MOLECULAR DYNAMICS OF THE QUASI-CARNO CYCLE FOR RETINAL ISOMERIZATION MOLECULAR MACHINE

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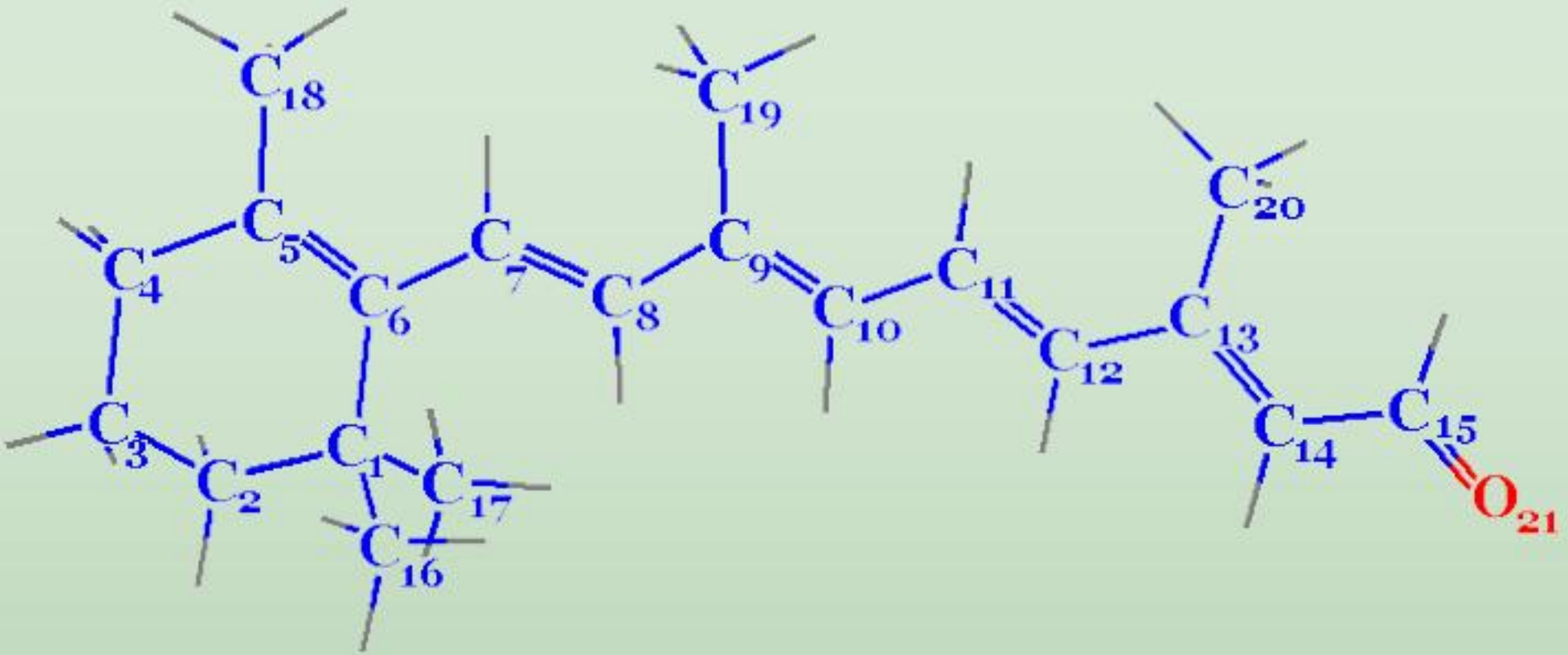
The system of protein rhodopsin or bacteriorhodopsin with a chromophore retinal is one of examples of molecular biological system with surprising effectiveness.

Retinal absorbs light.

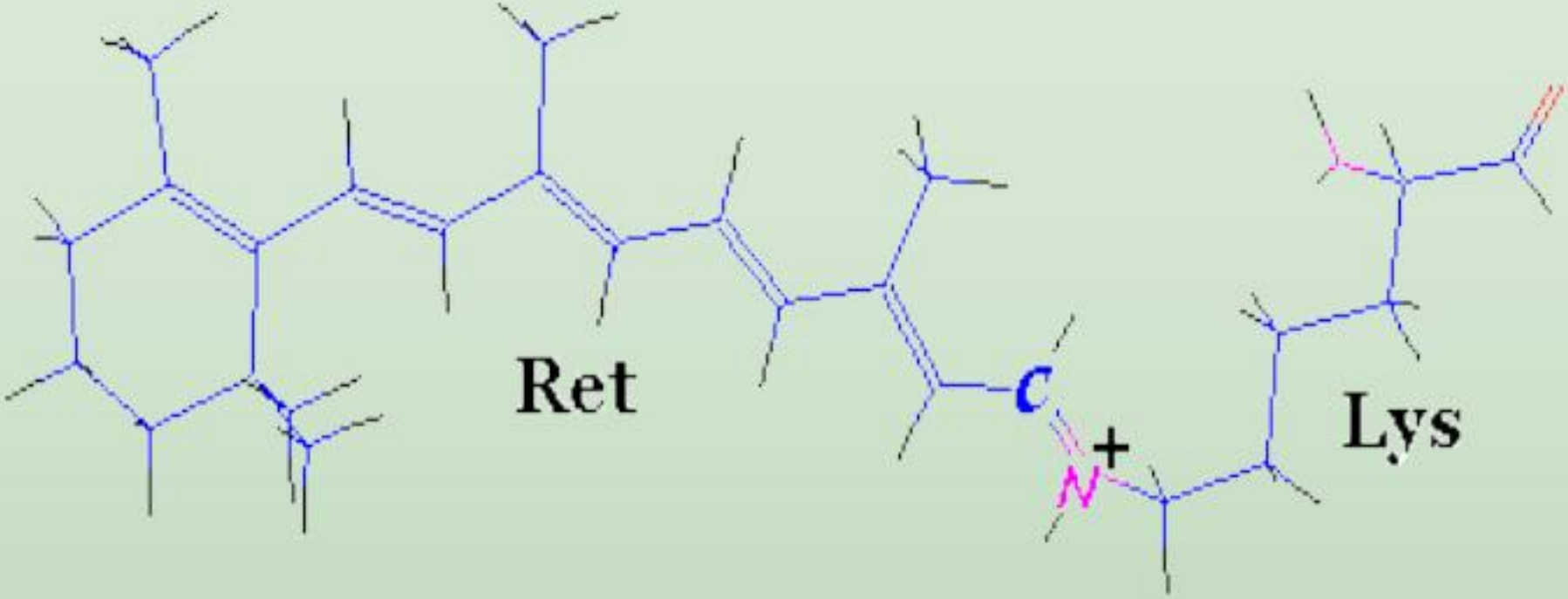
Then in a system there are particular conformational rearragements.

As a result of such modifications it gains ability to transfer a proton, starting thus a chain of the subsequent reactions.

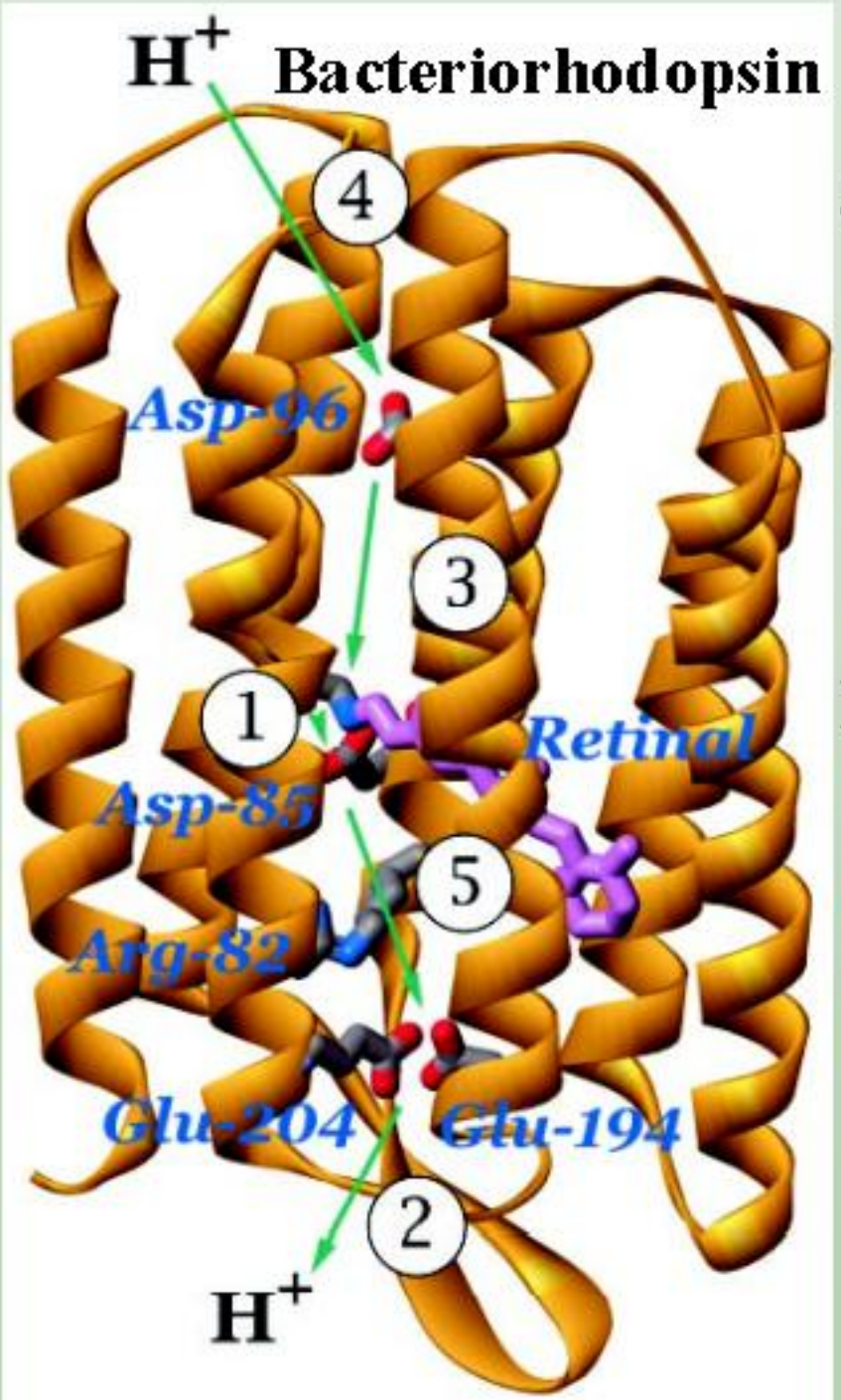


Structure and atom labeling of the all-trans retinal molecule.

Initial conformation for bacteriorhodopsin

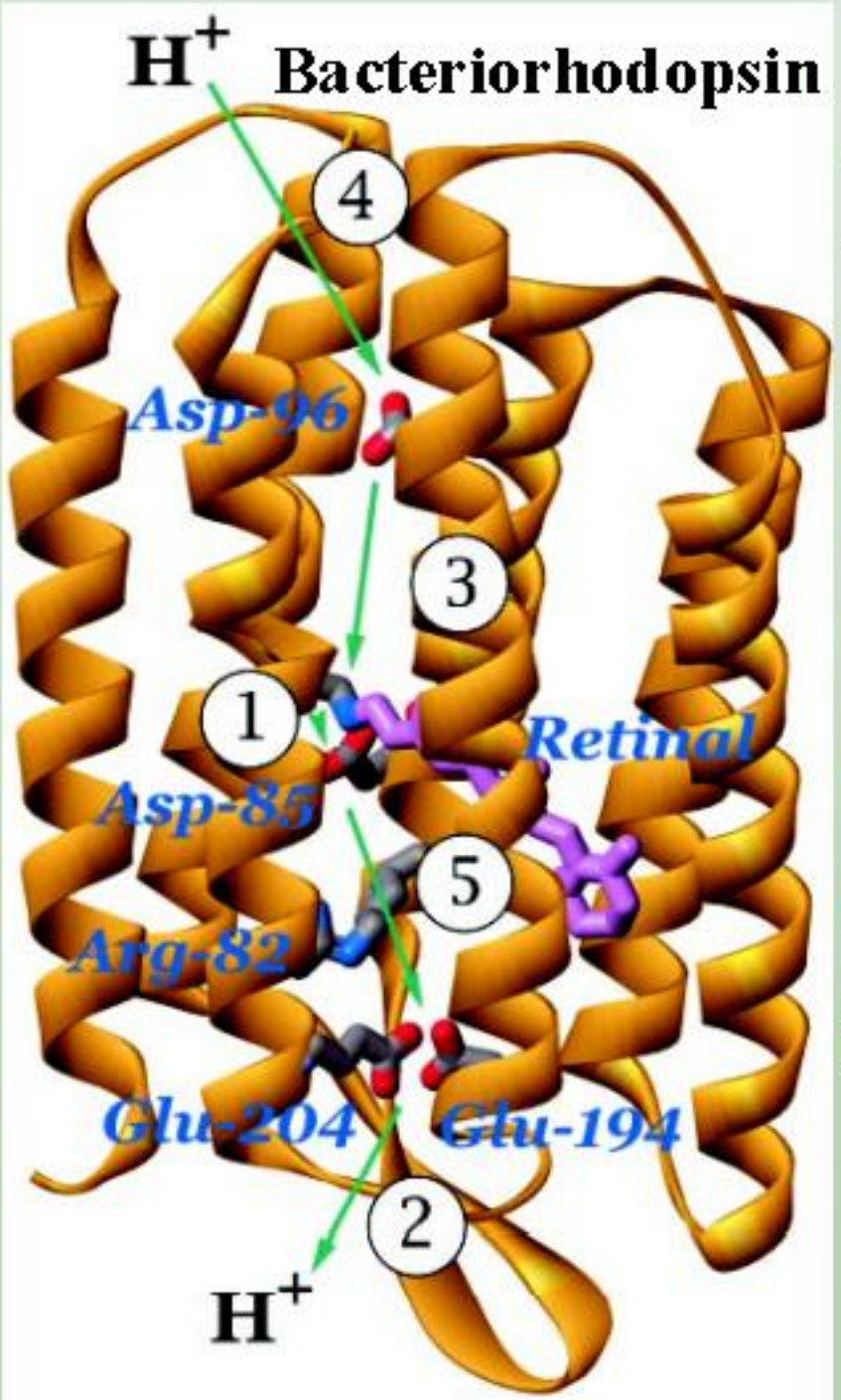


In rhodopsin proteins retinal is bonded with lysine by means of Schiff base.



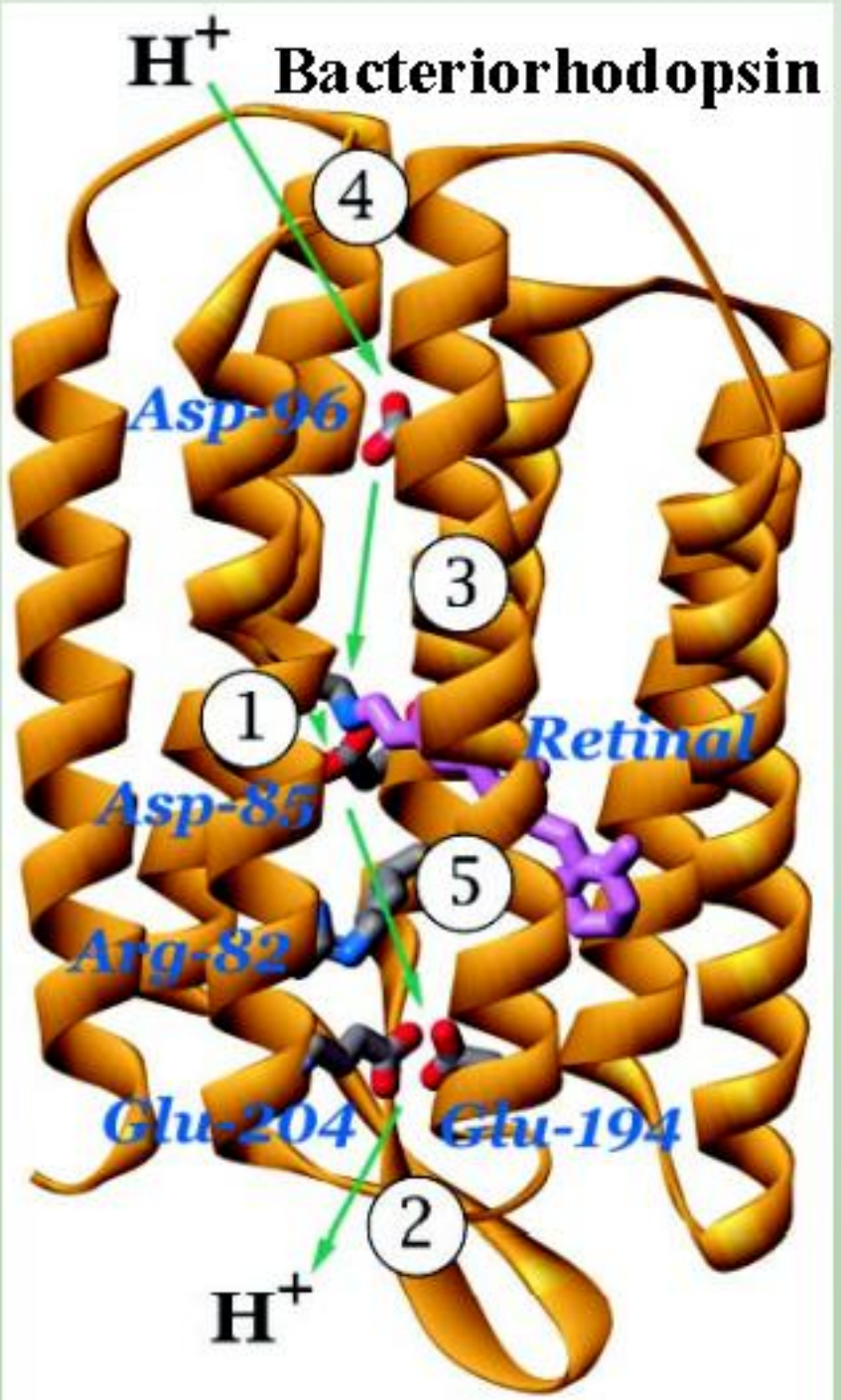
Bacteriorhodopsin and visual rhodopsin are integral membrane proteins with 7 trans–membrane α-helices.

These helices form a pocket around of bound strained retinal.

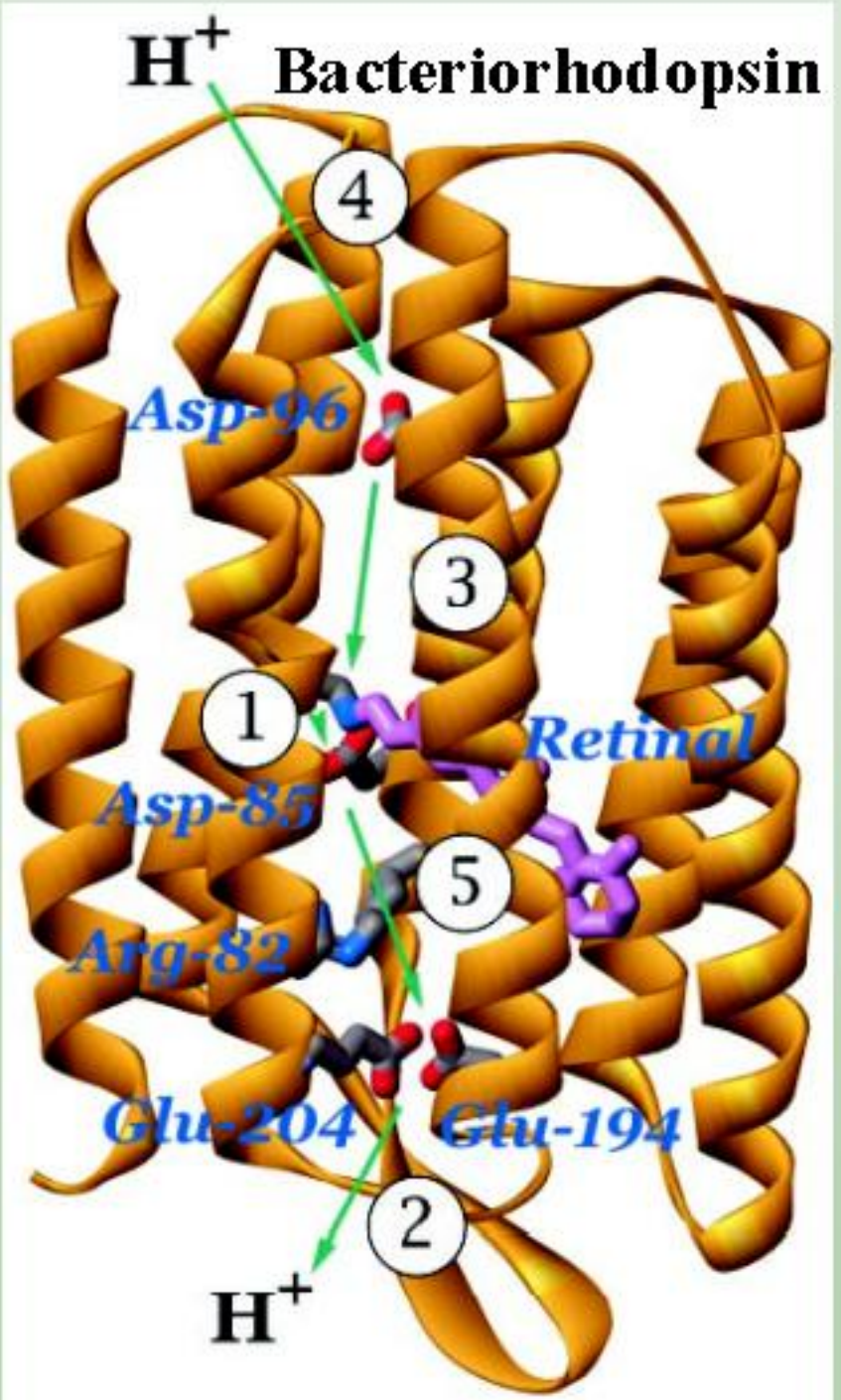


Initially inside bacteriorhodopsin there is all - trans retinal.

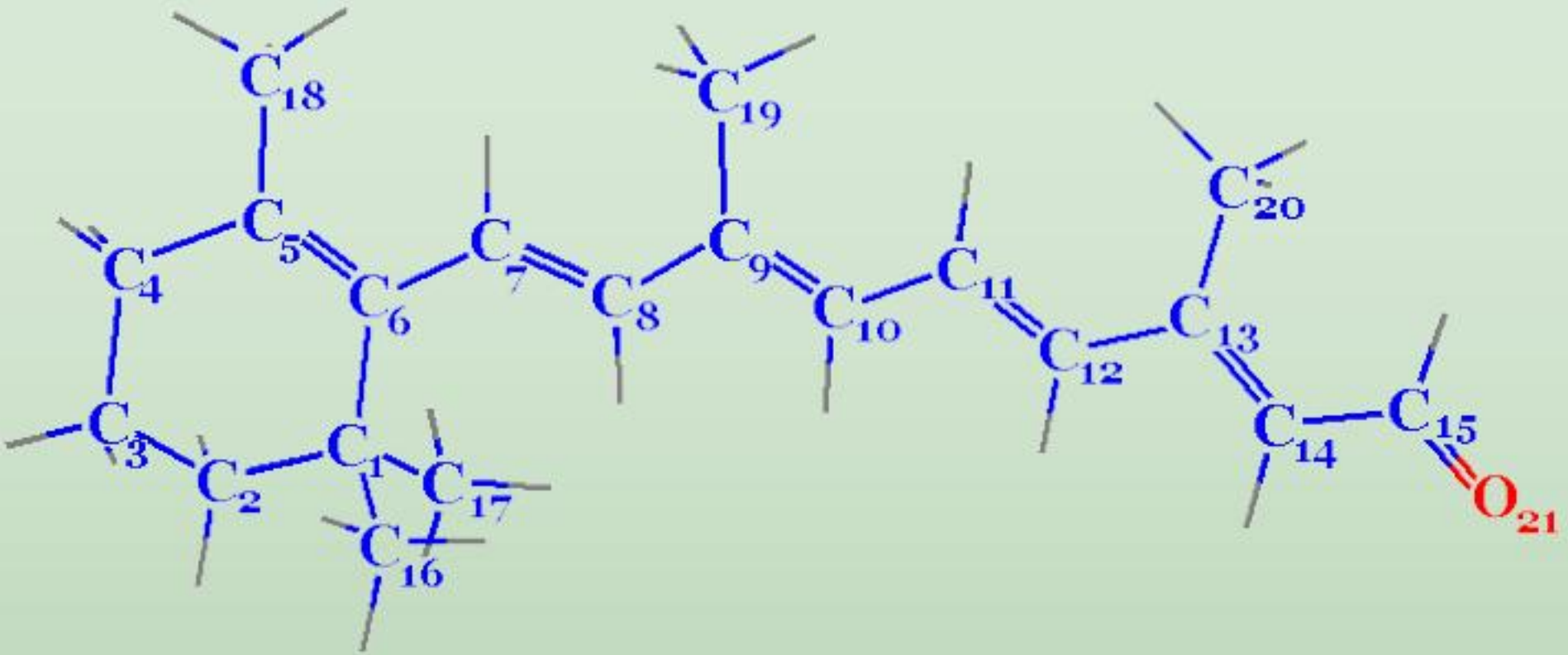
After an absorption of a light quantum it isomerizes to the 13-cis form.



Inside visual rhodopsin there is 11-cis retinal, being isomerized after an absorption of a light quantum to a all - trans form



After isomerization there is a deprotonation of retinal and proton transposition on acceptor group.



Retinal contain six coupled double bonds. Therefore theoretically the isomerization may take place on any of them.

The quantum yield of retinal isomerization in solution is about 10 percent.
Reaction time is picoseconds.

In contrast,
the protonated retinal in visual rhodopsin or bacteriorhodopsin photoisomerizes with an efficiency about 67 percent.
Time is 200 femtoseconds.

Why is cis–trans transition in protein so strikingly effective and rapid?

Although

- **there are more free space in solution,**
- **protein microviscosity is higher.**

Therefore retinal isomerization in protein has to be slower than this process in solution.

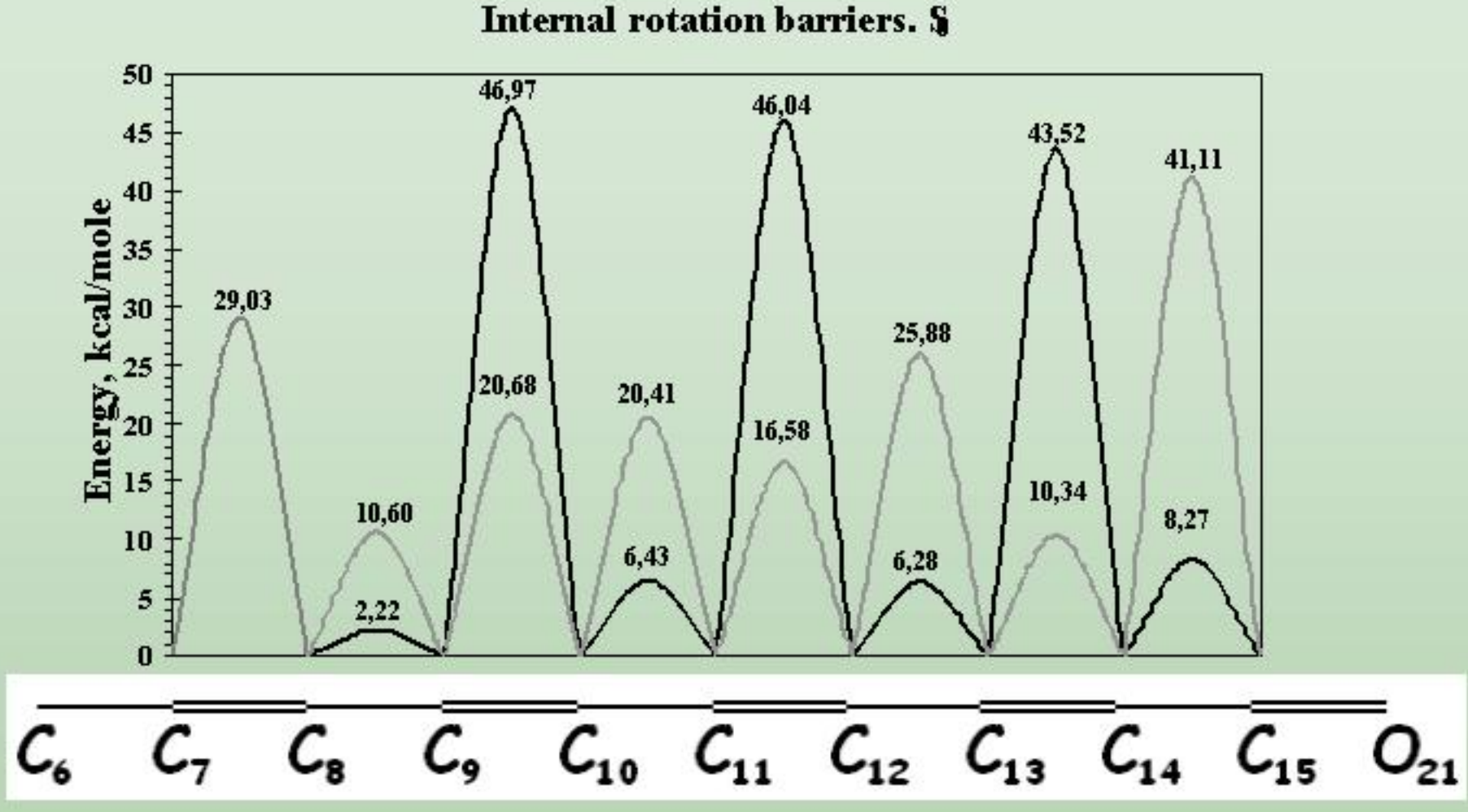
Factors were considered to solve this conflict:

- **potential barriers redistribution under electron excitation**
- **certain retinal group fixation inside protein**

Quantum chemistry and molecular dynamics technique were applied.

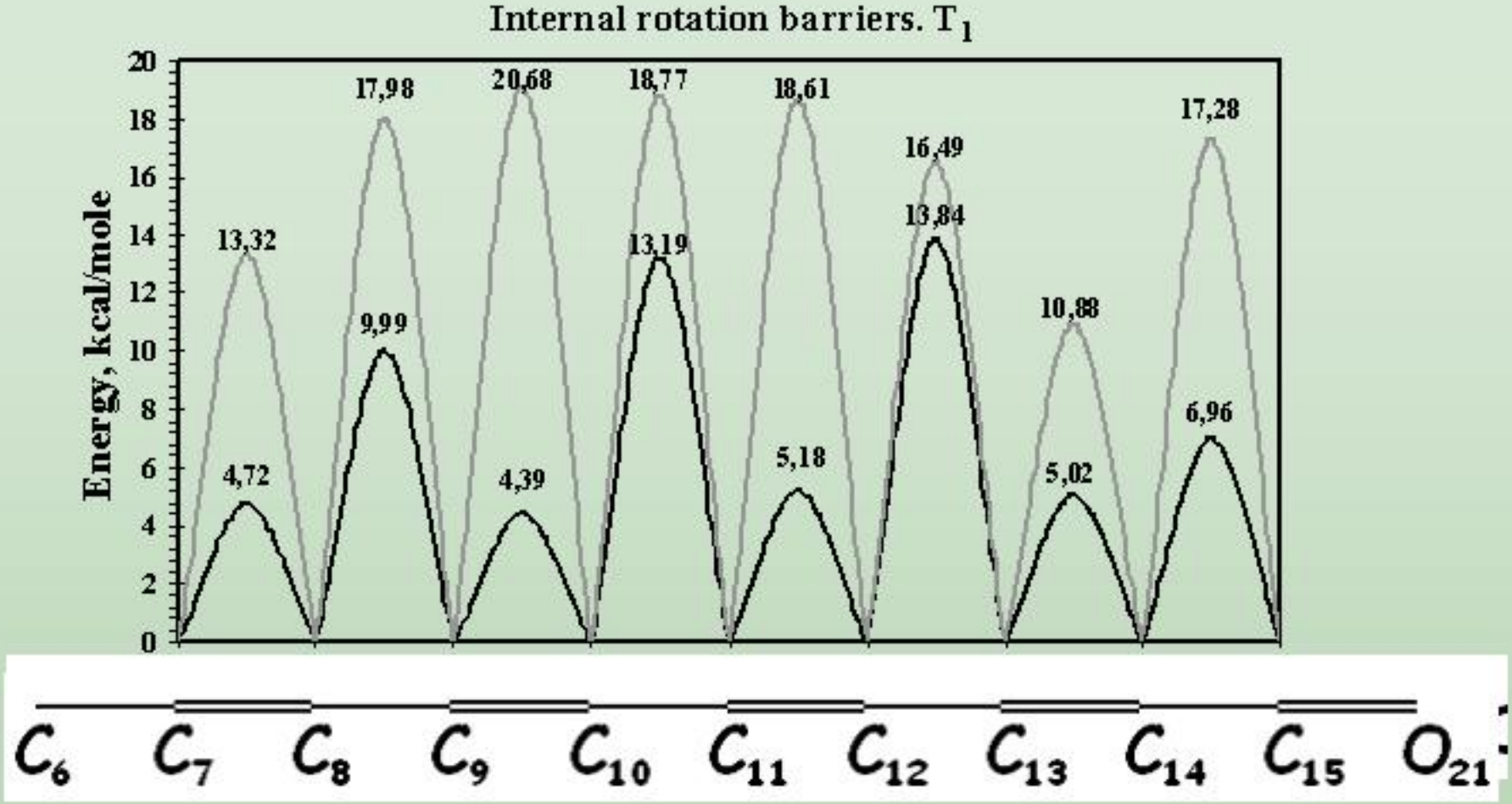
Quantum chemistry techniques:

- the Hartree–Fock method with 6-31G basis set
- the perturbation theory of second and fourth orders
- performances of the lowest triplet state T_1 were assumed to be close enough to parameters of the first excited singlet state S_1 (it was revealed for butadiene)



Internal rotation barriers of retinal in the ground state.

Black line is initial retinal, gray line is protonated retinal.



Internal rotation barriers of retinal in the first triplet excited state.

Black line is initial retinal, gray line is protonated retinal.

Molecular dynamics techniques:

- **AMBER–99 potential field**
- **parameters of retinal were added from quantum chemistry calculations**
- **the modeling time was 10 ns**
- **temperature was taken 2000 K for better agreement results with ergodic hypothesis**

Molecular dynamics techniques:

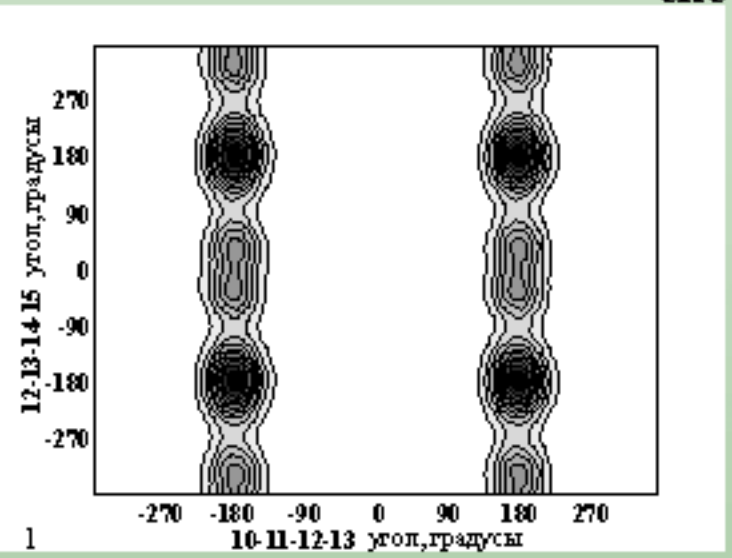
- **information was entered in trajectory file every 1fsec**
- **permittivity of medium was $\varepsilon = 1$**
- **mass of virtual particles in collision thermostat was taken 18 g/mole**
- **frequency of collision medium particles with atoms of calculated molecule was 55 $psec^{-1}$**

Molecular dynamics techniques:

Comparison study of excited and unexcited retinal was carried out.

To simulate the protein environment, the distance between the ends of the retinal was taken to be constant.

Probability distribution of torsion angles $C_{10}–C_{11}=C_{12}–C_{13}$ and $C_{12}–C_{13}=C_{14}–C_{15}$ in the ground state of retinal.



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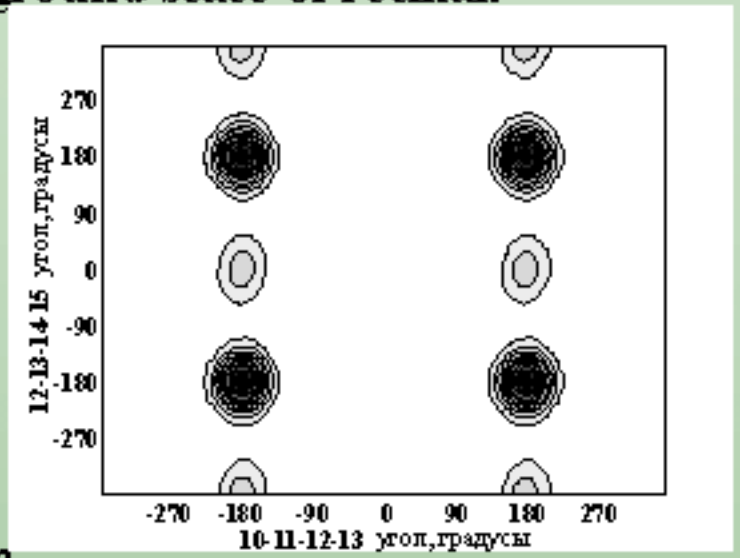
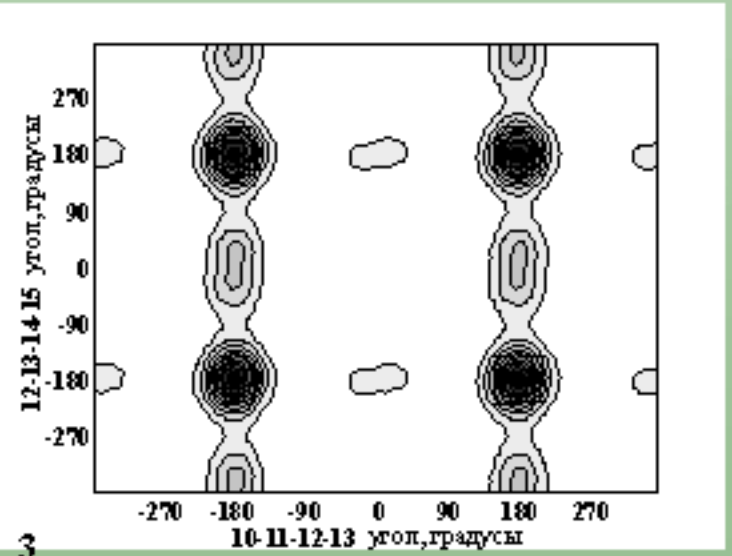


2

1–Distance between the ends of retinal is not fixed;

2–Distance between the ends of retinal is 14 angstrom;



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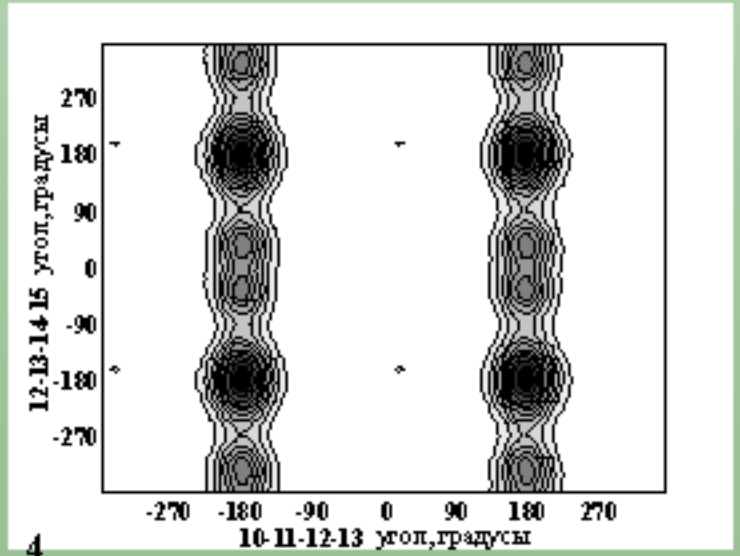
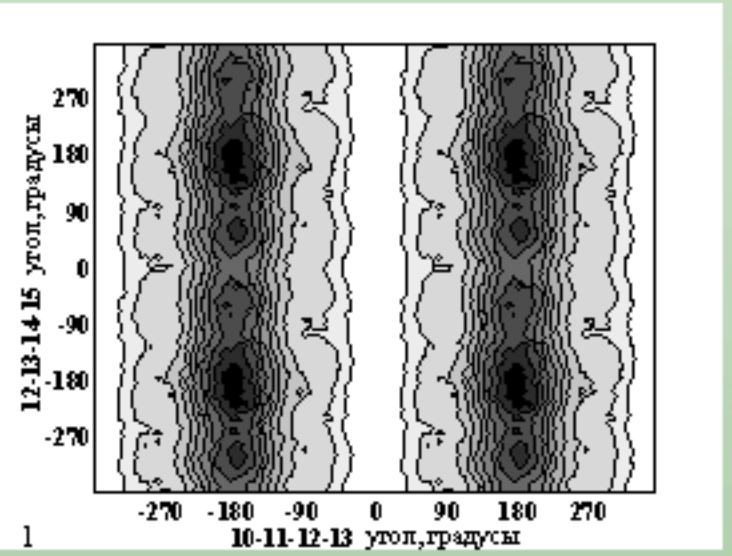


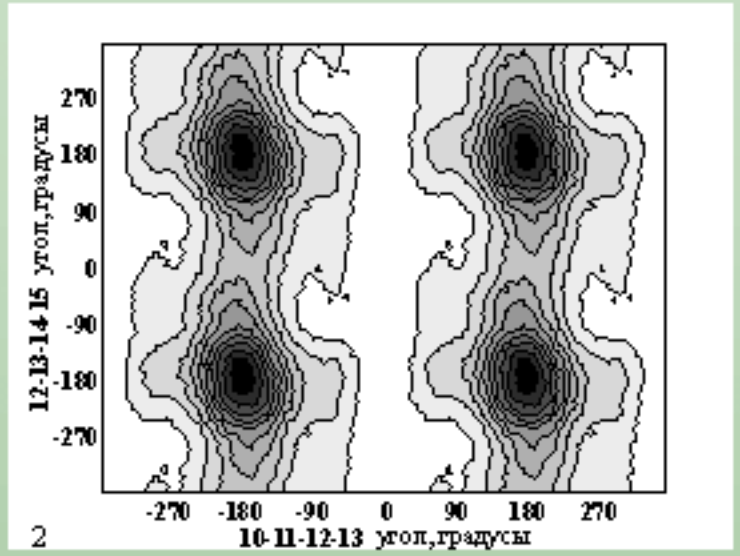
4

3–Distance between the ends of retinal is 10 angstrom;

4–Distance between the ends of retinal is 5 angstrom.

Probability distribution of torsion angles $C_{10}–C_{11}=C_{12}–C_{13}$ and $C_{12}–C_{13}=C_{14}–C_{15}$ in the first triplet state of retinal.





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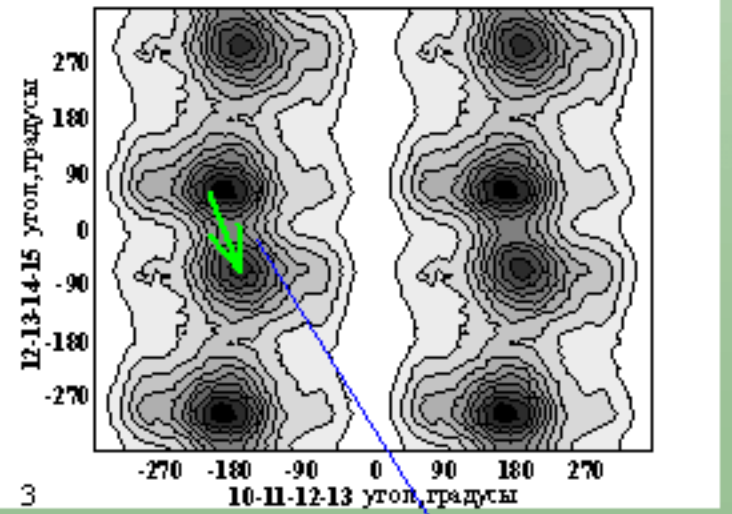

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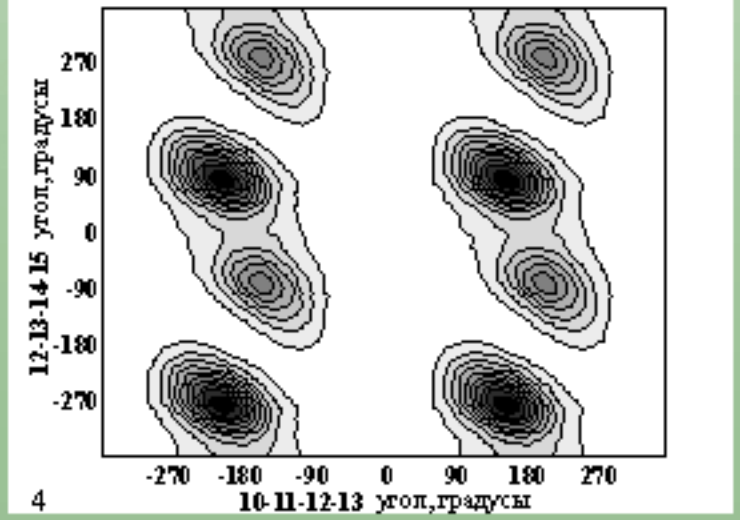


4–Distance between the ends of retinal is 5 angstrom.

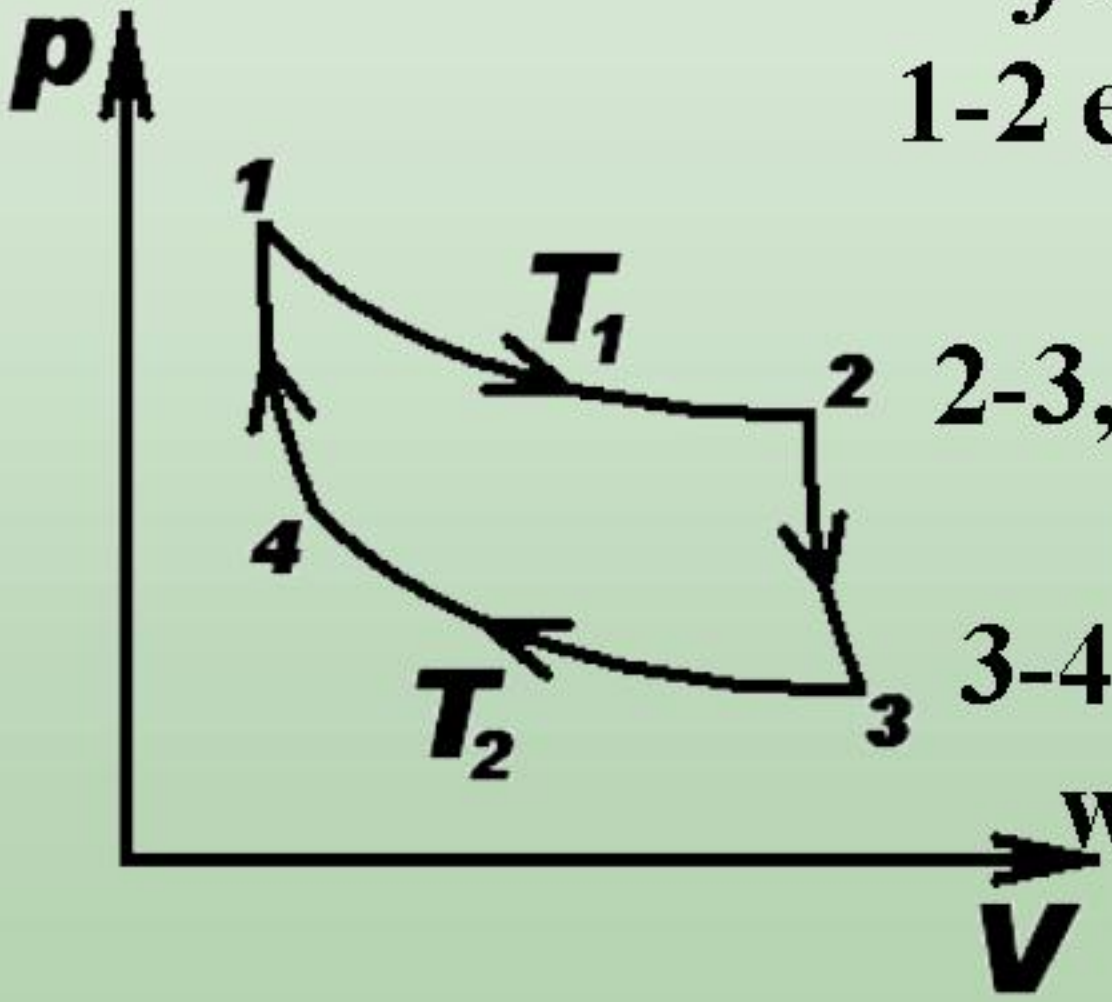
Collective degree of freedom transition

Conclusions:

1. The protein environment was found to exert a considerable effect on the isomerization process.
2. Collective degrees of freedom were discovered in excited retinal with fixed ends.
3. The process of isomerization can be considered as a cycle similar to the Carno cycle for the heat engine.

Carno cycle:

for ideal gas

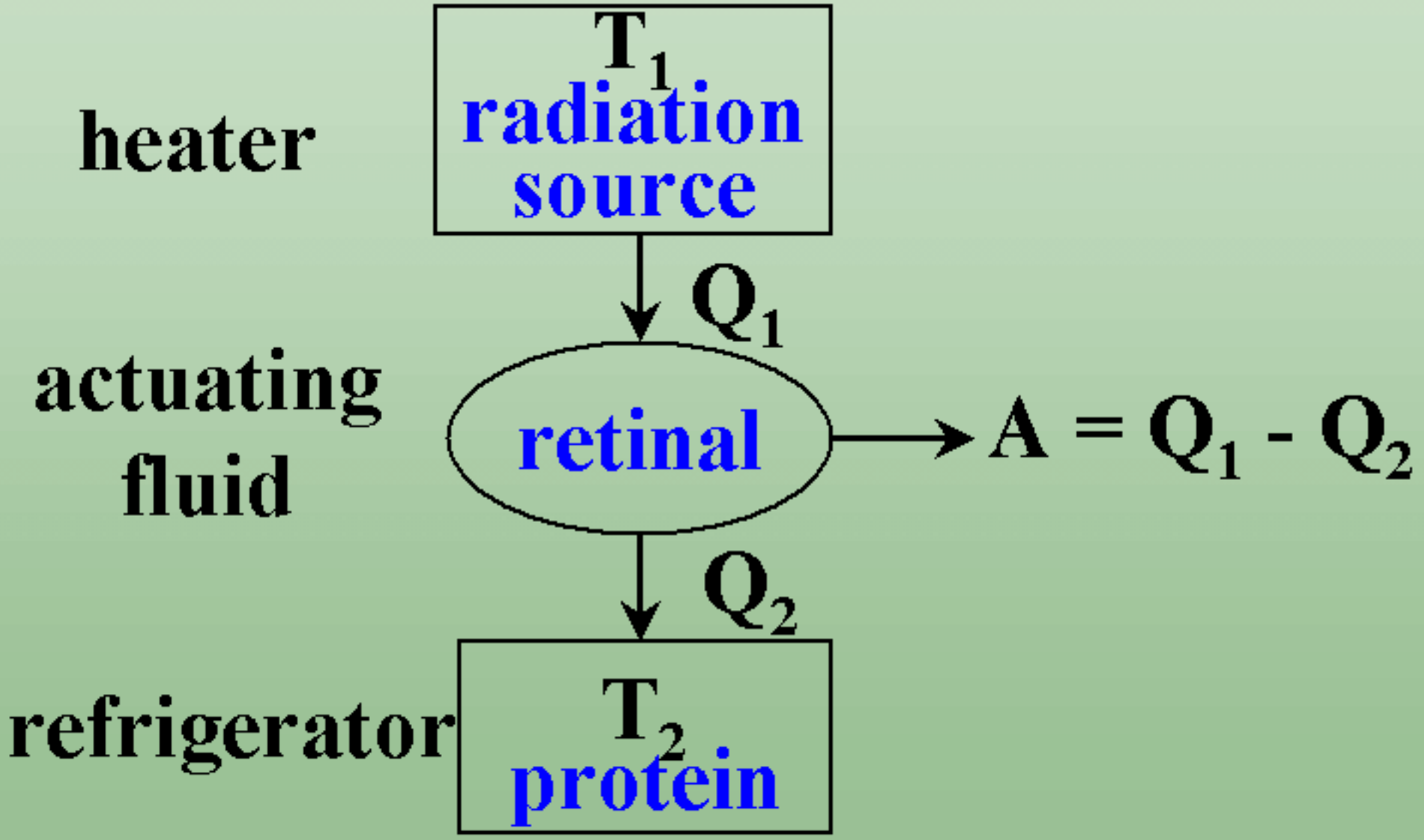


1-2 expansion with heating

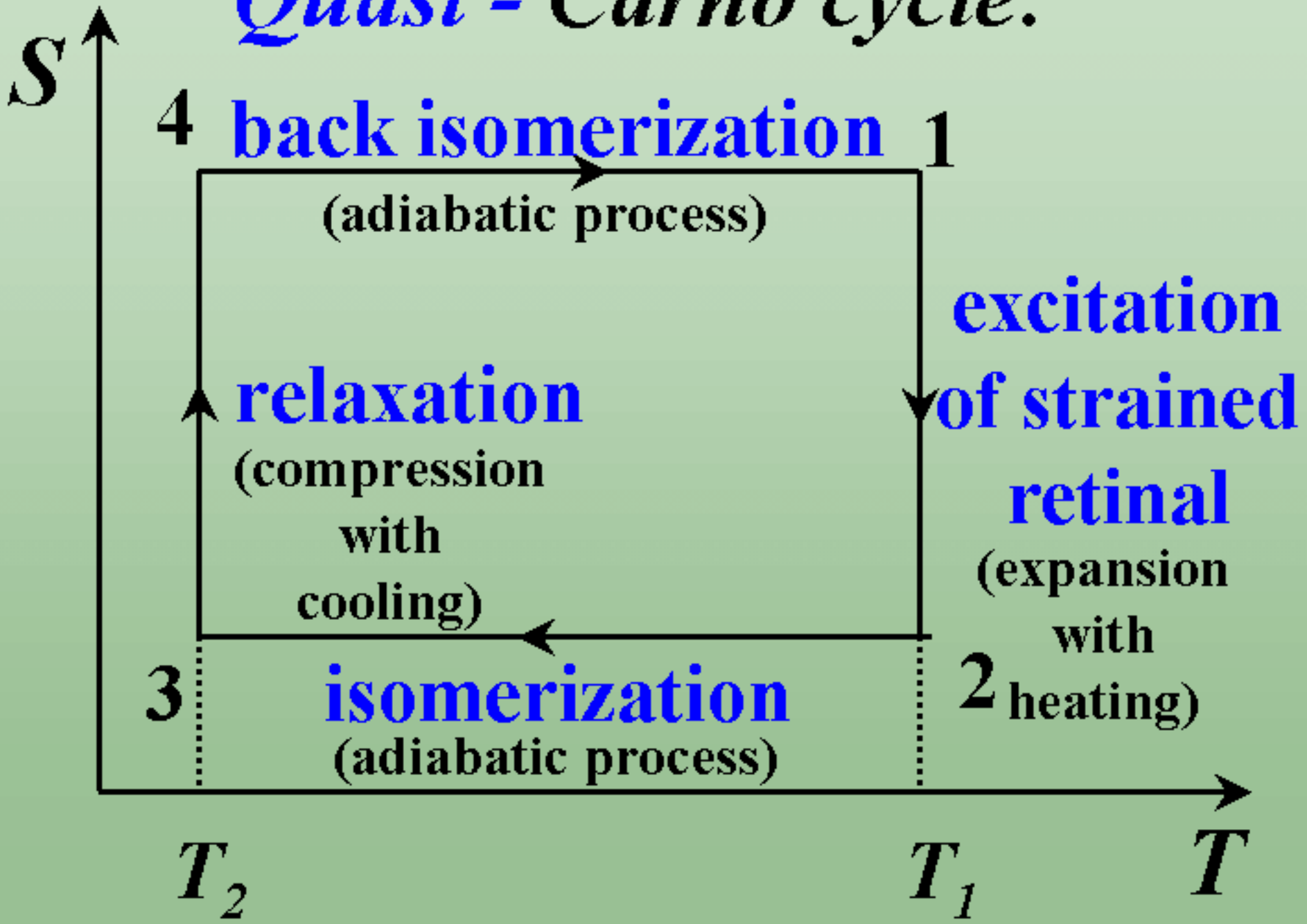
2-3, 4-1 adiabatic processes

3-4 compression with cooling

Quasi - Carno cycle:



Quasi - Carno cycle:



Thank you for your attention