Theoretical Study of the Binding of Collagen-Like Peptide Units on Carbon-Based Surfaces and Materials

CLAUDIO CAZORLA[▸]
CARME ROVIRA[⋆]

Recent progress in understanding bio-inorganic interfaces and the physico-chemical processes taking place on them has lead to major developments in a number of scientific areas like nanotechnology, modeling of biomaterials, food industry, design of drug-delivery nanodevices and energy storage-production, to cite some examples. Intimately related to this progress is the discovery of carbon nanotubes (CNTs), which since the early 1990s has sparked an impassioned theoretical and experimental research on carbon-based nanostructures (CNSs). Given their very unique electronic, structural and mechanical properties, CNSs have been proved as excellent chemical sensors, components of integrated circuits, platforms for hydrogen storage, etc., and there is considerable expectancy also on using them in novel biological and biomedical applications (1,2). Even so, comprehension of the interactions between molecules important for life and CNSs is still far from satisfactory as witnessed by the yet controversial possible toxicity of CNTs in physiological environment. Therefore, gathering further quantitative knowledge on organic-inorganic systems is determinant to keep further progress on a number of scientific fields and to secure the design of biologically safe standards. The main motivation of this project was to study the interactions of collagen-like peptides with carbon-based surfaces and materials at the quantum level of description.

In particular, the **specific aims** of this project were to:

- characterize the quantum interactions of collagen-like peptide units, basically composed of glycine (Gly), proline (Pro) and hydroxiproline (Hyp) amino acids, with carbon-based surfaces (CSs), like **graphene**, and materials, like **calcium graphite** (CaC_6) (see Figure 1)
- unravel whether simple collagen-like peptides adsorb or not onto CSs and Ca-doped CSs
- envisage ways of tailoring the interactions of collagen-like peptides with CSs in order to impel developments in bio- and nano-technology fields

Collagen is the main building-block of connective tissue in animals and the most abundant protein in mammals. Regenerative medicine/tissue engineering is a rapidly growing multidisciplinary field that pursues to develop functional cells and tissue to relieve or partly cure affections deriving from lack or defective production of collagen. Development of novel biomaterials and scaffolds designed to direct the growth, differentiation and organization of the cells in new functional tissue, is a very promising area within this field and biomedicine in general. CNTs and graphene (one-atom thick planar sheet of carbon atoms densely packed in a honeycomb crystal lattice -see Figure1-) appear to be gifted materials for this end since apart from presenting very intriguing physical qualities they can be assembled to form three-dimensional porous structures (which encourages bone cell in-growth) and are affordable to produce. Interestingly, in a recent study (3) it has been demonstrated that the binding of small amino acids to graphene can be enhanced dramatically by doping the carbon surface with calcium atoms. In view of this finding, exploration of the interactions of collagen peptide units with Ca-/C-based materials like CaC_6 (a graphite intercalation compound for which corresponding synthesis methods

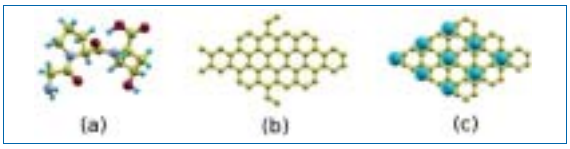

Fig. 1. Optimized geometry of the collagen peptide unit (a), Graphene (b) and Ca-doped Graphene (c). Oxygen atoms are colored in red, Nitrogen in purple, Carbon in yellow, Calcium in blue (big spheres) and Hydrogen in blue (small spheres).

and atomic structure are well-known (4)) turns to be appealing from a biomaterials modeling perspective.

In this project, we employed density functional theory (**DFT**) as the computational method of choice for coping with the specific objectives outlined above.

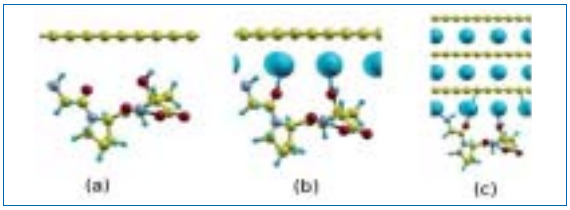

Fig. 2. Optimized geometry of the collagen peptide unit adsorbed on Graphene (a), Ca-doped Graphene (b) and CaC_6 (c). Atoms are colored as in Figure 1.

DFT is a first-principles quantum approach that has proved accurate in describing a deal of material properties, physico-chemical processes and binding of molecules to carbon-based nanostructures. The main findings of our work can be summarized as:

- collagen-like peptide units do adsorb onto graphene though the corresponding binding energies are always very small (physi-adsorption, binding energies amount to $\sim -10^{-1} - 10^{-2}$ eV)
- by doping graphene with calcium atoms, the biding of collagen-like peptides is enhanced dramatically (chemi-adsorption, binding energies amount to $\sim -10^{-1} - 10^{0}$ eV) as a result of electron-charge transfers from the Ca impurities to the oxygen atoms contained in the carboxyl groups of the peptide (see Figure 2)
- equivalent results than obtained in the Ca-doped graphene case are found in the hybrid peptide-CaC_6 system (see Figure 2)

Future work is being planned to address the effect of water molecules on the quantum hybrid interactions analyzed in this project. This knowledge is necessary to gauge the potential of the studied systems as realizable biomaterials. It is worth noticing that the results obtained in our investigations can be used for benchmarking/refinement of existing force fields that subsequently can be employed to perform large-scale molecular dynamic simulations of these and/or similar organic-inorganic systems.

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▸ *Department of Chemistry, University College London, UK*
⋆ *Centre de Recerca en Quimica Teorica, Parc Cientific de Barcelona, Spain*