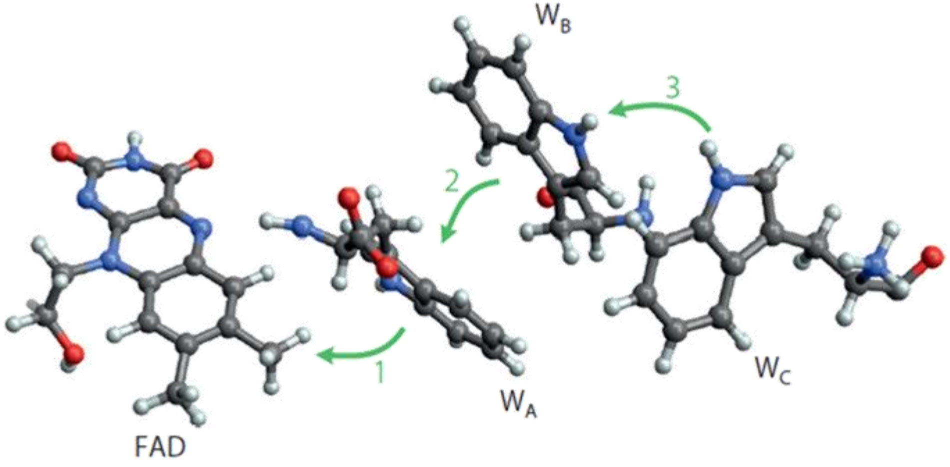
OCC

Cryptochrome, Radical pairs

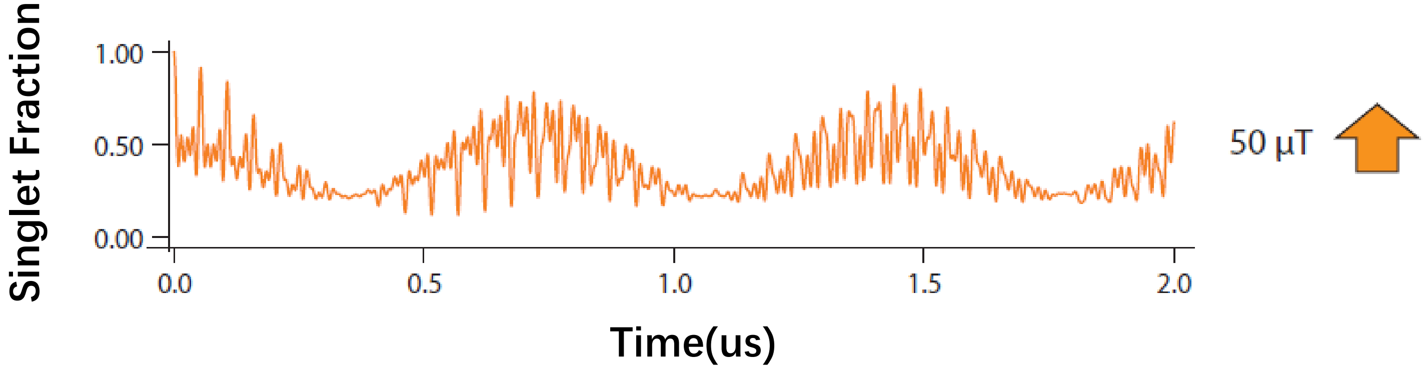
Principle of radical pair mechanism

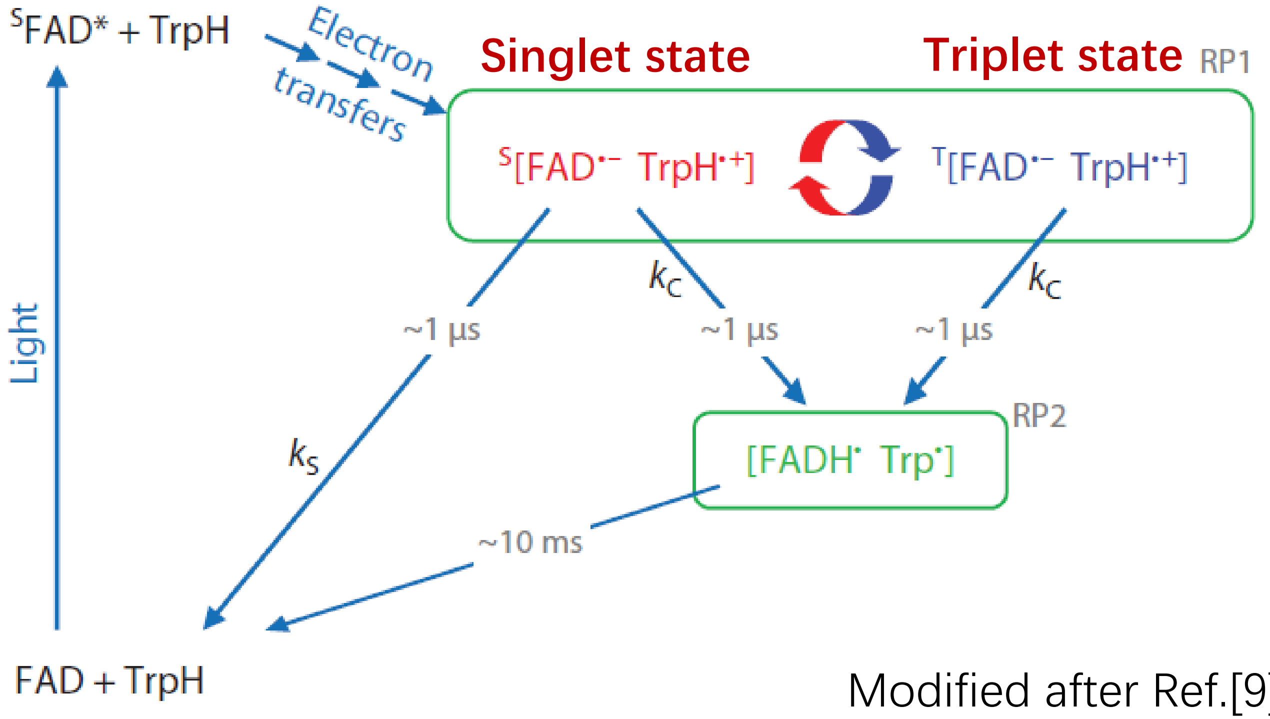


Cryptochrome



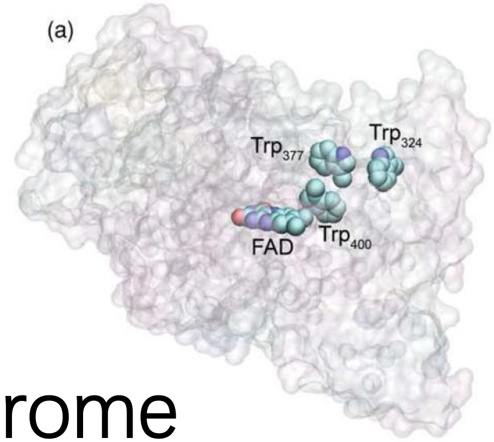
FAD - Flavin adenine dinucleotide
Trp(W) - Tryptophan



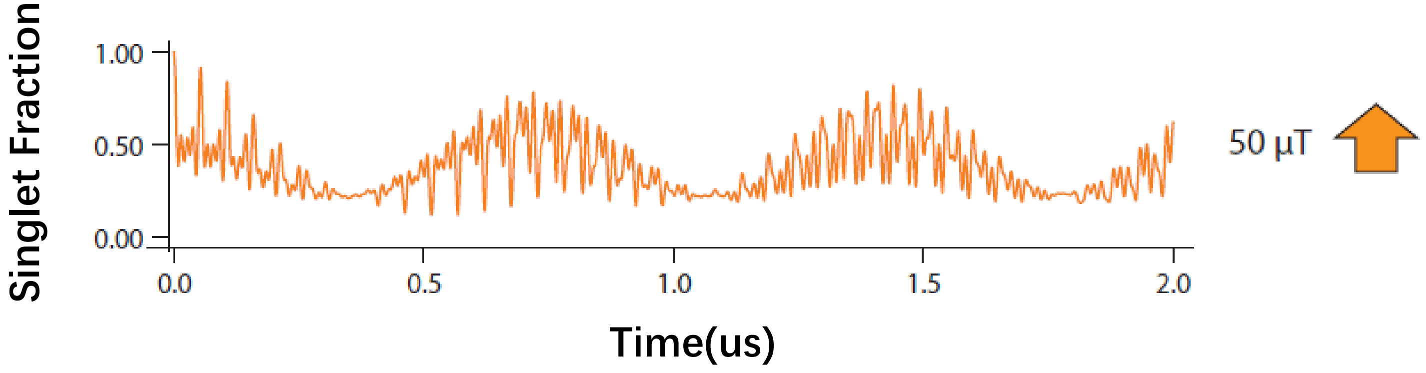


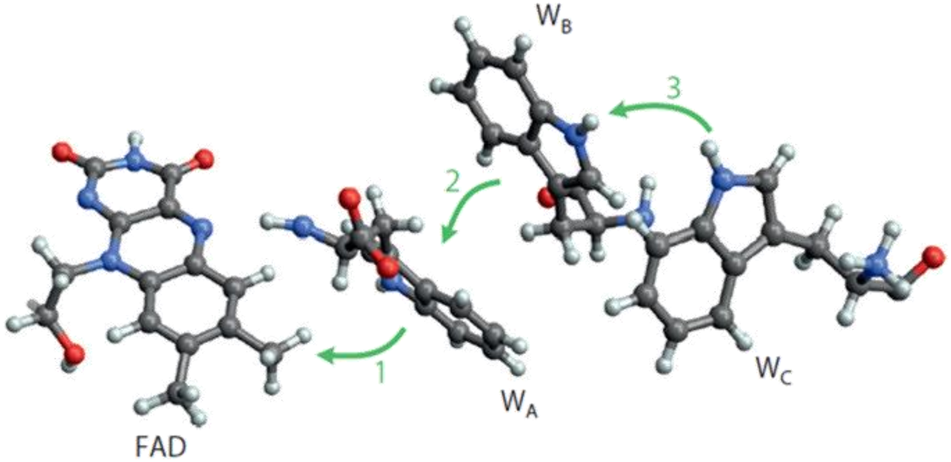
Modified after Ref.[9]

Principle of radical pair mechanism



Cryptochrome





FAD - Flavin adenine dinucleotide
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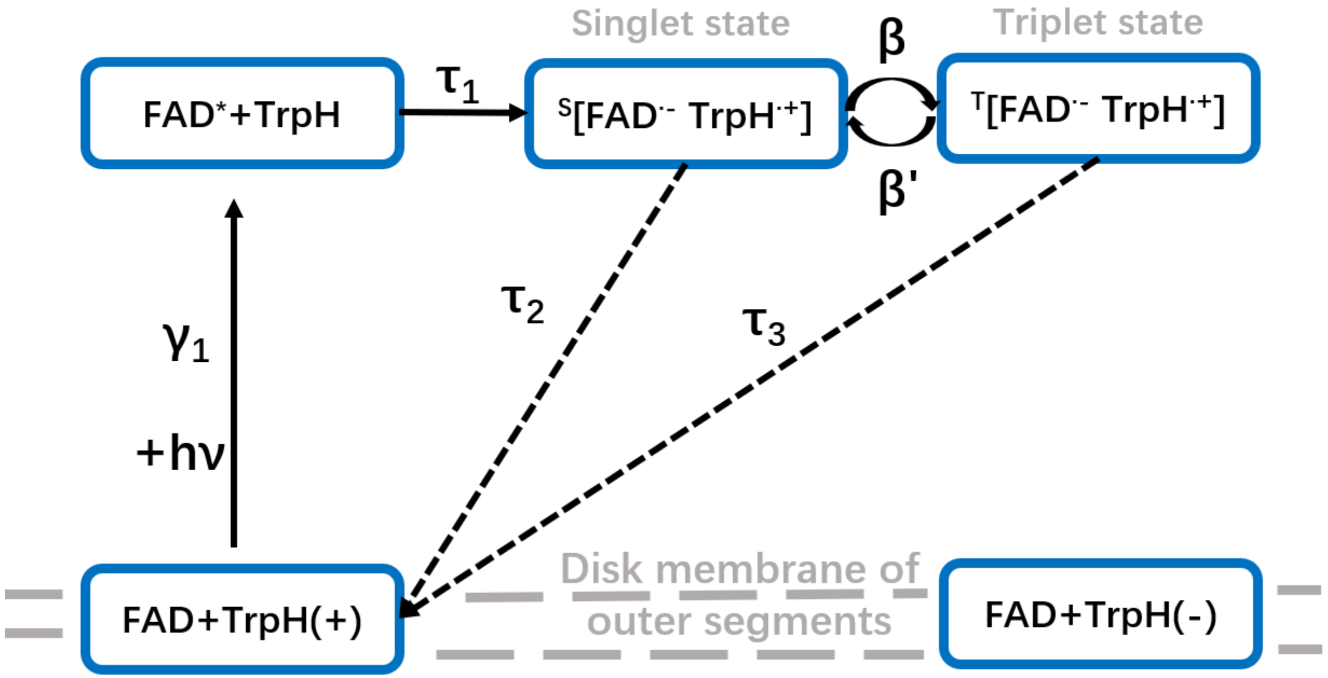
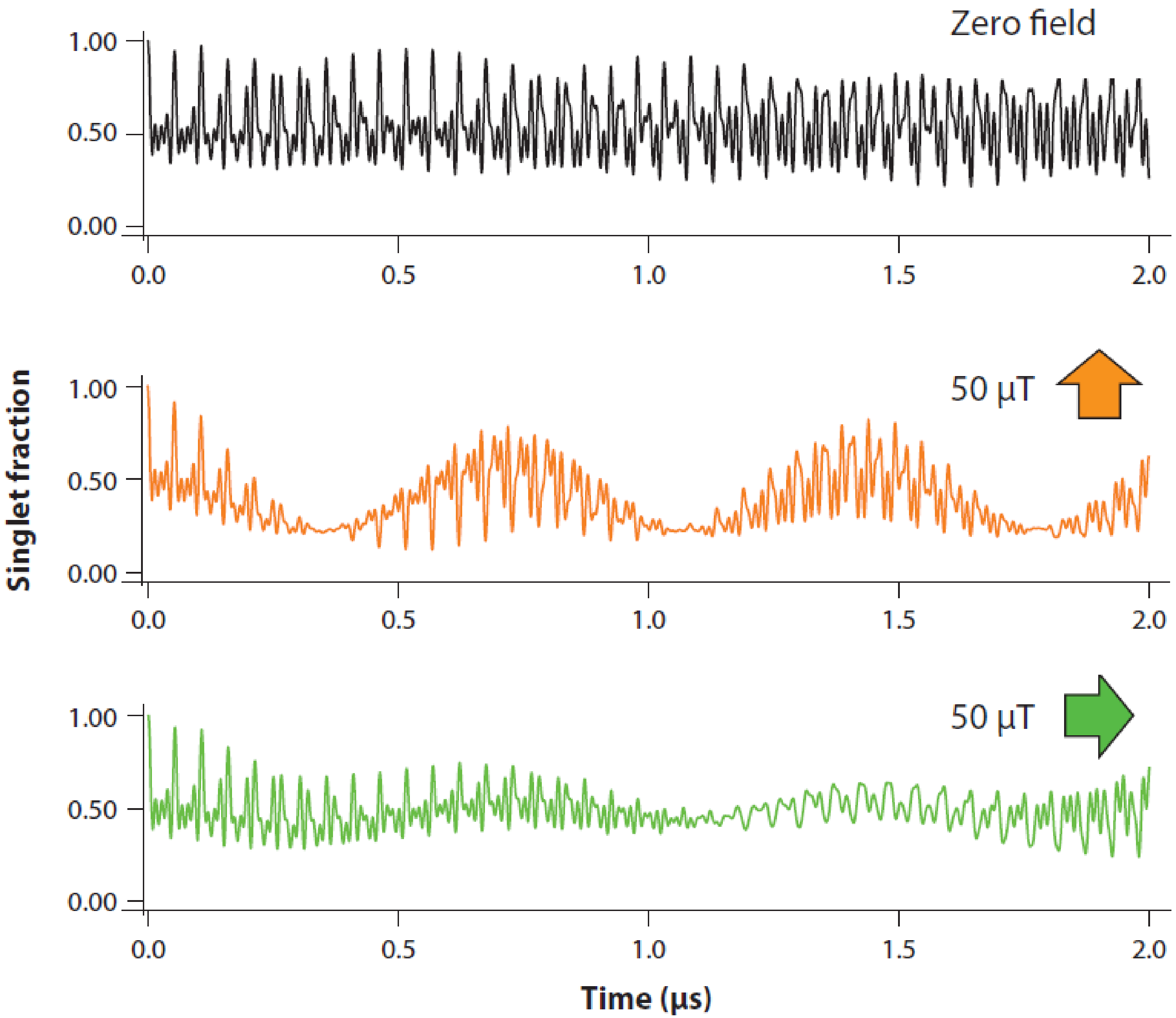
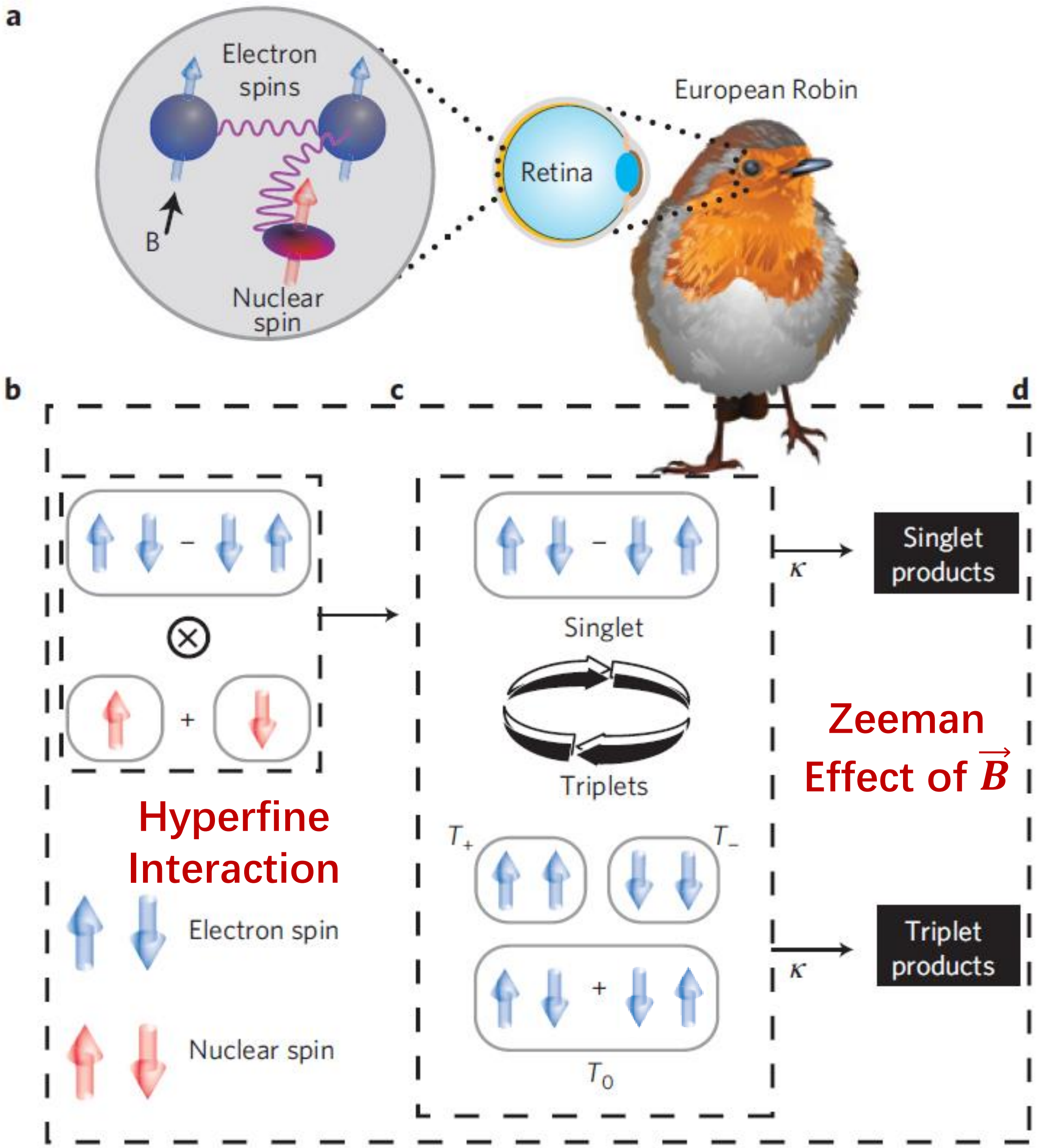


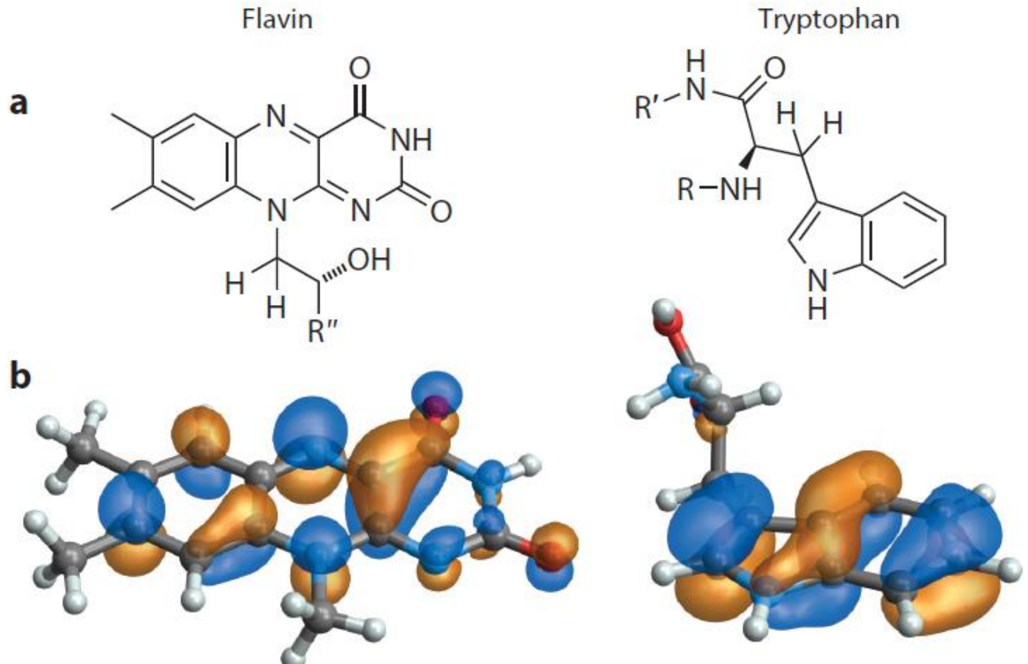
Spin dynamics



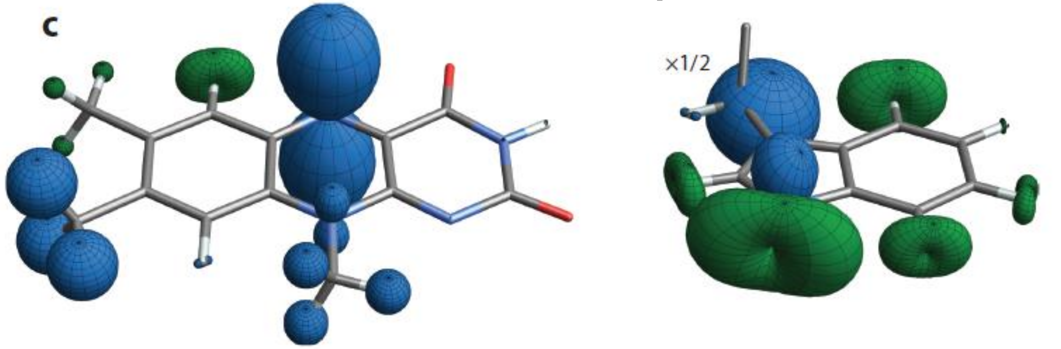


Modified after Ref.[11]

Quantum effect



Molecular orbitals of a unpaired electron



Hyperfine interactions

Modified after Ref.[9]

The fractional yield of singlet and triplet state product is $\phi_S = 1 - \phi_T$ is an integral of the real part of $T(t)$ which is the singlet fraction at arbitrary time t.

$$\phi_T = k_T \int_0^\infty T(t)dt$$

$$T(t) = Tr[Q^T \rho(t)]$$

Q^T is the projection operator of triplet state while $\rho(t)$ is the density matrix of the radical pair at arbitrary time. The triplet state fraction is a trace operation of the density matrix projected on the triplet state product.

$$\rho(t) = \frac{1}{N} e^{-\frac{iHt}{\hbar}} \rho(0) e^{\frac{iHt}{\hbar}}$$

Assume there is only singlet product at time 0, where $\rho(0) = Q^S e^{-kt}$, here to make it simple, we let $k = k_S = k_T$. N is the number of nuclear spin.

The hamiltonian for two electron spins are H_1 and H_2 respectively. $\vec{B}$ is the magnetic field vector with a specific direction.

$$H = H_1(\vec{B}) + H_2(\vec{B})$$

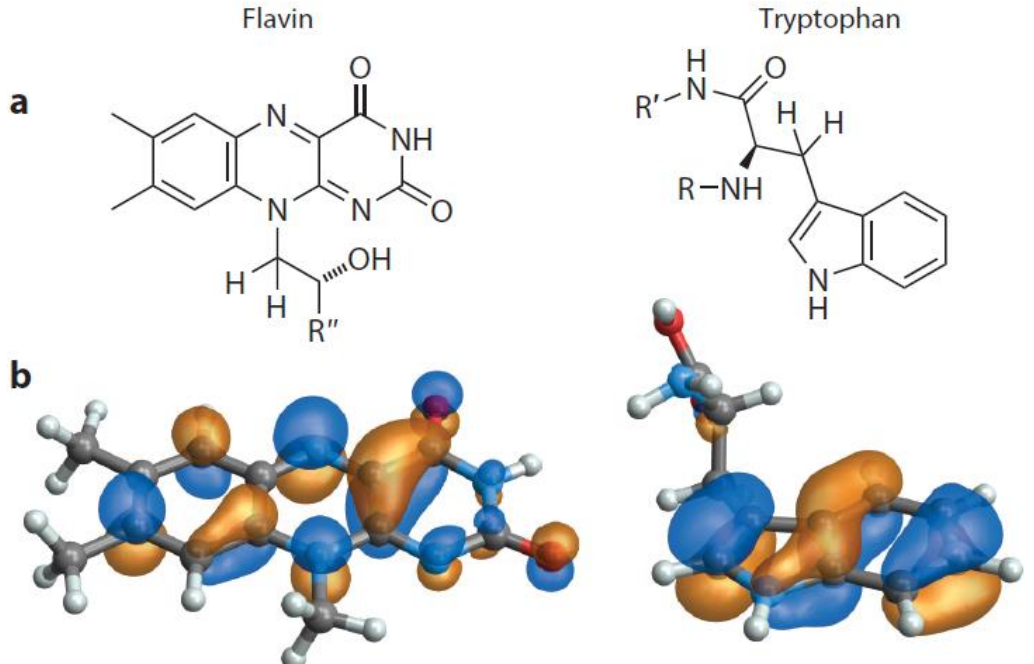
$$H_j = g\mu_B \vec{S_j} \cdot (\vec{B} + A_j \vec{I_j})$$

$\vec{S_j}$ is the electron spin operator whereas $\vec{I_j}$ is the nuclear spin operator correlated with the nuclear spin in vicinity. A_j is the anisotropic coefficient of the nuclear spin.

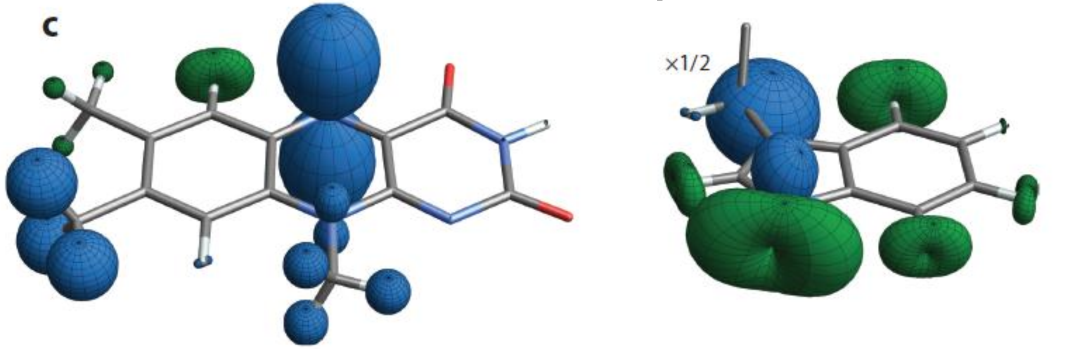
$$T(t) = \phi_S = 1 - Tr[Q^T \frac{1}{N} e^{-\frac{iHt}{\hbar}} Q^S e^{-kt} e^{\frac{iHt}{\hbar}}]$$

$$\phi_S = 1 - \frac{1}{N} \sum_{mn} Q^T_{mn} Q^S_{nm} \frac{k^2}{k^2 + (\omega_m - \omega_n)^2}$$

Quantum effect



Molecular orbitals of a unpaired electron



Hyperfine interactions

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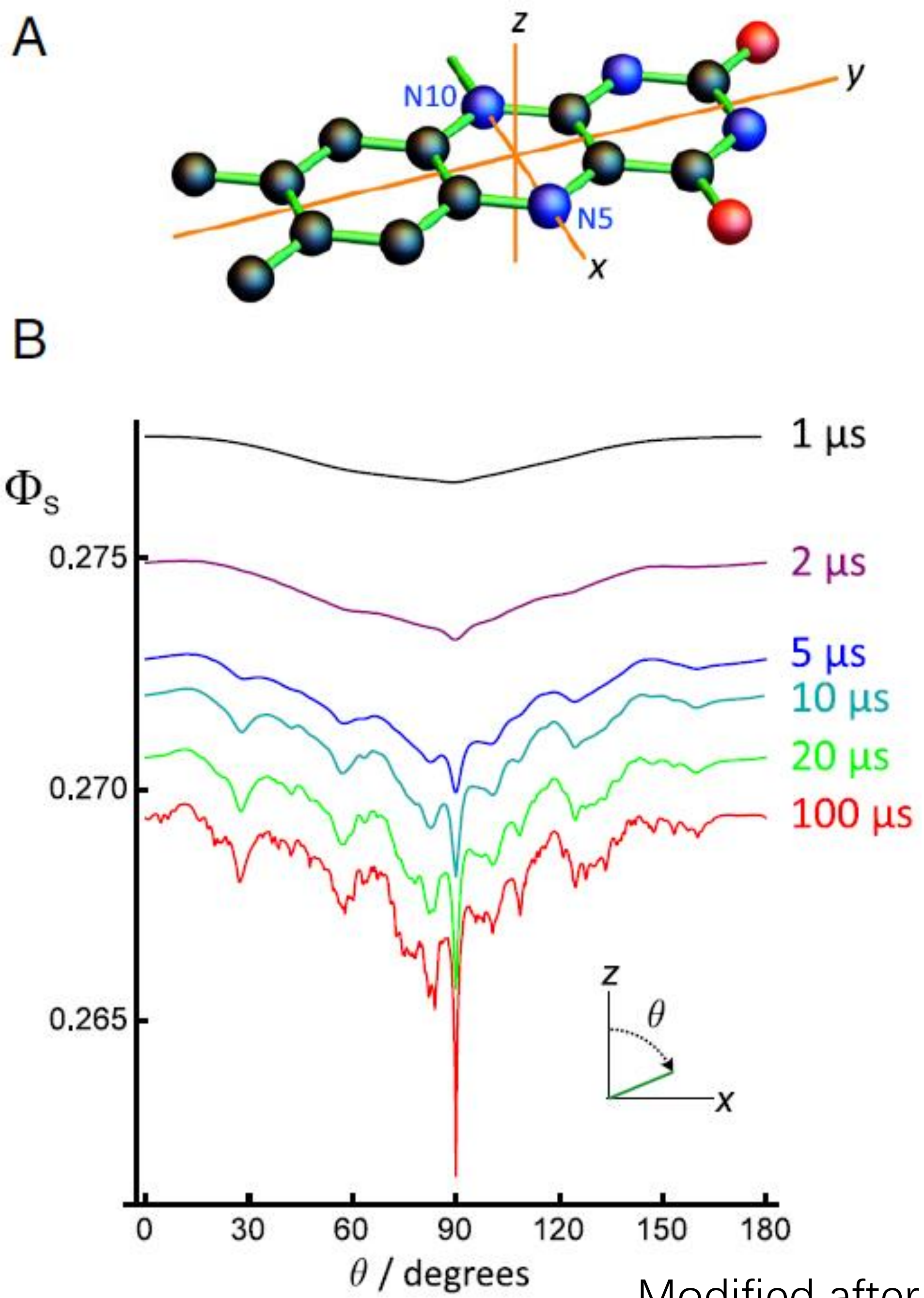
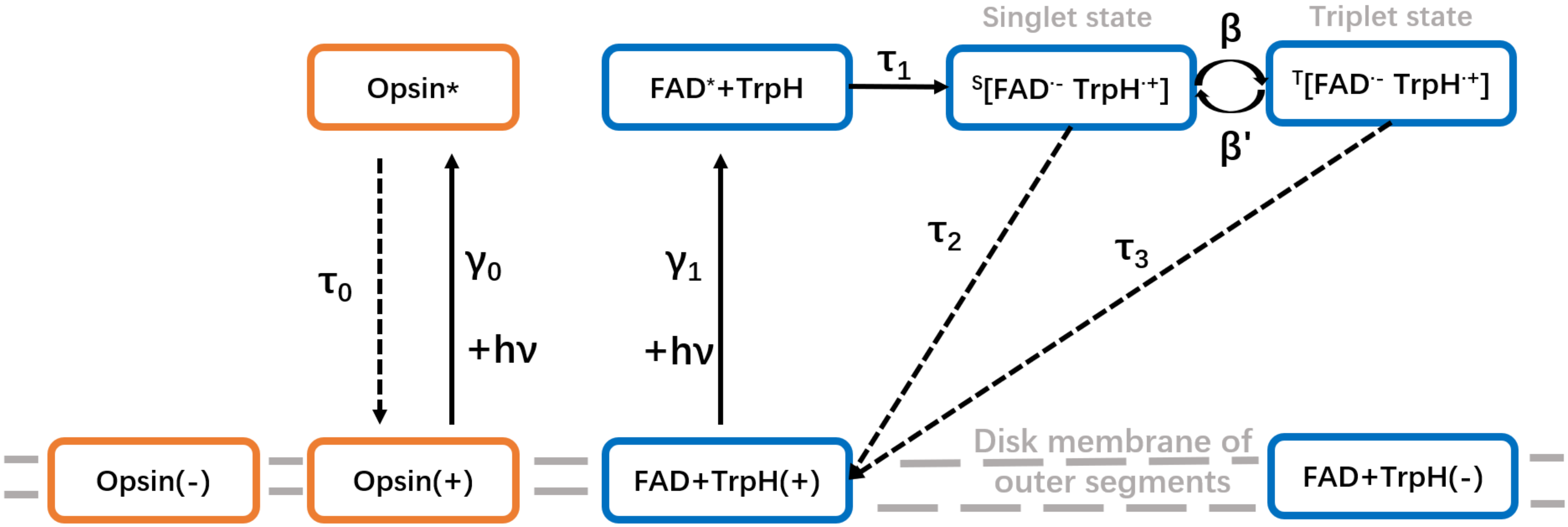


Modified after Ref.[10]

OCC

Photon Competition

Opsin-Cryptochrome Competition model

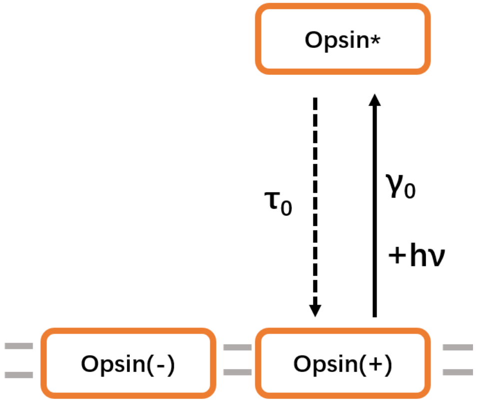


(+) represents the ground state of a molecule absorbed by one photon; (*) represents the excitation state of a molecule after photon absorption; (s) and (t) represent the singlet and triplet state of a molecule.

Model formulation

$$N_{op}^{(+)} + N_{FAD}^{(+)} = N_{photon} \tag{9}$$

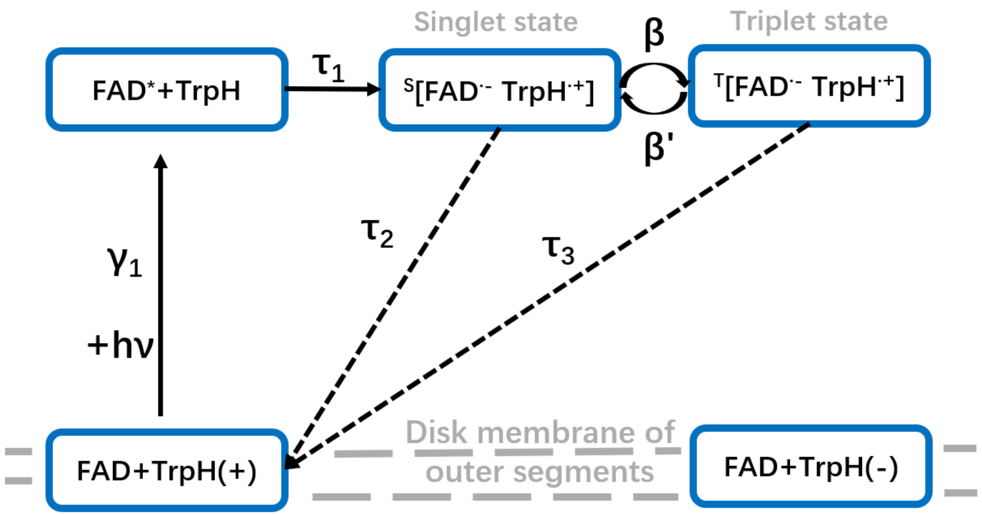
$$R_{opsin} = \frac{N_{op}^{(+)}}{N_{photon}} \tag{10}$$



$$N_{op}^{(+)} + N_{op}^{*} + N_{op}^{(-)} = C_1 \tag{1}$$

$$\frac{d(N_{op}^{(+)} + N_{op}^{(-)})}{dt} = -\gamma_0 N_{op}^{(+)} + \frac{1}{\tau_0} N_{op}^{*} \tag{2}$$

$$\frac{dN_{op}^{*}}{dt} = \gamma_0 N_{op}^{(+)} - \frac{1}{\tau_0} N_{op}^{*} \tag{3}$$



$$N_{FAD}^{(+)} + N_{FAD}^{*} + N_{FAD}^{Singlet} + N_{FAD}^{Triplet} + N_{FAD}^{(-)} = C_2 \tag{4}$$

$$\frac{d(N_{FAD}^{(+)} + N_{FAD}^{(-)})}{dt} = -\gamma_1 N_{FAD}^{(+)} + \frac{1}{\tau_2} N_{FAD}^{Singlet} + \frac{1}{\tau_3} N_{FAD}^{Triplet} \tag{5}$$

$$\frac{dN_{FAD}^{(*)}}{dt} = \gamma_1 N_{FAD}^{(+)} - \frac{1}{\tau_1} N_{FAD}^{*} \tag{6}$$

$$\frac{dN_{FAD}^{Singlet}}{dt} = \frac{1}{\tau_1} N_{FAD}^{*} - \frac{1}{\tau_2} N_{FAD}^{Singlet} - \beta N_{FAD}^{Singlet} + \beta' N_{FAD}^{Triplet} \tag{7}$$

$$\frac{dN_{FAD}^{Triplet}}{dt} = \beta N_{FAD}^{Singlet} - \beta' N_{FAD}^{Triplet} - \frac{1}{\tau_3} N_{FAD}^{Triplet} \tag{8}$$

A stationary solution: let all derivatives=0

$$N_{op}^{(+)} + N_{FAD}^{(+)} = N_{photon} \tag{9}$$

$$R_{opsin} = \frac{N_{op}^{(+)}}{N_{photon}} \tag{10}$$

$$N_{op}^{(-)} + B * N_{op}^{(+)} = C_1 \tag{11}$$

$$N_{FAD}^{(-)} + A * N_{FAD}^{(+)} = C_2 \tag{12}$$

$$(A - B) N_{op}^{(+)2} + (C_1 + C_2 - N_{photon}(A - B)) N_{op}^{(+)} - N_{photon} C_1 = 0 \tag{15}$$

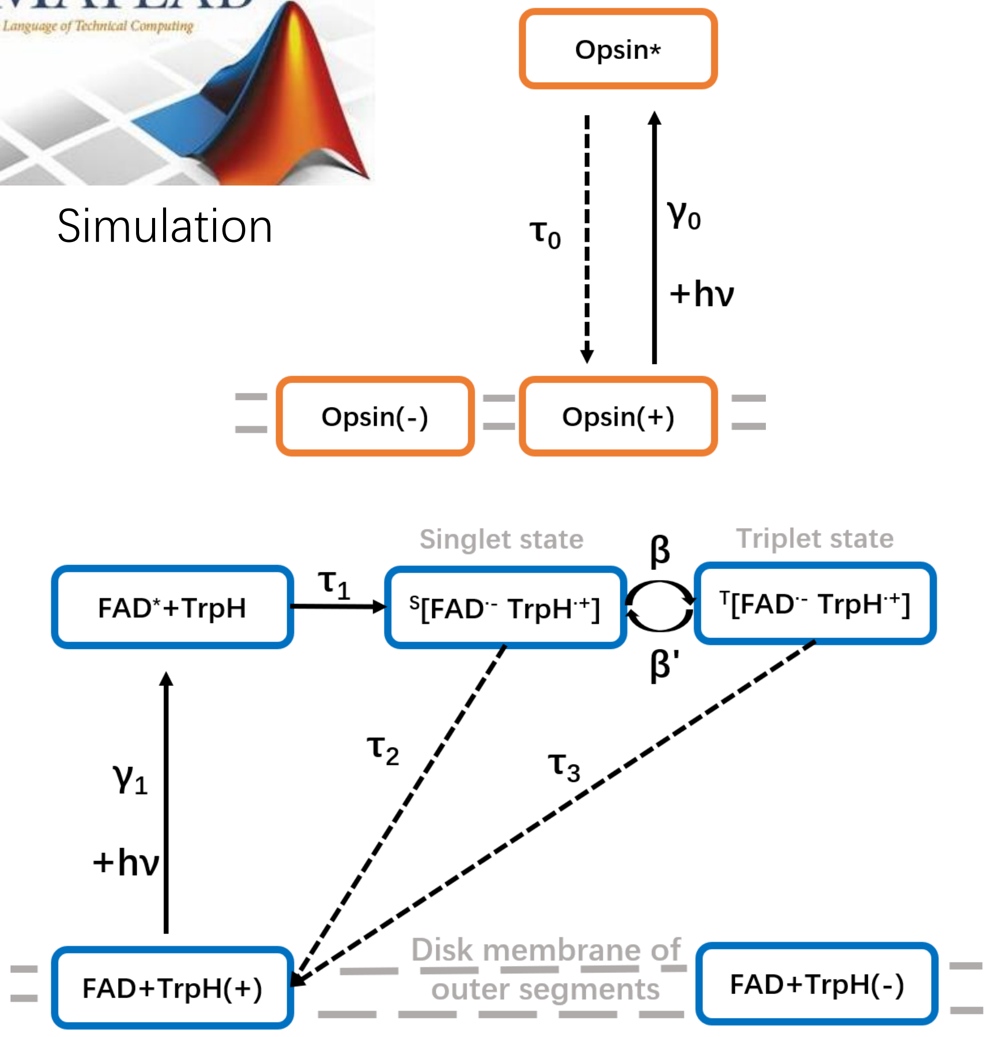
$$R_{opsin} = \frac{-(C_1 + C_2 - N_{photon}(A - B)) + \sqrt{(C_1 + C_2 - N_{photon}(A - B))^2 + 4 N_{photon} C_1 (A - B)}}{2 N_{photon}(A - B)} \tag{16}$$

$$A = 1 + \gamma_1 \left(\tau_1 + \frac{1}{\frac{\beta'}{\tau_2 \beta} + \frac{1}{\tau_2 \tau_3 \beta} + \frac{1}{\tau_3}} + \frac{1}{\frac{1}{\tau_2} + \frac{\beta}{\tau_3 \beta' + 1}}\right) \qquad B = \tau_0 \gamma_0 + 1$$

Simulation

Parameter initiation

Simulation



- **Singlet-triplet oscillation β coefficient:**

  $\beta' = 0;\ \beta = \dfrac{\Delta(\Phi T)}{\Delta(\tau_2)}$ in terms of angle

- **Reciprocal of rate constant(lifetime):**

  $\tau_0 = 4.2ms;\ \tau_1 = 1ns;$

  $\tau_2 = 1us;\ \tau_3 = 10ms;$

- **Rate constant of light absorption:**

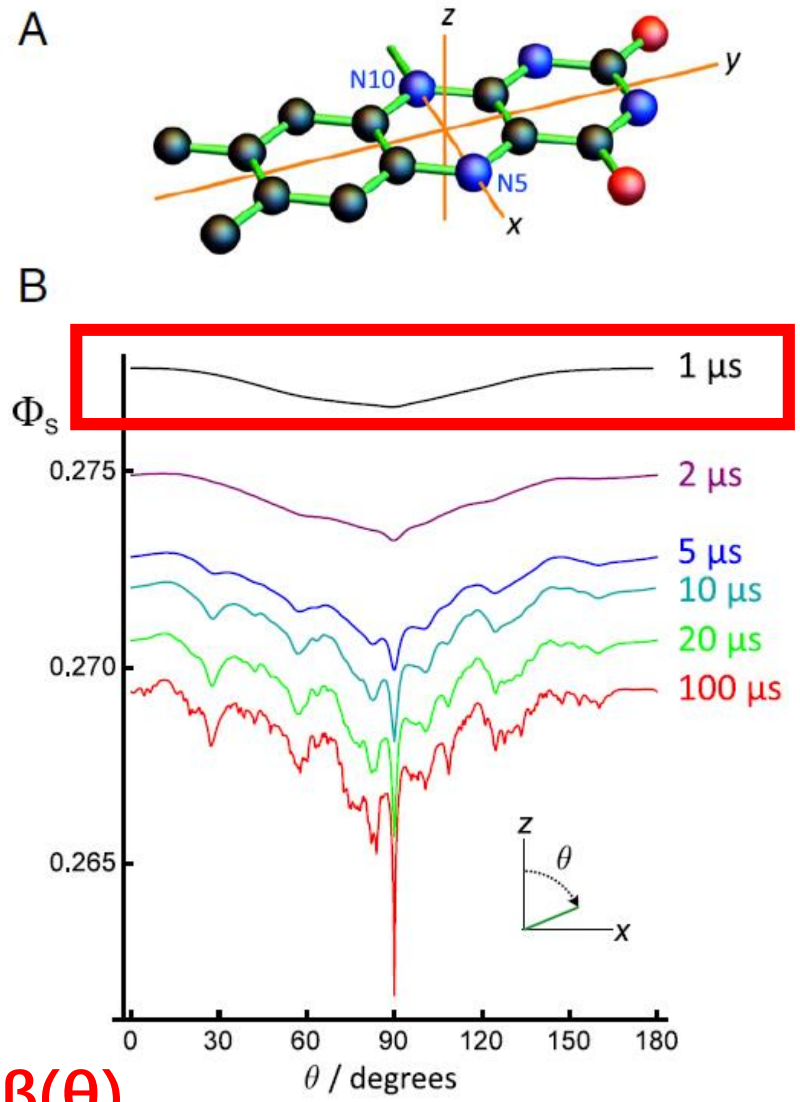
  $\gamma_0 = \gamma_1 = 10^9/s;$

- Assume the **protein number** of opsin and cryptochrome is the same: $C_1 = C_2$

- **Incident photon number** N_{photon}

  where $N_{photon}:C_1 = 10^{-3}$

Parameter initiation

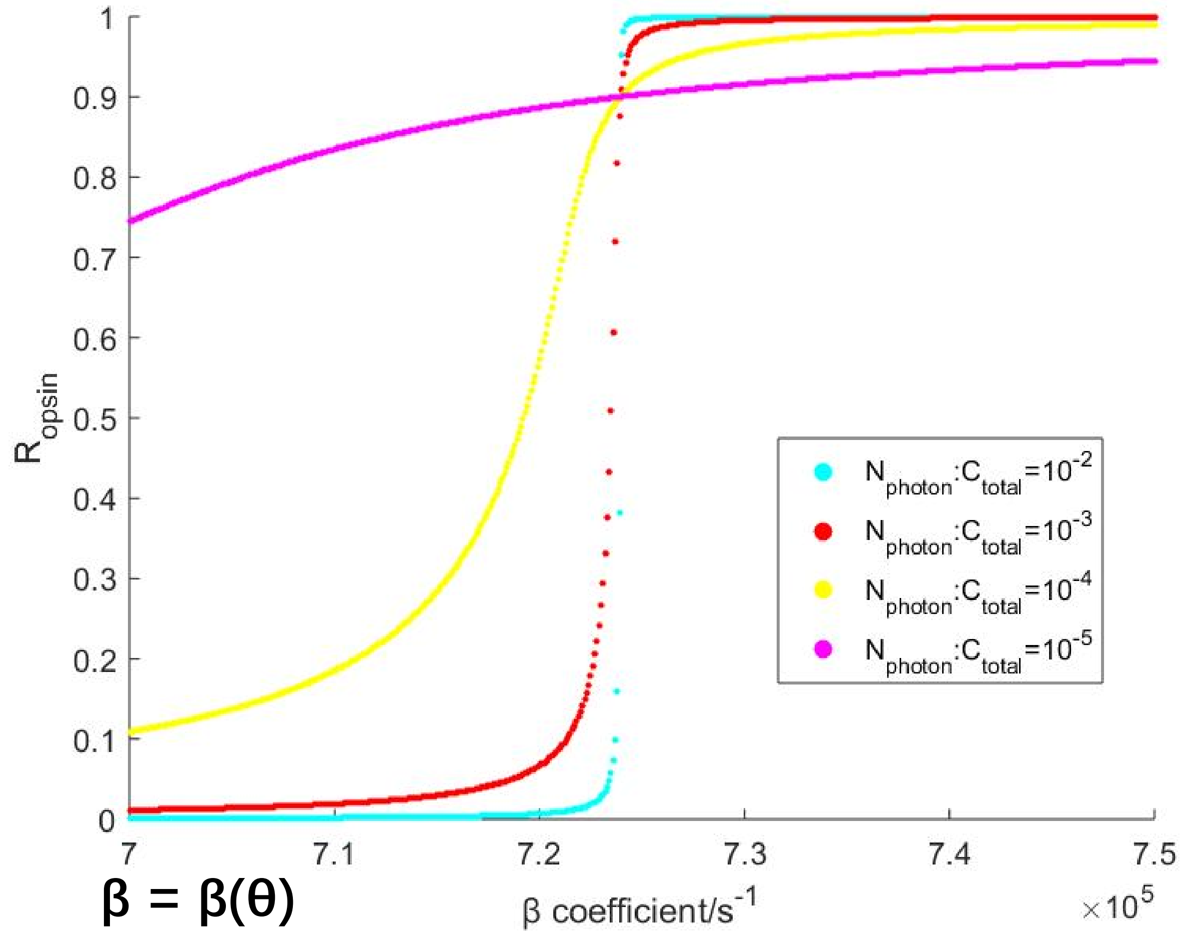


$\beta = \beta(\theta)$

- Singlet-triplet oscillation β coefficient:
  $\beta' = 0$; $\boldsymbol{\beta = \frac{\Delta(\Phi T)}{\Delta(\tau_2)}}$ **in terms of angle**
- Reciprocal of rate constant(lifetime):
  $\tau_0 = 4.2ms$; $\tau_1 = 1ns$;
  $\tau_2 = 1us$; $\tau_3 = 10ms$;
- Rate constant of light absorption:
  $\gamma_0 = \gamma_1 = 10^9/s$;
- Assume the protein number of opsin and cryptochrome is the same: $C_1 = C_2$
- Incident photon number N_{photon}
  where $N_{photon}:C_1 = 10^{-3}$

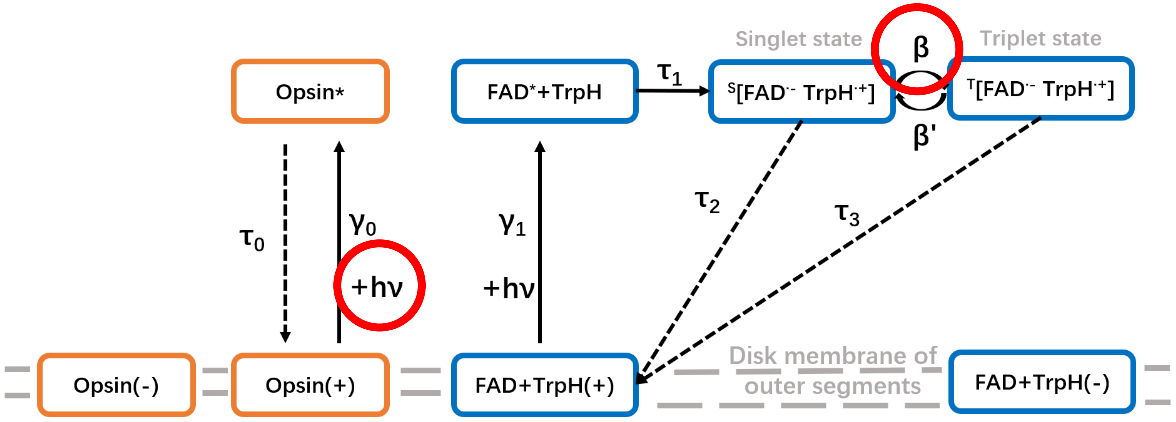
Secondary amplification effect

$$R_{opsin} = \frac{-(C_1 + C_2 - N_{photon}(A - B)) + \sqrt{(C_1 + C_2 - N_{photon}(A - B))^2 + 4N_{photon}C_1(A - B)}}{2N_{photon}(A - B)}$$



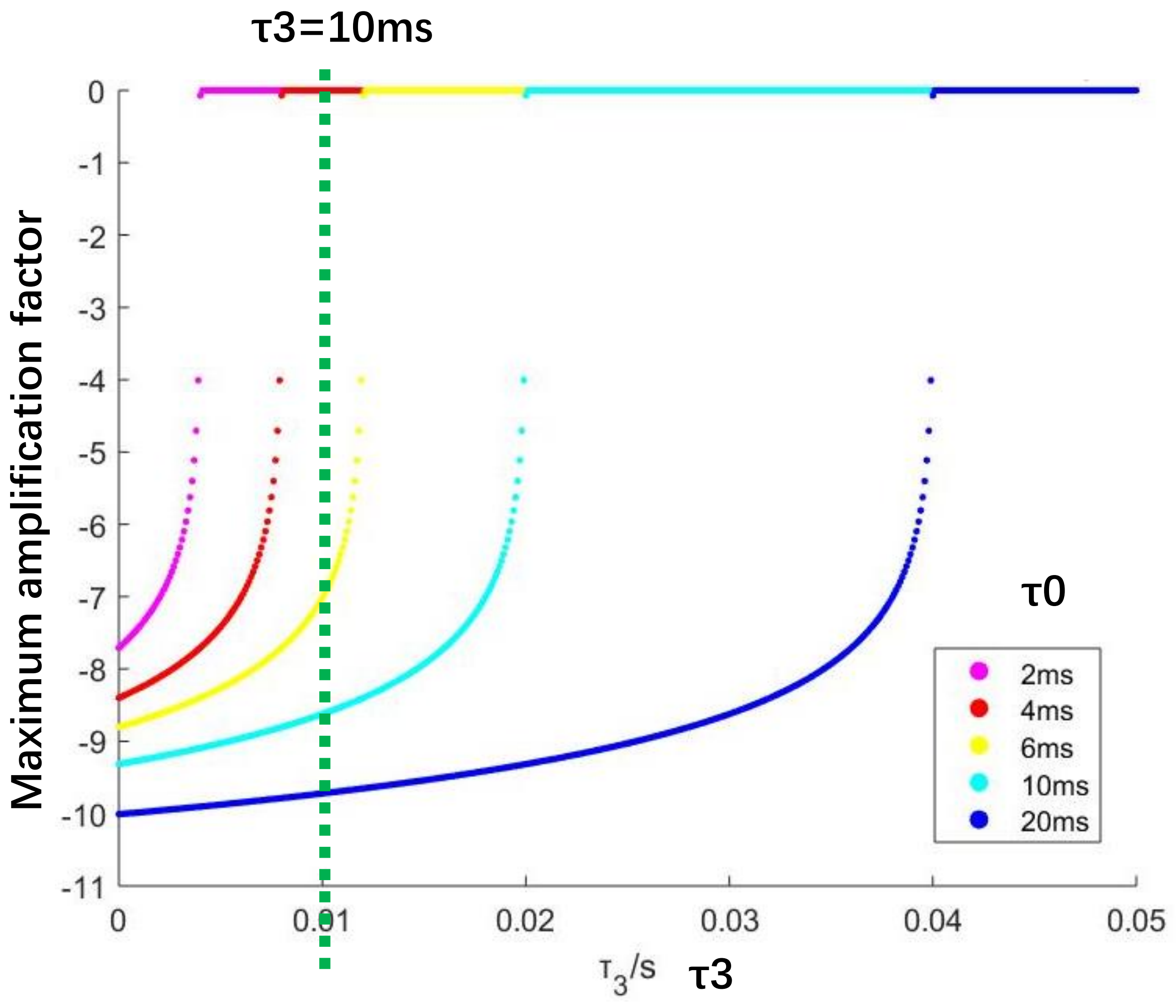
β = β(θ)

$R_{opsin} \in (0, 1)$ representing the percentage of incident photons that are absorbed by rhodopsin.

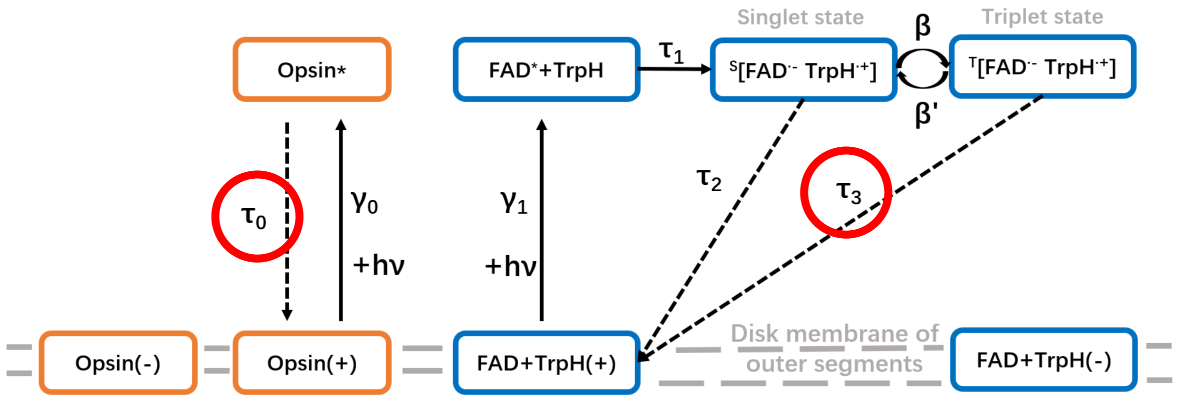


- Ratio of incident photons and protein numbers are critical for amplification **indicating a photon threshold** for magnetoreception.

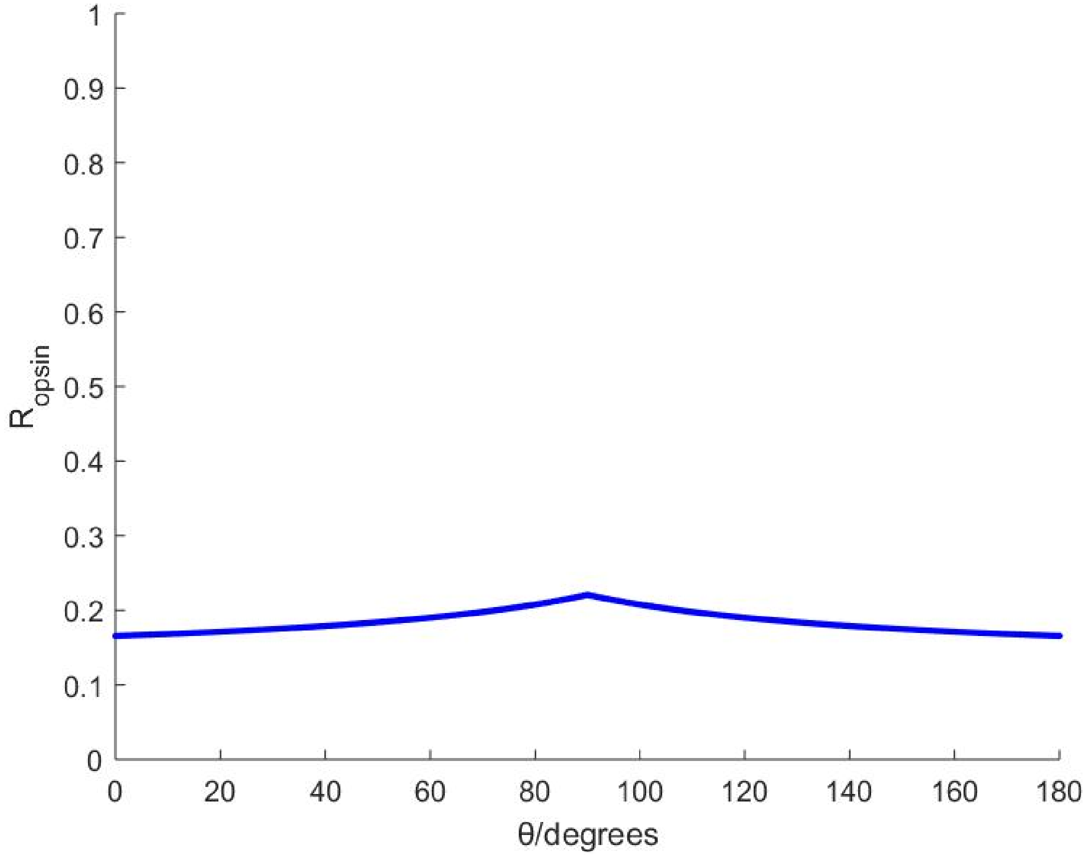
Secondary amplification effect

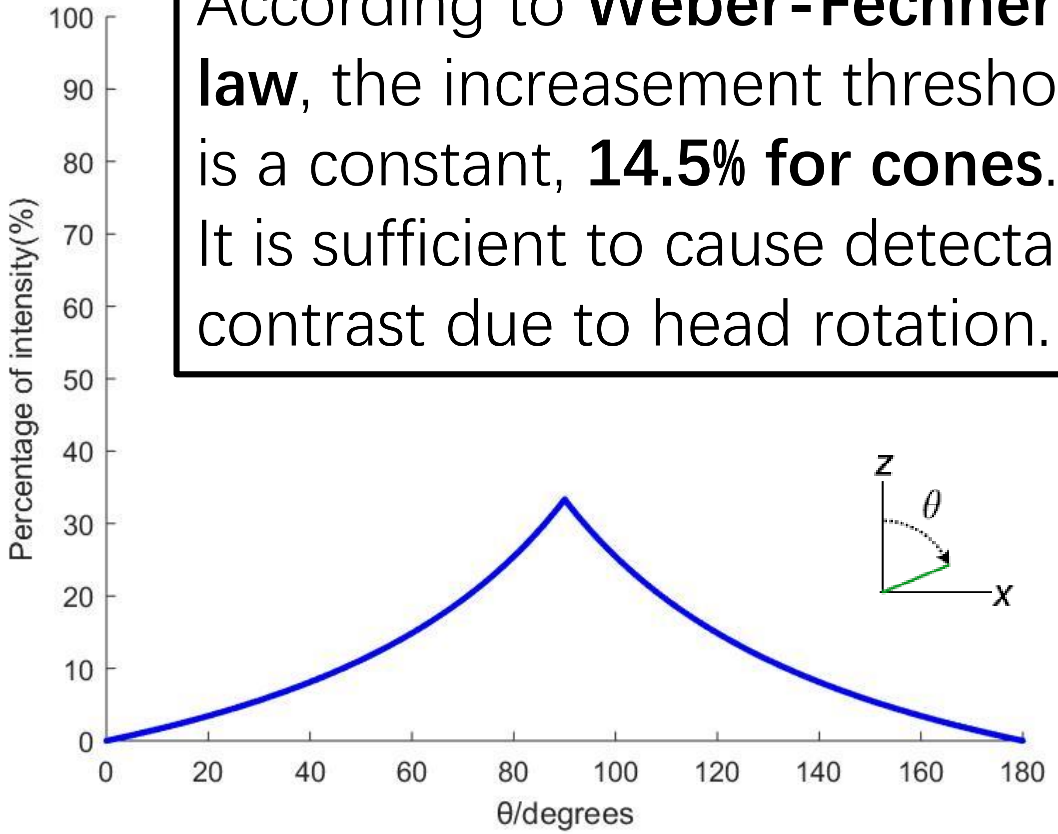


- **The quantity of τ0** is critical for the amplification effect.
- The secondary amplification effect is a key step to **convert a physical cause into biological consequence**.



Photon competition simulation result

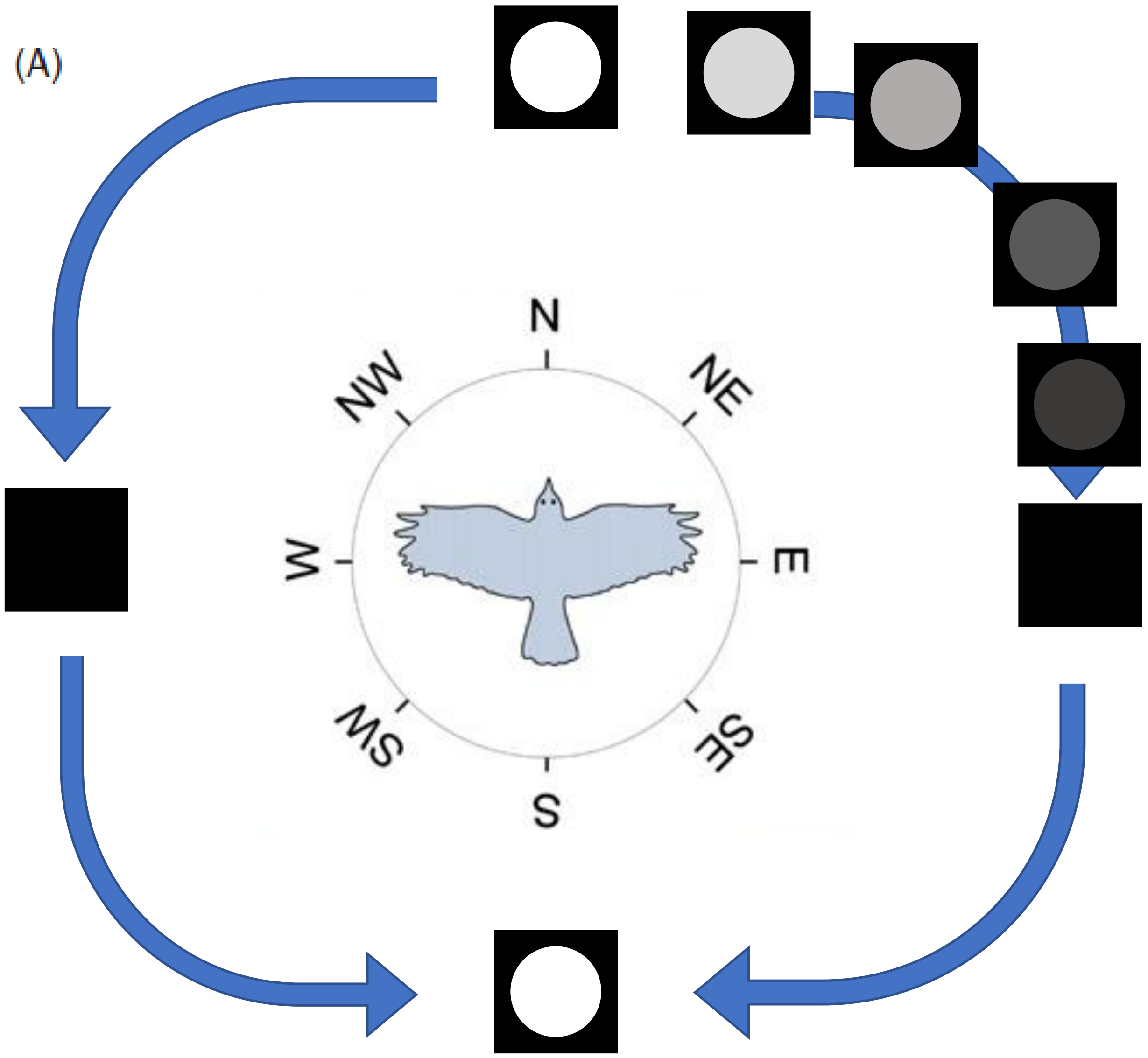


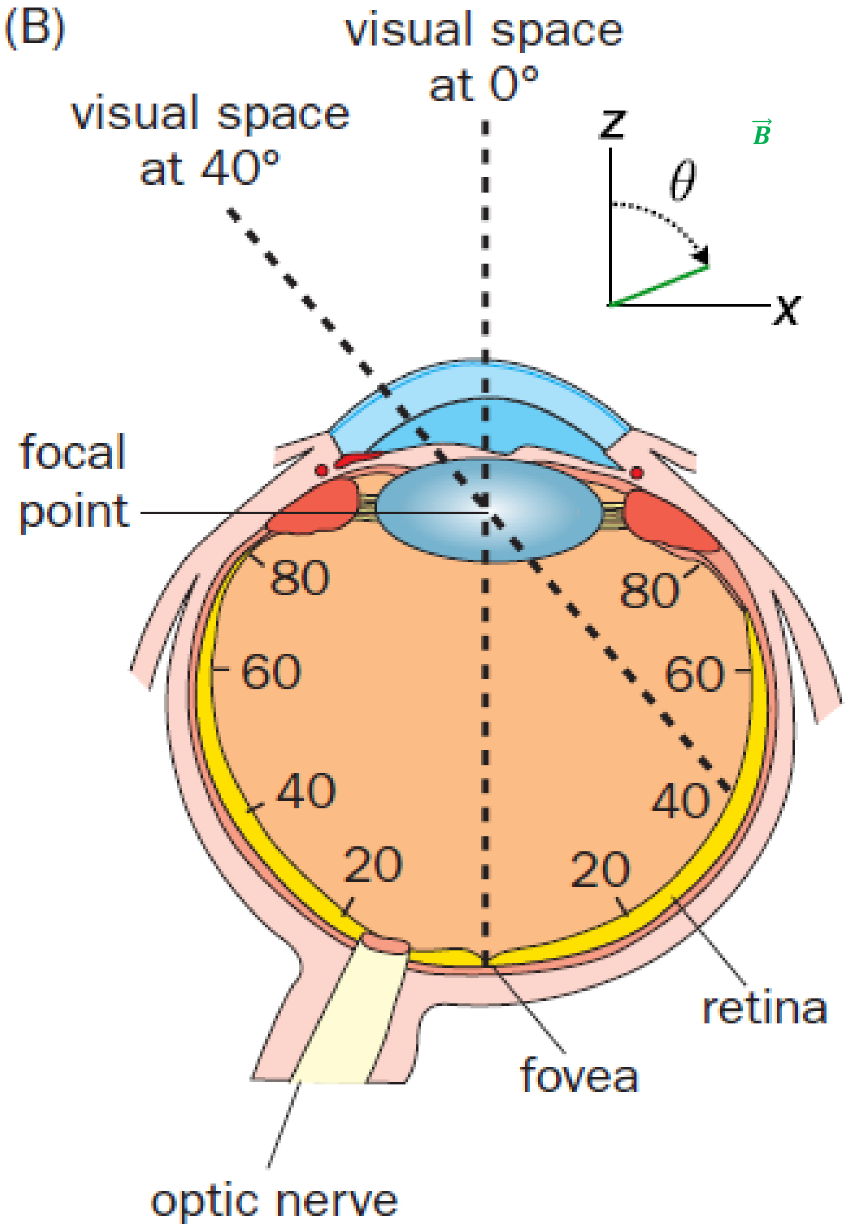


According to **Weber-Fechner law**, the increasement threshold is a constant, **14.5% for cones**.
It is sufficient to cause detectable contrast due to head rotation.

$R_{opsin} = R_{opsin}(\beta)$ **and** $\beta = \beta(\theta)$

Incresement threshold = $\frac{\Delta I}{I}$


(A)
N
NE
E
SE
S
SW
W
NW


(B)
visual space
at 0°
visual space
at 40°
z
x
θ
$\vec{B}$
focal
point
80
60
40
20
80
60
40
20
retina
fovea
optic nerve

Experimental predictions

- Our model give a prediction that **cone cells are magnetic sensors** with two properties:

(1) **Incident photon threshold** for magnetic sensing.

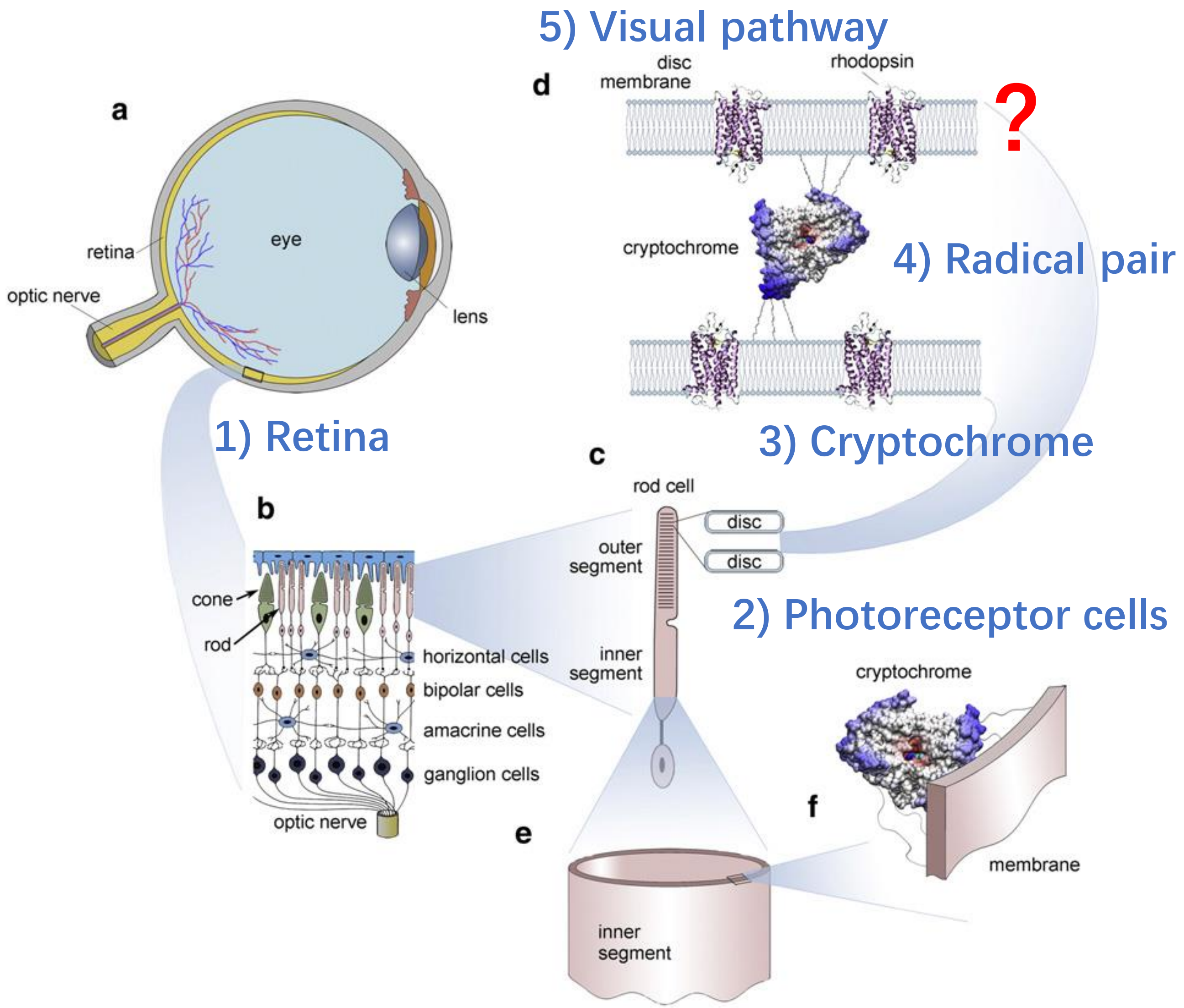
- There are lower and upper photon thresholds for competition of opsin and cryptochrome. Controlled light intensity of background can be a on-off effect for magnetoreception.

(2) **Disruption/Analogy** of the magnetic sensing.

- Under zero magnetic field, generate an artificial light pattern resembling the earth magnetic field effect.
- Use changing spatial intensity of incident light on the retina to disrupt the existing light pattern caused by earth magnetic field .

Summary

? ➡ OCC?



- A popular hypothesis of (4)-(5) is an noncanonical biological pathway of visual system that can modulate night vision. **No such signaling pathway** is found till now.
- We propose that no downstream signaling involved and instead a photon competition plays a key role.

A novel biophysical model:

Opsin-Cryptochrome competition model(OCC model).

<u>Experiments to verify this model are proposed.</u>

Discussion

- Our model only works under **the radical-based magnetoreception** in **migratory birds** under **total overcast and under dim light**.
- European robin, pigeon and turtle seems use a inclination magnetic compass whereas other animals use intensity or polarity compass.

Parameter setting:

- Recovery time of retinal: τ_0
- Singlet-triplet oscillation β
- Singlet product τ_2
- Triplet products τ_3

1. Decoherence time – molecular motion
2. Photon threshold and visual pattern
3. Protein distribution
4. Number ratio of cry4 and opsin protein
5. Intensity perception of rods and cones

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Acknowledgement

- Thanks for Dr. Jiansheng Wu for the helpful instructions in theoretical realization of the biophysical model and warm guidance during the project.

https://github.com/LokyWei/Biophysical-model

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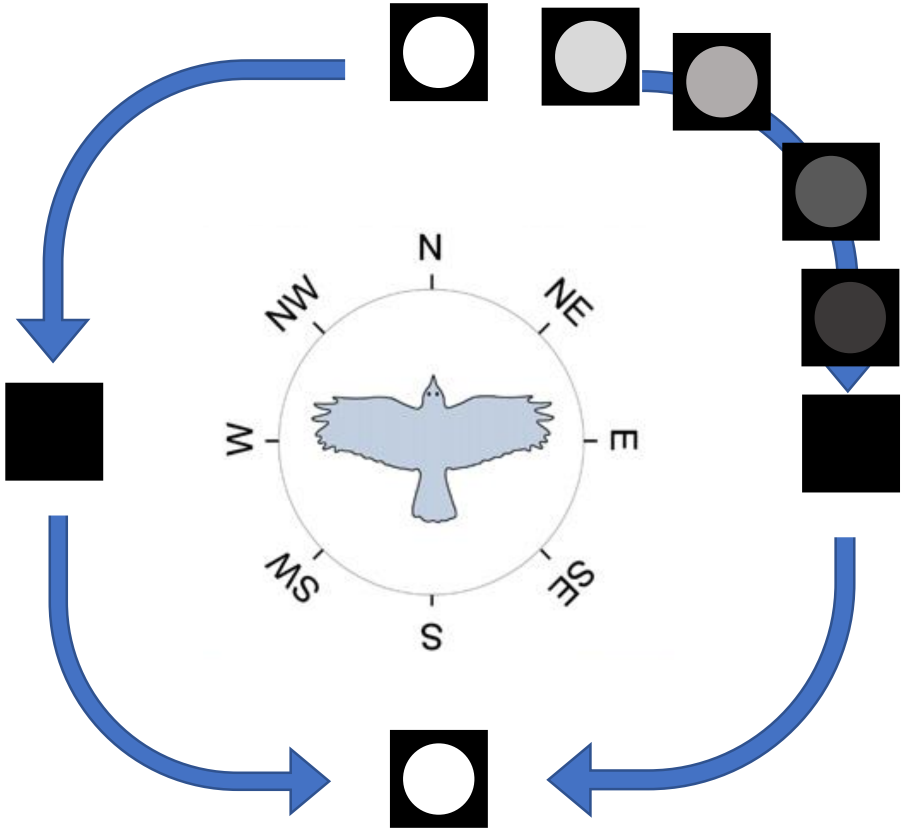
Thank you



Appendix

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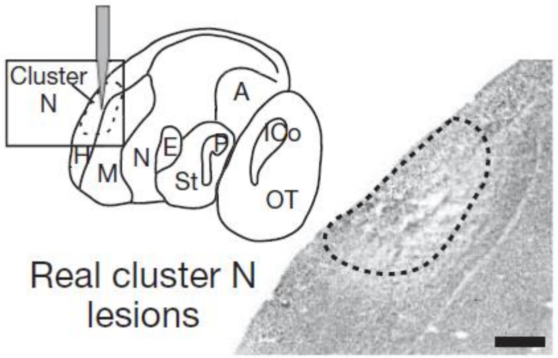
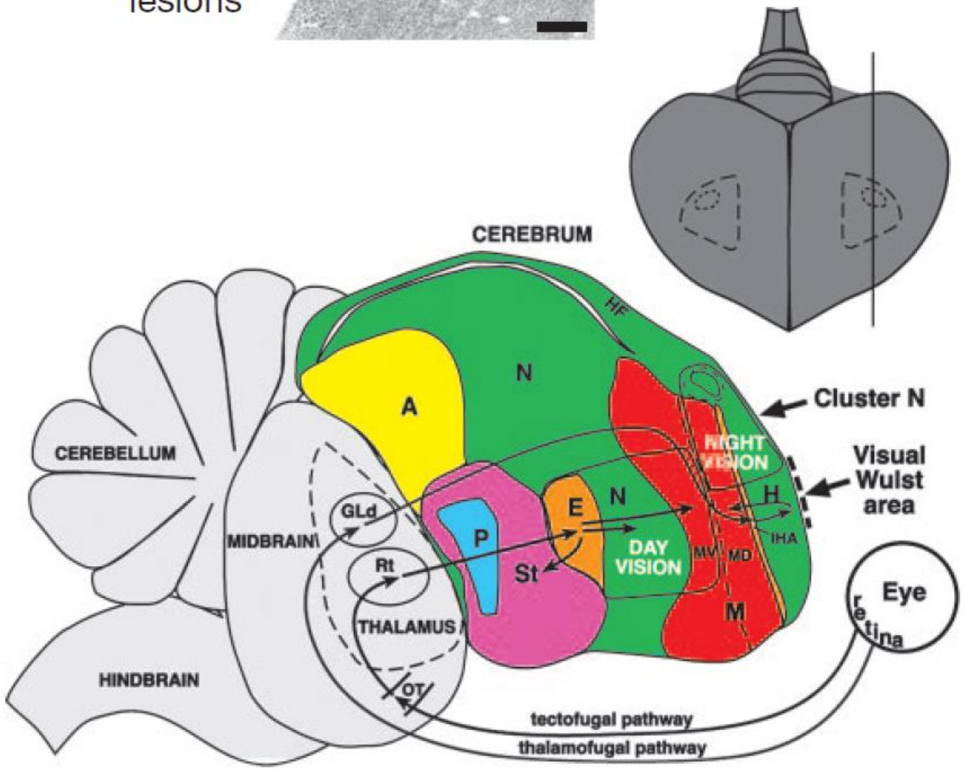
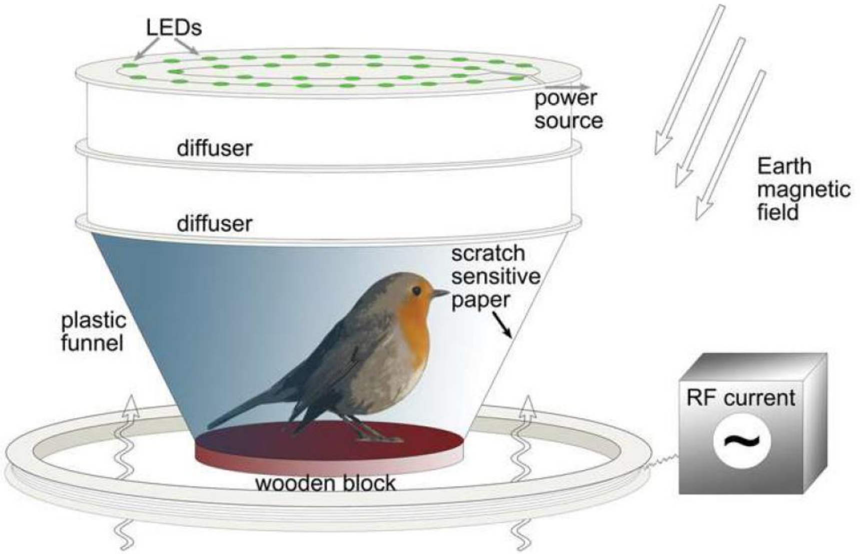
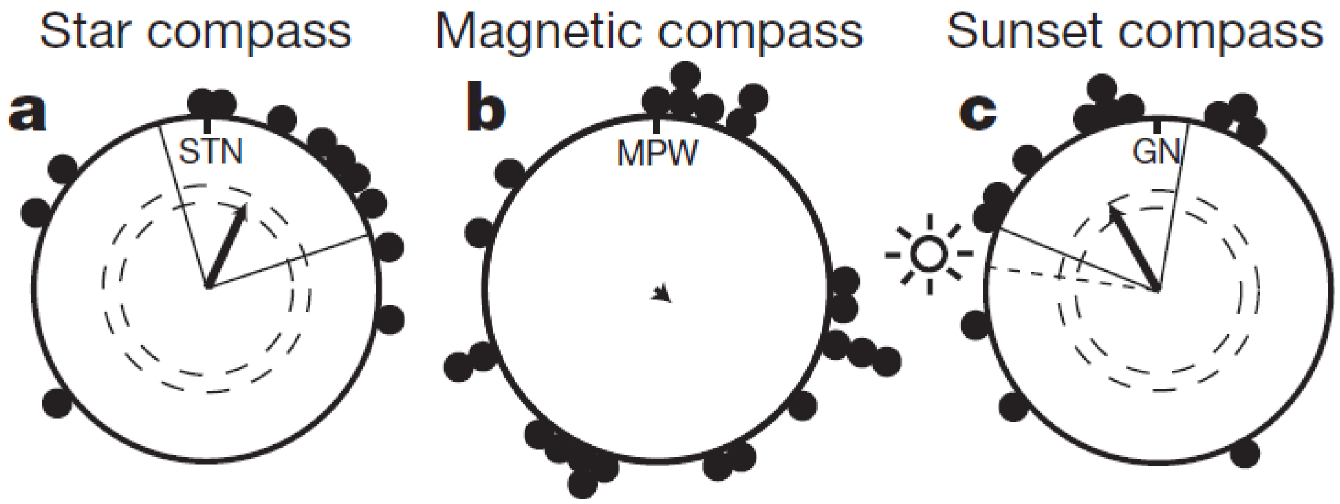
- 1) A neural connection between night vision and magnetic sensing in European robin.

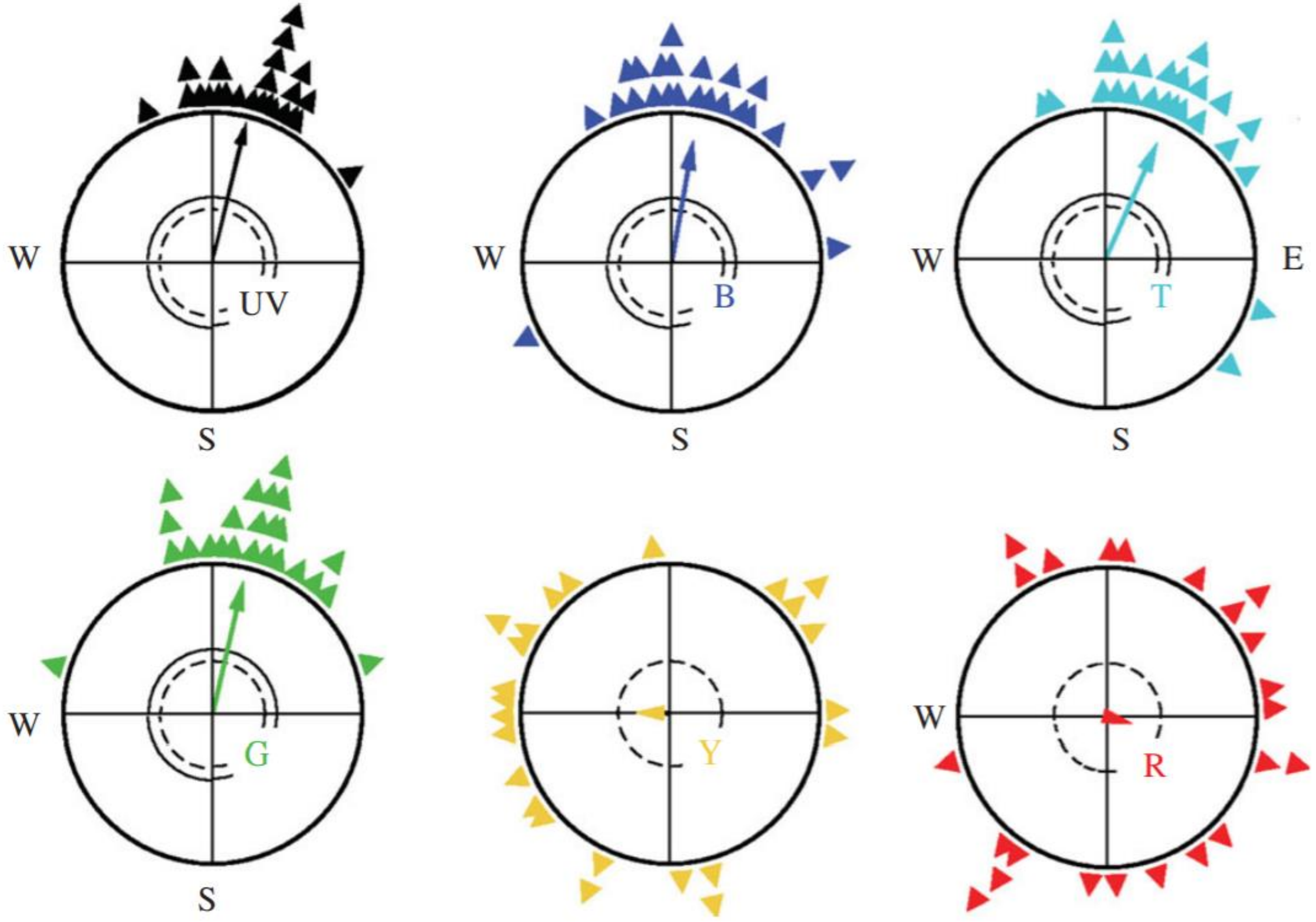




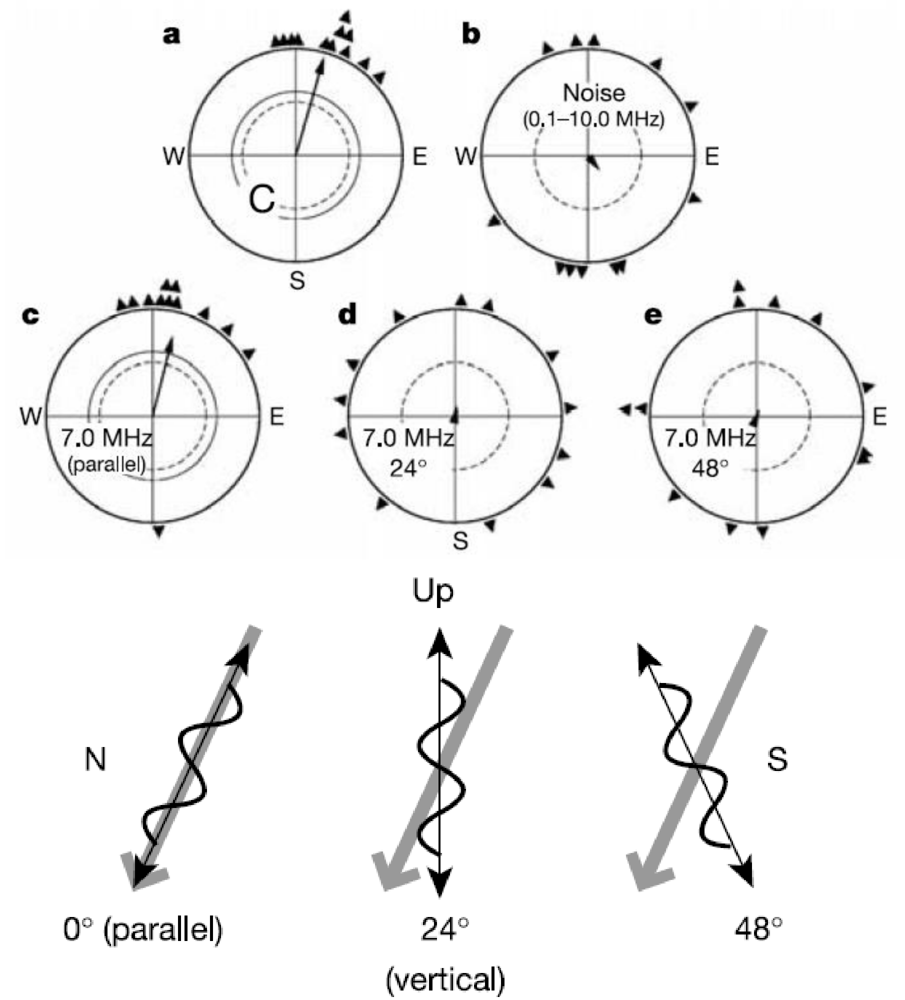




- 2) Different wavelength of incident light can disrupt magnetic orientation of European robin.

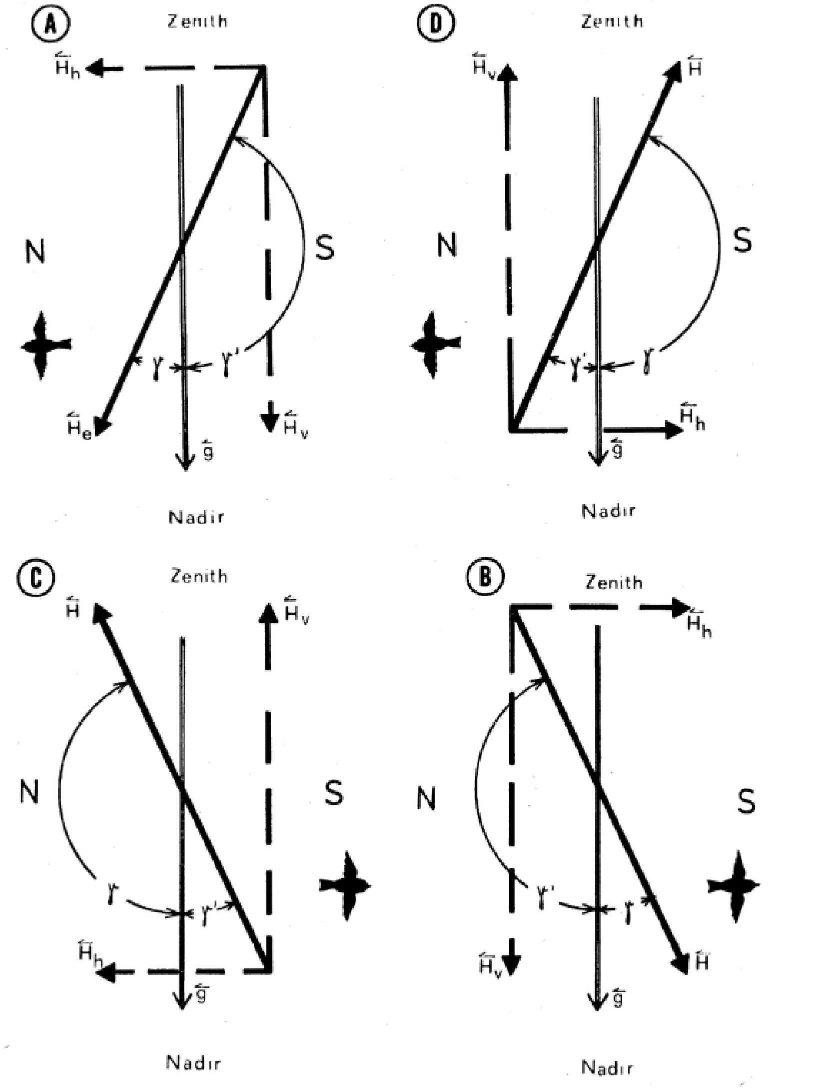


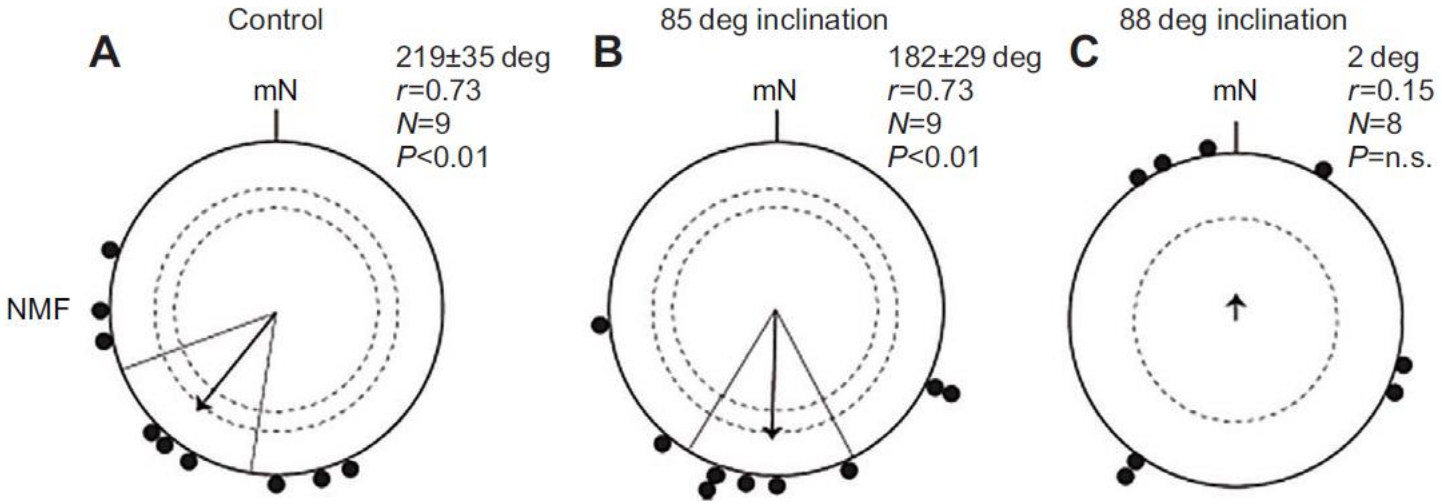
Orientation of European robin under monochromatic light of different wavelengths



Robins were disoriented when exposed to a vertically aligned broadband (0.1–10 MHz) or a single-frequency (7-MHz) field in addition to the geomagnetic field.

- 3) The magnetic compass of European robin is a inclination compass with <5° precision, which can be explained by radical pair mechanism instead of any other hypothesis.



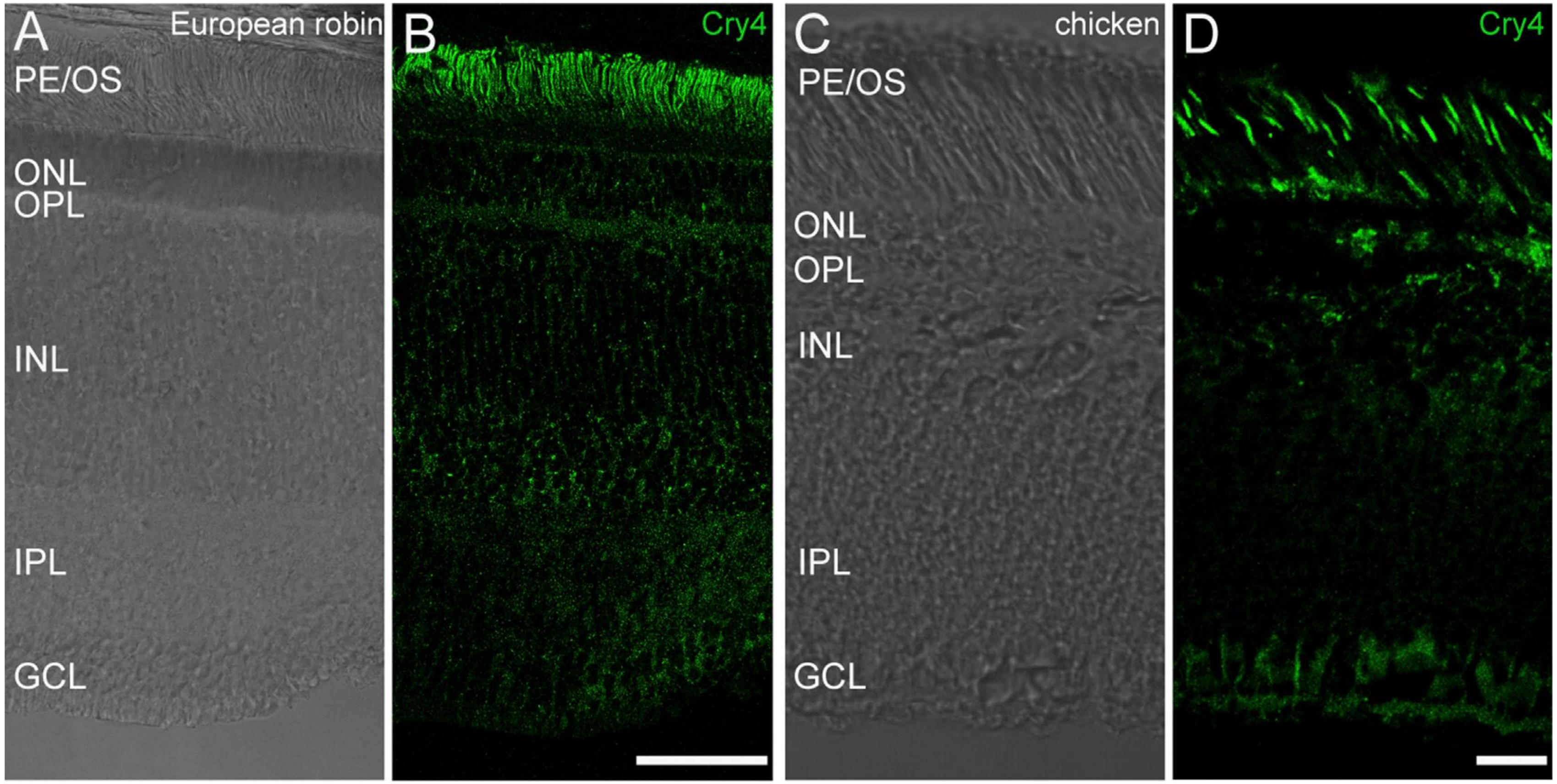


The orientation of individual blackcaps was tested in magnetic fields with 67, 85 or 88 degree inclination

The magnetic compass of European robins **does not use the polarity of magnetic field** for detecting the north direction.

The birds derive their north direction from interpreting the **inclination of the axial direction** of the magnetic field lines in space, where **field lines and gravity vector form the smaller angle**.

- 4) Cry4 protein, a member of cryptochrome family, is found recently located on the outer segment in cones in birds' retina.



Cry4 Is Expressed in the Outer Segments of Specific Photoreceptor Cells in the Retina of European Robin and Chicken