Experimental report

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Proposal: DIR-173 **Council:** 4/2019

Title: Quantum effects investigated on the dynamics of a protein

Research area: Physics

This proposal is a new proposal

Main proposer: Judith PETERS

Experimental team: Judith PETERS
Dominik ZELLER
Aline CISSE
Philippe OGER

Local contacts: Michael Marek KOZA
Jacques OLLIVIER

Samples: protonated Green Fluorescent protein (H-GFP)
deuterated GFP (d-GFP)

Instrument	Requested days	Allocated days	From	To
IN5	3	3	04/10/2019	07/10/2019

Abstract:

There is a growing number of indications that quantum mechanics might play a role for the functioning of certain biomolecules and within living cells, as for instance through tunnelling effects or quantum entanglement. However, not much is reported in the literature about experimental results, certainly because the expected effects are rather small. As quantum effects depend on the mass of the scatterer, their signature should be detectable when comparing a protonated protein with its per-deuterated counterpart. We propose therefore to study Green fluorescent protein (GFP) in the two versions, at very low temperature where these effects should be highest, but also by doing a temperature scan for elastic scattering and recording the density of states and QENS at low, intermediate and high temperature to permit data analysis within a newly developed approach taking into account quantum effects.

QUANTUM EFFECTS INVESTIGATED ON THE DYNAMICS OF A PROTEIN

Experiment on IN5, 4 – 7/10/2019

Y. Suenaga, Chiba University, Japan
P. Oger, INSA Lyon
A. Cisse, UGA Grenoble

For decades the functioning of biological systems was considered to be governed by mechanisms which can be described in terms of classical physics. As a full quantum mechanical approach is moreover very complex, most studies were conducted with traditional approaches. Recently, new insights revealed that quantum effects could have to some degree importance in different domains of life as for enzymatic activity, olfaction, photosynthetic energy capture and bird's magnetodetection (1). What is common to all these effects is that they are based on a transition from one state to another which can be calculated from Fermi's golden rule. To which extend such effects contribute to the functioning of proteins has not much been studied so far except that they can explain the high efficiency of certain enzymatic activities due to tunneling effects. However, proteins are atomistic systems and quantum mechanics provides the most accurate description of them. So it seems reasonable that such effects contribute to some extend to the observed phenomena in this domain.

To explore the possibility that quantum effects are indeed involved in proteins function, we investigated Green fluorescent protein (GFP). This protein has the advantage to be relatively small (27 kDa), to have an activity which can be easily monitored (through fluorescence) and to have been extensively characterized. GFP is a spontaneously fluorescent protein isolated from *Aequoria victoria* which can be expressed in bacteria, archaea and eucarya, and is therefore widely used as a cellular tag (2). The protein is in the shape of a cylinder (β-barrel), consisting of 11 strands of β-sheets with an α-helix containing the covalently bound chromophore 4-(p-hydroxybenzylidene)-imidazolidin-5-one (HBI) running through the center of the protein (3). The β-barrel structure is a nearly perfect cylinder, 42Å long and 24Å in diameter, which is unique to the GFP family of proteins. Inward-facing sidechains of the barrel induce specific cyclization reactions in Ser65–Tyr66–Gly67 that provoke ionization of HBI to the phenolate form and chromophore formation (4). The hydrogen-bonding network and electron-stacking interactions with these sidechains influence the color, intensity and photostability of GFP. Arg96 is the most important stabilizing residue due to the fact that it prompts the necessary structural realignments that are necessary from the HBI ring to occur. The tightly packed nature of the barrel excludes solvent molecules, protecting the chromophore fluorescence from quenching by water. GFP is quite thermostable, very resistant to chemical and pressure-induced denaturation. Last, the transfer of electron in the chromophore at the origin of fluorescence is perfectly known.

To test the implication of a quantum effect in the function of that protein, we measured GFP in a protonated and a per-deuterated form. The latter one was produced by the D-lab and we acknowledge the efforts the colleagues did. An example of first results of the density of state (DOS) of the two samples is shown in figure 1. Clear differences are visible. We are aware that partly they are simply due to a mass effect between H and D, but further data analysis should show that in addition there are clear effects which can be attributed to

quantum effects. As an appropriate approach and models are yet to be developed, data analysis is under progress in collaboration with the theoretician G. Kneller from University of Orleans.

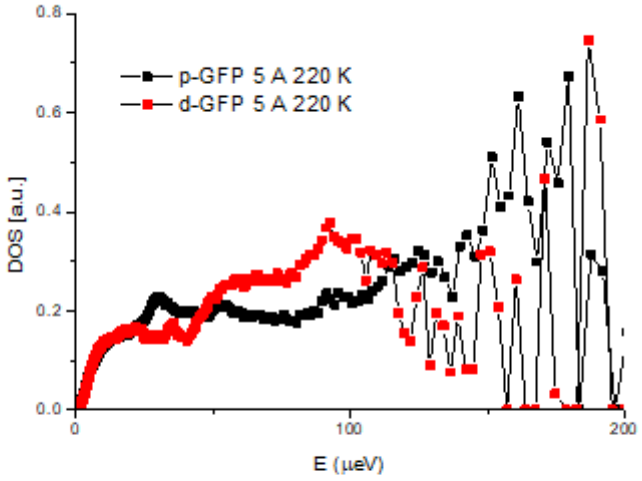

Figure 1: Density of states corrected for multi-phonon effects as function of energy transfer for both samples measured at 220 K.

References

1) Brookes JC. 2017. Proc. R. Soc. A 473: 20160822.
2) Tsien RY. 1996. The green fluorescent protein. Annual Reviews of Biochemistry 67:509-544.
3) Ormo M, Cubitt AB, Kallio K, Gross LA, Tsien RY, Remington SJ. 1996. Science 273:1392-1395.
4) Bublitz G, King BA, Boxer SG. 1998. Journal of the American Chemical Society 120:9370-93716.