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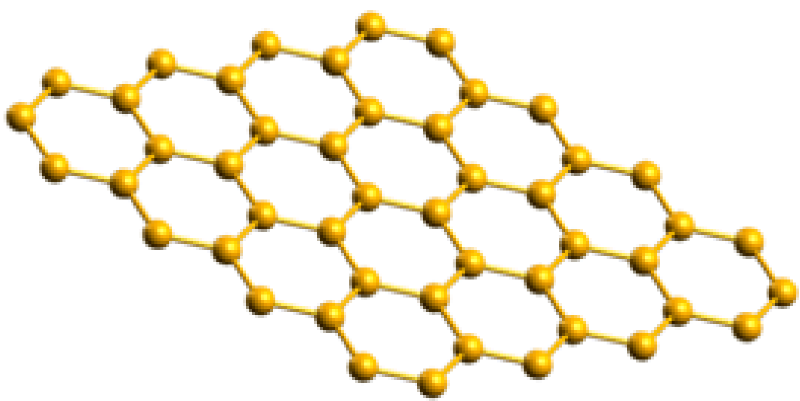

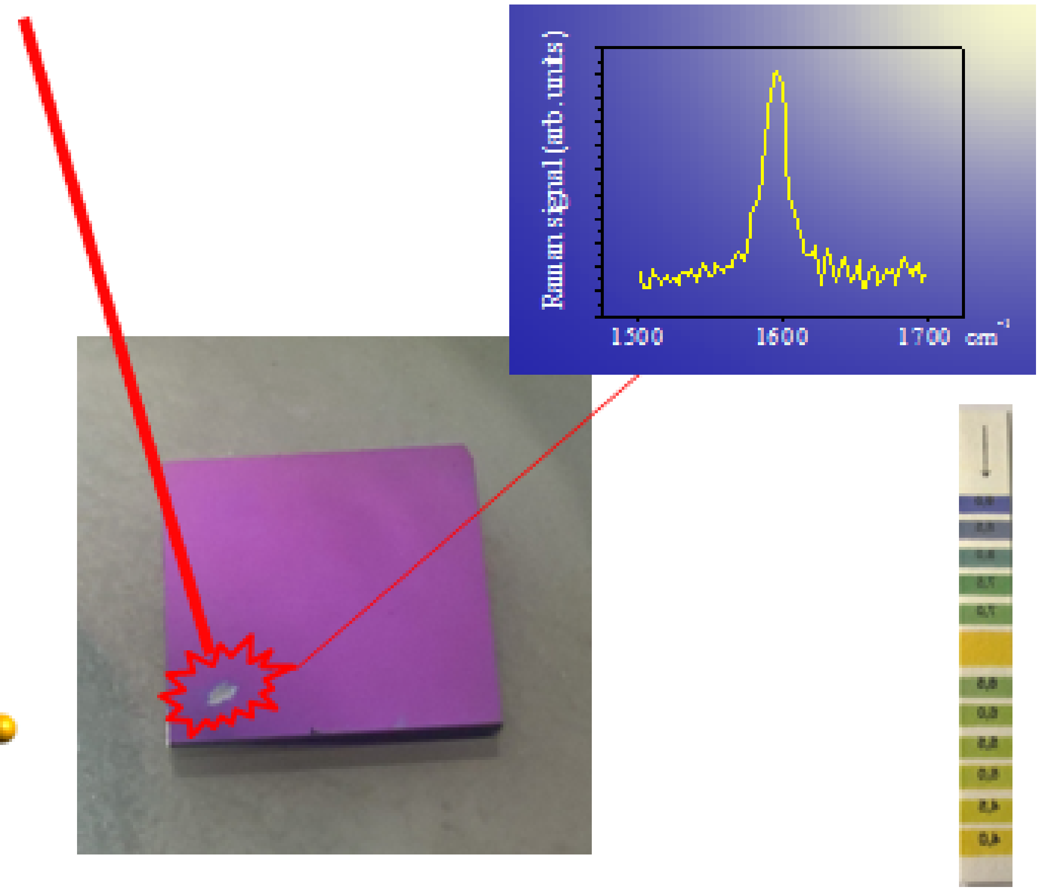


# Micro sensing of pH levels in biological samples by graphene-based Raman spectroscopy

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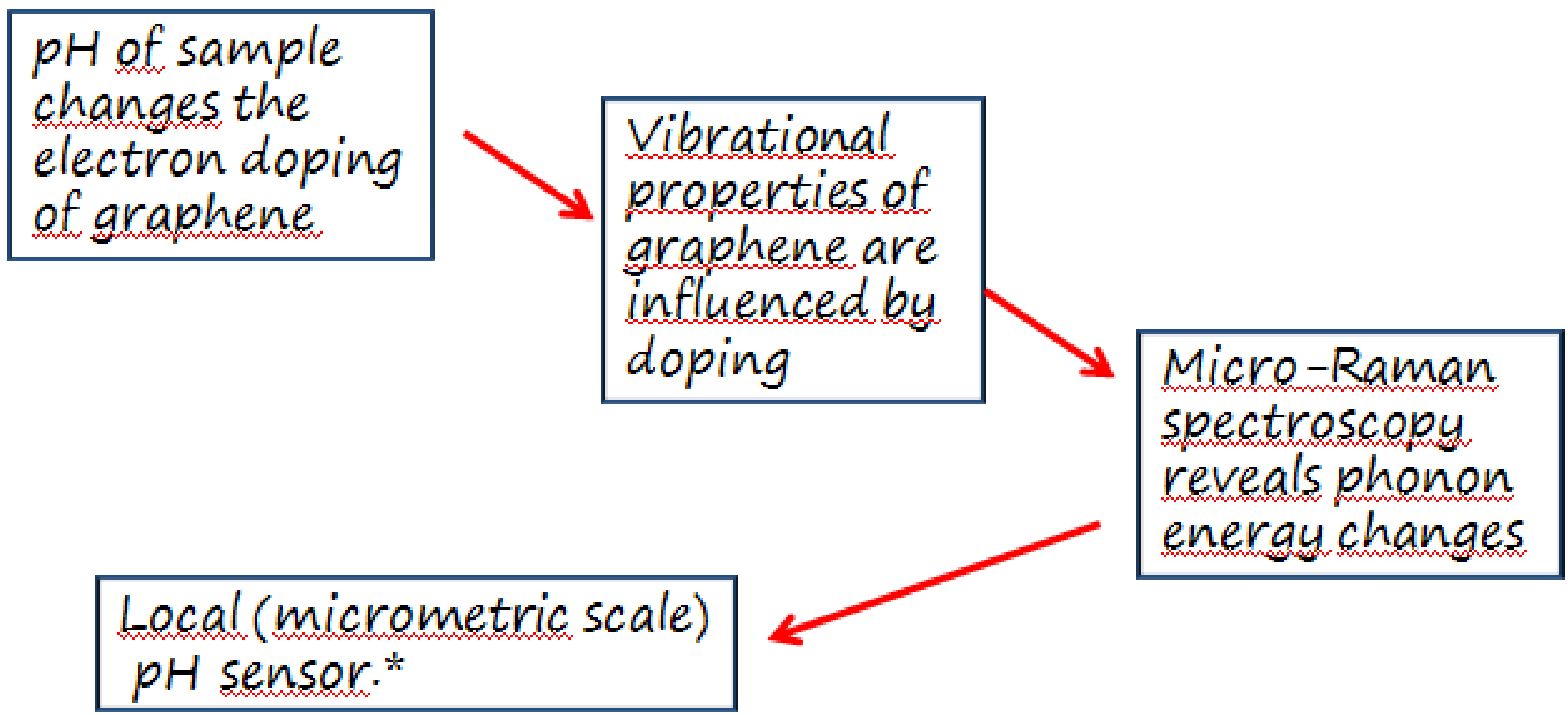
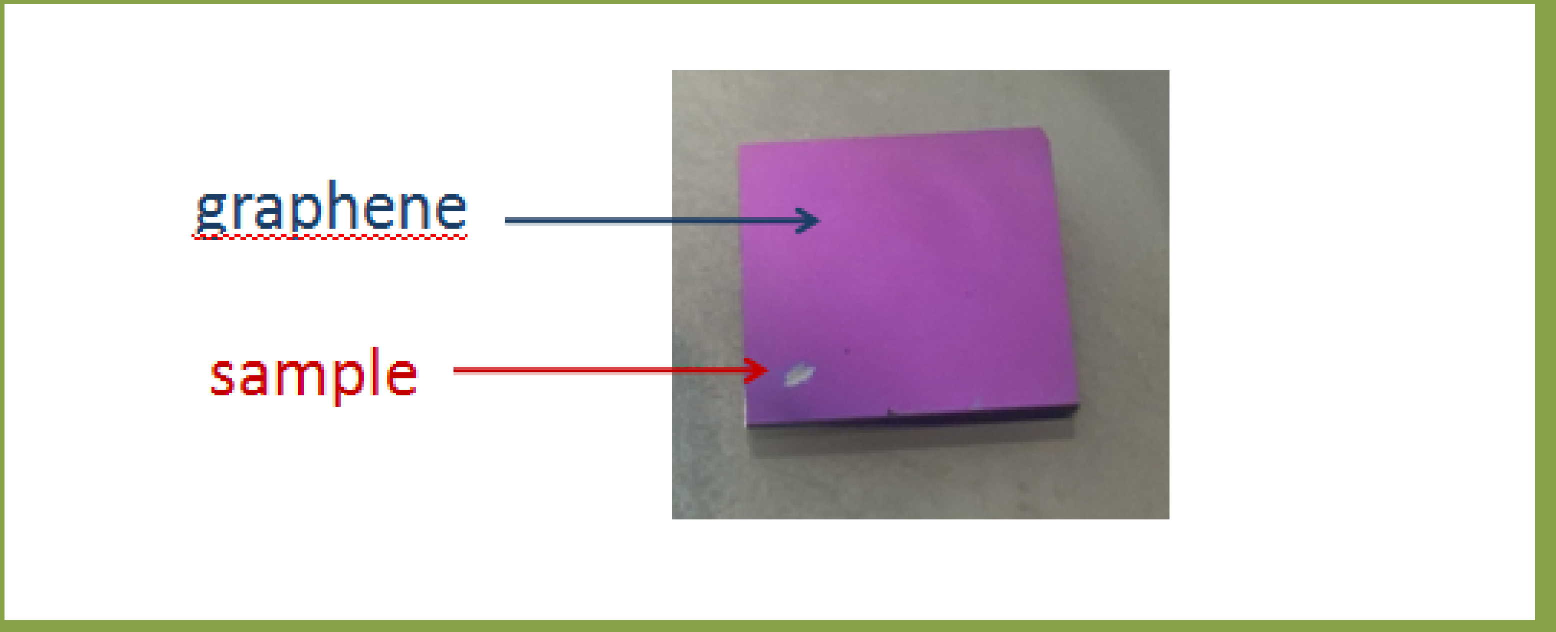
Graphene provides a unique way for sensing local pH level of substances on micrometric scale, with important implications for the monitoring of cellular metabolic activities where protonic excretion could occur.

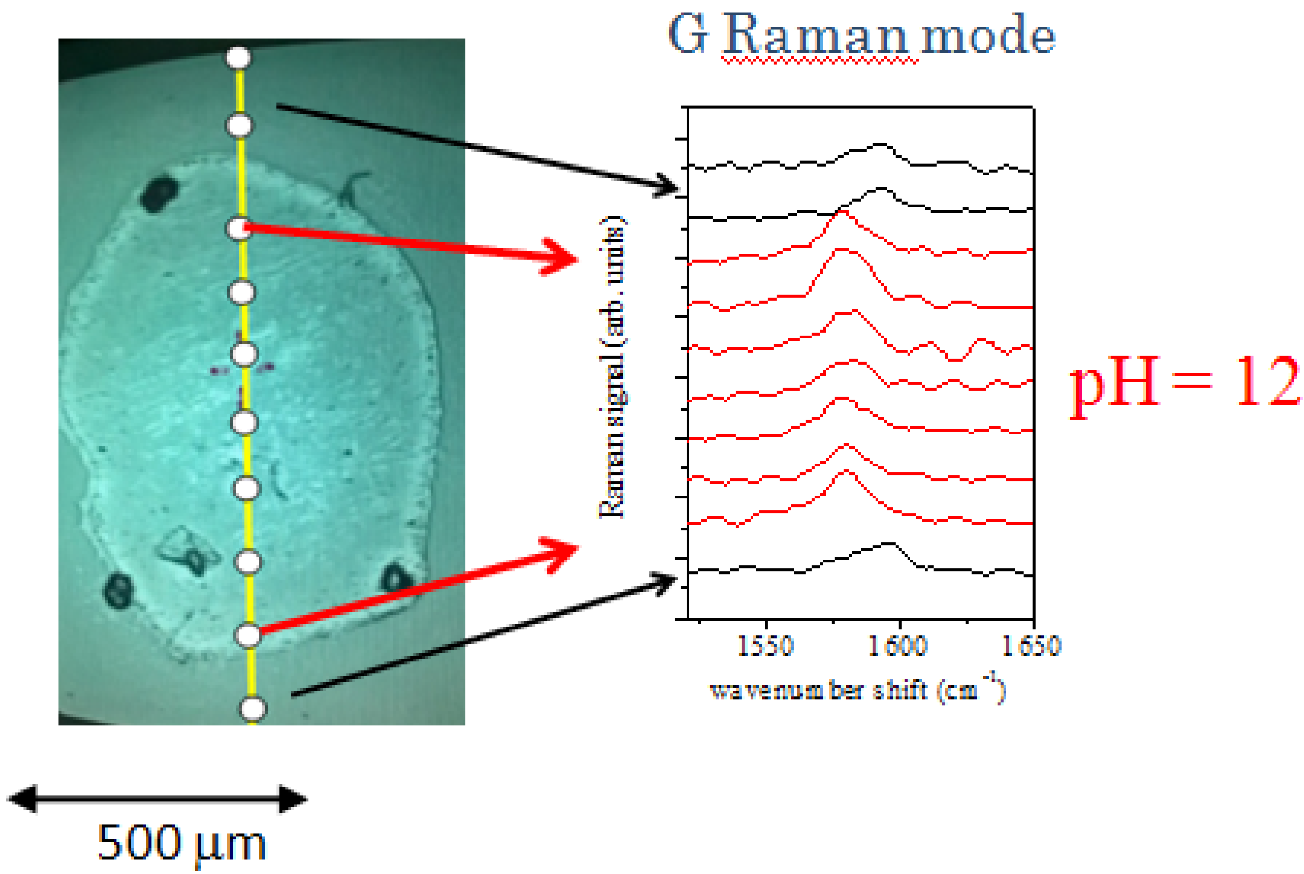



* Firstly proposed and tested by Geraldine L. C. Paulus et al, *Sci. Reports* **2014**, *4*, 6865.

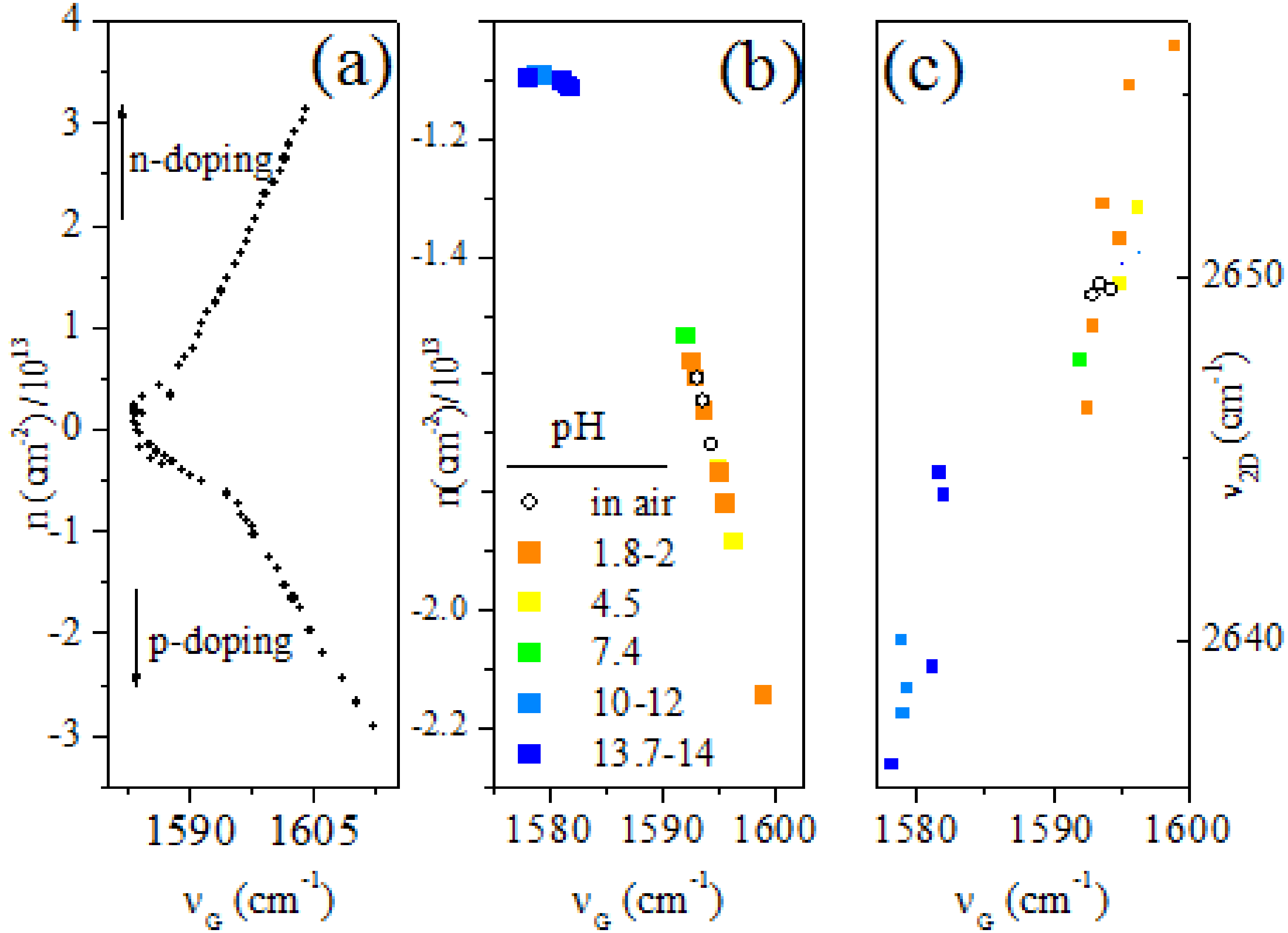
# Experimental



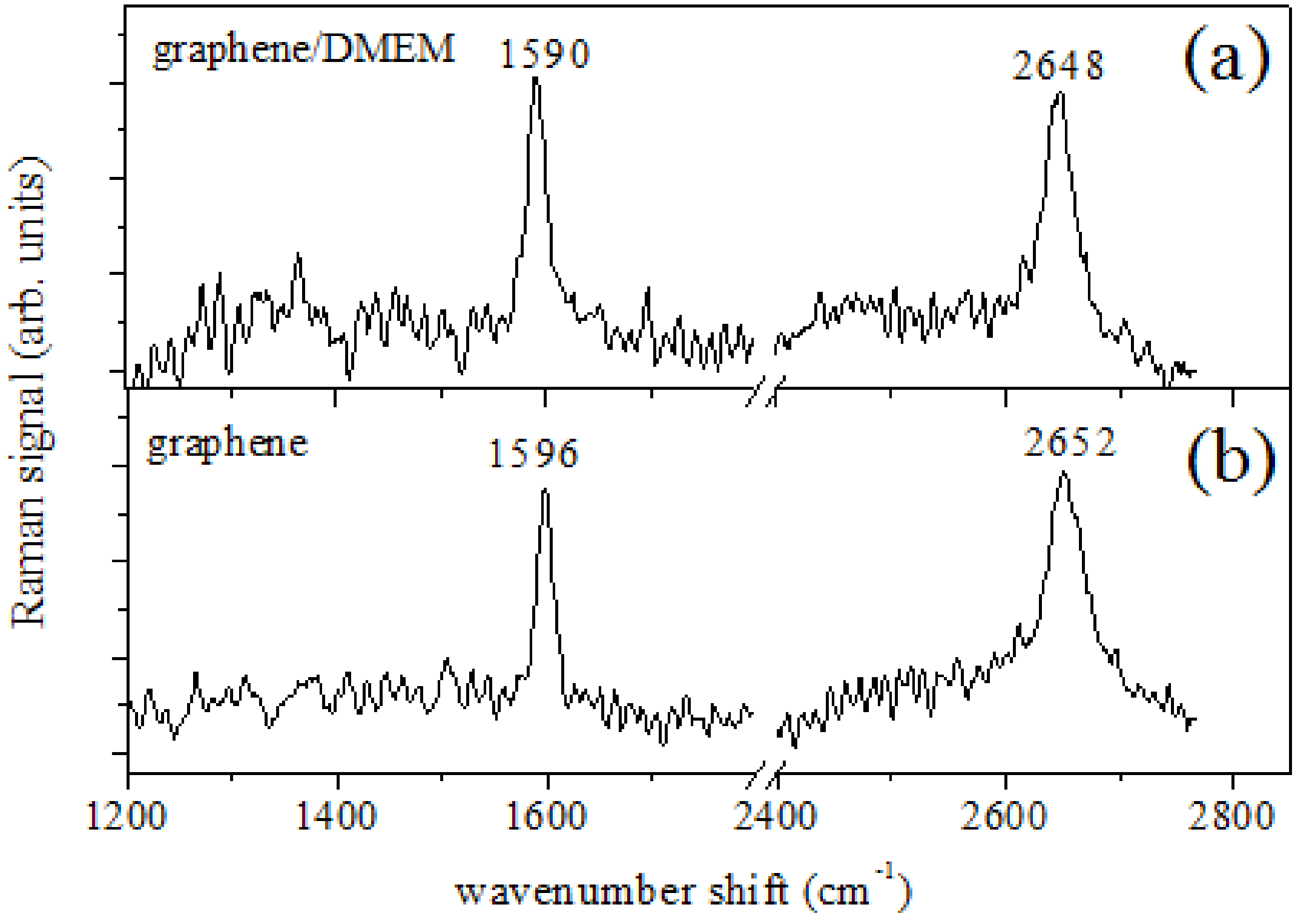

A drop of about 1 μl was considered for the Raman analysis. The micro-Raman spectroscopy was performed by using a Jobin-Yvon system (by Horiba Inst. Ltd, Kyoto) equipped by TriAx 180 monochromator, a liquid $N_2$ cooled CCD and an optical grating of 1800 grooves/mm, allowing a spectral resolution of 4 $cm^{-1}$. A He-Ne laser operating at a wavelength $\lambda$= 633 nm was used, (maximum nominal power of 17 mW). The laser light was focused on the sample surface by means of a 100× (n.a.=0.90) optical objective on an excitation area of about 1 μm of size. The spectra were obtained using an accumulation time of 180 seconds.



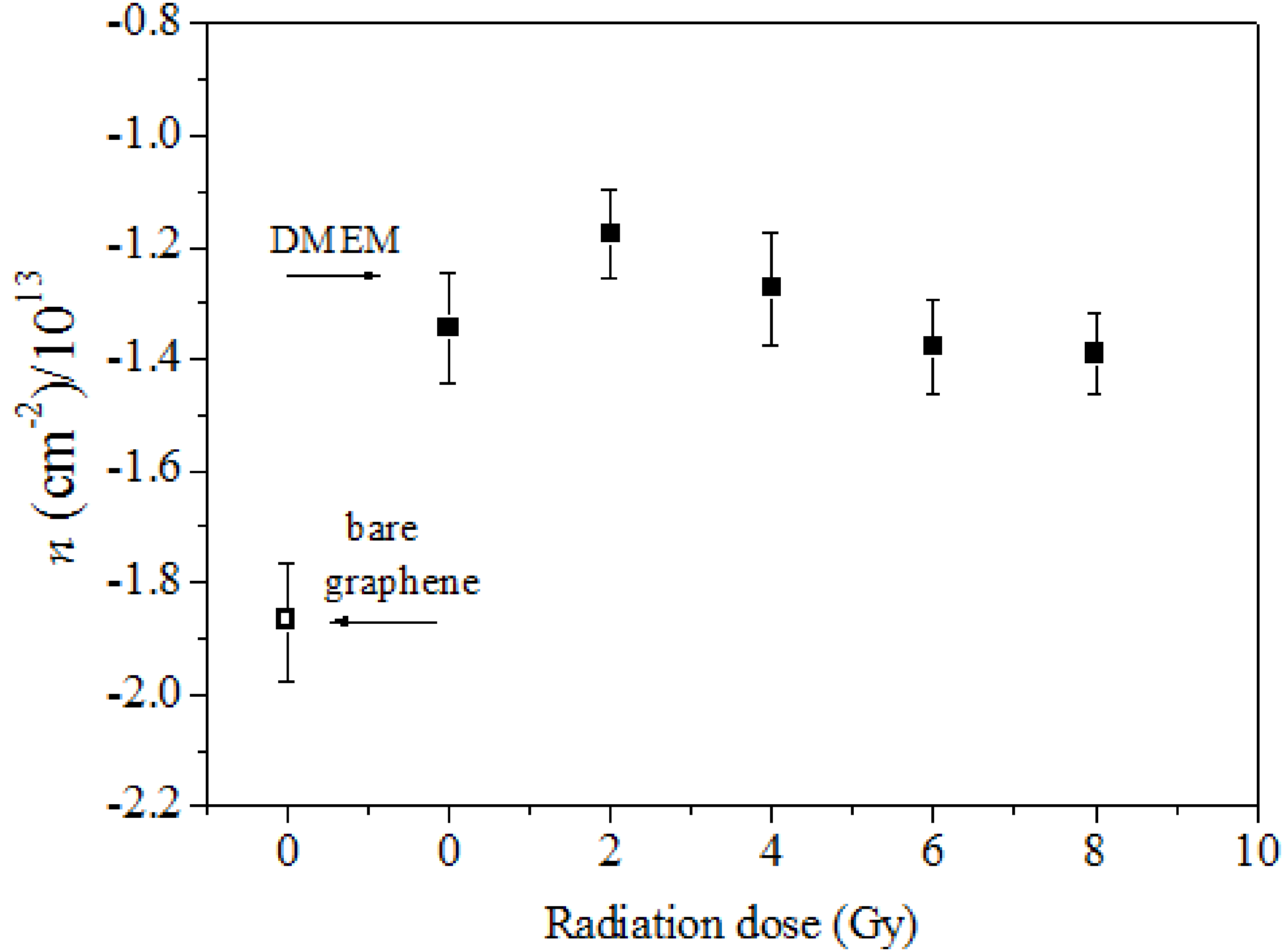

The alkaline solution (pH=12) changes the doping of the underlying graphene into the area covered by the solution drop. Micro-Raman spectroscopy feels the doping changes by revealing the wavenumber shift of the position of G Raman mode (red shift) with respect to pristine graphene.




(**a**) Relation between electron concentration and G mode wavenumber of graphene (data from A. Das et al, *Nature nanotechnology* **2008**, *3*, 210-215. ). (**b**) Experimental doping carrier concentration evaluated for aqueous solutions at different pH levels. Circles refers to bare graphene in air. (**c**) Correlation between wavenumber of the graphene 2D mode and G mode, at different values of pH.




In order to configure experiments for monitoring cell activities, the cell culture media (DMEM) were characterized. The Raman response of graphene covered by a drop of DMEM is reported in (**a**). When the spectrum is compared with the Raman spectrum of bare graphene, reported in (**b**), a spectral red-shift of the mode at 1590 cm$^{-1}$ (G mode) and at 2648 cm$^{-1}$ (2D) is clearly observed. The value evaluated for DMEM pH is of 8.6 ± 1.6.




Samples of DMEM exposed to ionizing radiation (250 kVp X-ray ), for doses of 0, 2, 4, 6 and 8 Gy . The value of *n* (carrier doping) is estimated and reported vs the dose. Changes of the pH value of DMEM were observed: at the dose of 2Gy a significant increase of pH (more alkaline state) occurs, but, increasing the irradiation doses, the level of pH decreases and reaches a pH value equal to 8.0 ± 1.8 at the dose of 8 Gy.

# Conclusions

Based on the unique properties of graphene, the dependence of the electronic doping of this material induced by the proximity of alkaline or acid liquids was probed by micro-Raman spectroscopy.

The method allows the determination of the pH level of solutions even when very small quantities are considered (smaller than 1 μl), or with high spatial resolution (of order of 1 μm) when a scan of the sample is performed.

A pH characterization of cell culture medium (DMEM) depending on the X-Ray irradiation doses has been done. A non monotonic dependence of pH on radiation dose was observed, mainly ascribed to the complex behavior of water hydrolysis induced by radiation, that mainly determines the pH level of the sample by regulating the amount of hydroxyl and hydrogen ions.

Based on this preliminary study, more detailed investigation on cell culture medium is in progress, in order to monitor cell activities after ionizing irradiation stages.

Collaboration : CNR-SPIN , Università della Campania “L. Vanvitelli” and Università di Napoli “Federico II” .

SPIN

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