Biology at the nanoscale: probing the molecular phenomena at the nano-bio interface

In association with

Dr Sourav Bhattacharjee from the UCD School of Veterinary Medicine outlines his research activities which encompass nanomedicine, biophotonics and quantitative structure-activity relationship

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As a physician with expertise in nanomedicine and nanochemistry, the research conducted in my group is varied and often runs in collaboration with other research groups in UCD Conway Institute or from abroad. Overall, my research activities follow either of the following three trajectories: nanomedicine, biophotonics and quantitative structure-activity relationship.

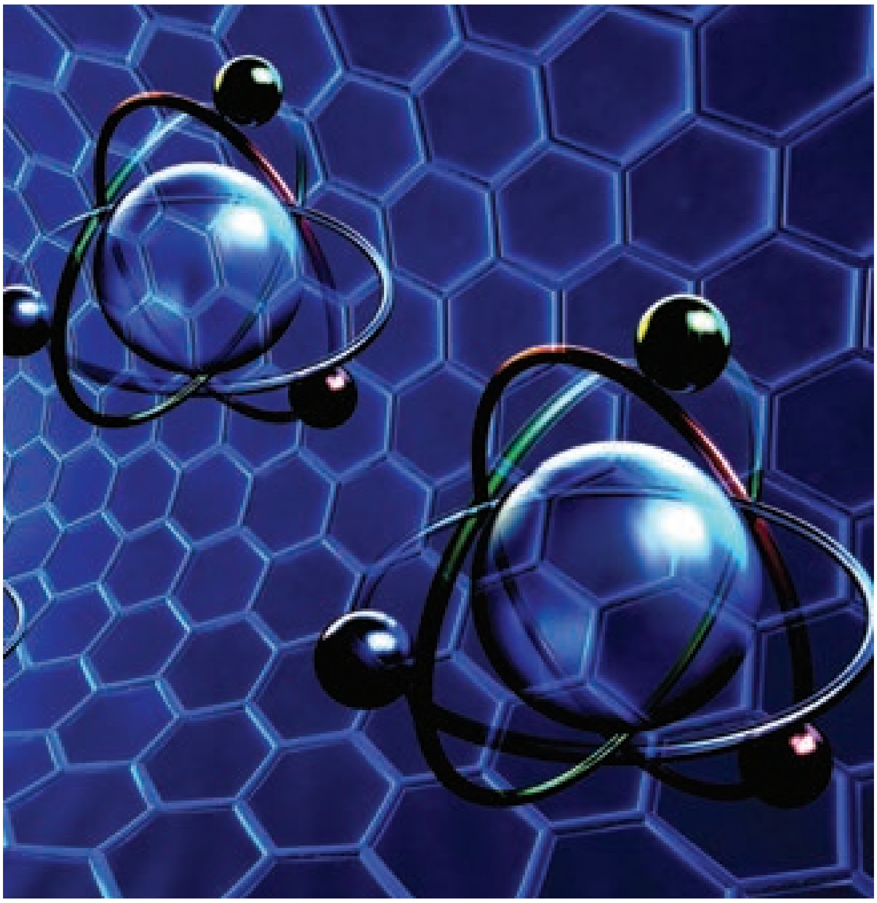

Figure 1. The unique physicochemical properties of nanoscale materials are used to perform various activities, including drug delivery, biomedical imaging, and diagnostics (representative image). Photo: Sourav Bhattacharjee.

NANOMEDICINE

Nanomaterials are materials with at least one of their dimensions less than 100nm. The physicochemical properties of nanomaterials, including nanoparticles and nanotubes, due to extremely small particulate size, demonstrate unprecedented attributes when compared to the bulk materials, such as conductivity and fluorescence. Moreover, such a small size makes the particles highly reactive and provides access to those parts of animal bodies that are otherwise inaccessible to larger particles, such as the microparticles. Interestingly, the combination of minuscule size, high reactivity, and tunable properties makes nanoparticles an exciting and emerging class of materials for drug delivery (see Figure 1). Advancements made in the field of synthesis, particularly in polymer engineering, provide further support toward designing novel nanoscale materials that can deliver an encapsulated cargo of biomacromolecules, including peptides, drug molecules, and imaging agents, in a precise and site-specific manner. My research interest lies in designing smart nanoscale drug-delivery systems (DDSs) that can be used to encapsulate a drug payload and release it in a controlled fashion, often under a range of extrinsic and intrinsic stimuli, for example, heat, tissue-specific pH, and magnetic field. Apart from drug delivery, I am also interested in using the diverse photochemistry of nanoscale materials toward developing highly sensitive, robust, and reproducible diagnostic platforms compatible with real-life biological samples, such as urine and blood.

BIOPHOTONICS

In collaboration with the Bioimaging Core facility at the UCD Conway Institute, I am engaged in biophotonics research where a range of advanced microscopic tools is used to investigate molecular phenomena occurring at a nano-bio interface. The microscopic platforms used are epifluorescence, confocal laser scanning microscopy (CLSM), and fluorescence lifetime imaging microscopy (FLIM). Recently, my group has established optimised protocols to image and analyse isolated tissue specimens based on autofluorescence (see Figure 2).

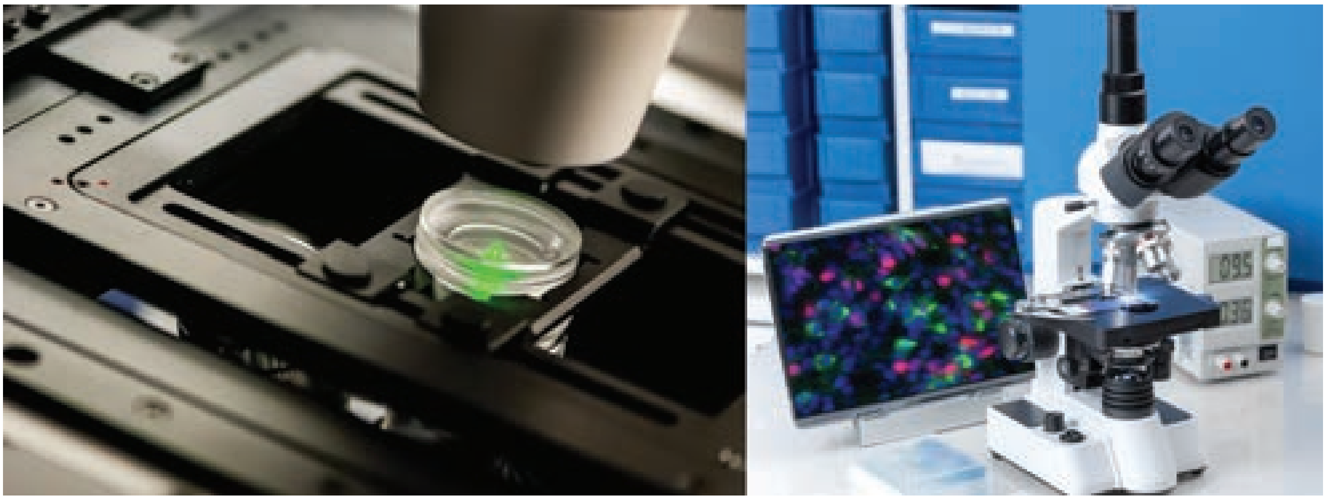

Figure 2: A range of biophotonic tools is currently being used to investigate how nanomaterials interact with biological samples (representative image). Photo: Sourav Bhattacharjee.

Utilising autofluorescence ensures minimal tissue manipulation and excludes the use of external dyes known to interfere with the native tissue fabric. Due to the high sensitivity of the technique, it can detect subtle changes within tissue samples. Interestingly, such protocols are quite useful in detecting nascent changes within tissue blocs, often prepared from a biopsied material, due to cancer onset. The ability to detect cancer at such an early stage, often termed carcinoma in situ (CIS), is crucial as early detection holds the key in managing cancer patients, such as improving prognosis and five-year survival rates. I am now collaborating with experts in the field to develop an integrated, robust, and automated imaging modality that will obviate the variation due to an empirical interpretation of histopathological tissue samples.

QUANTITATIVE STRUCTURE-ACTIVITY RELATIONSHIP (QSAR)

Molecular chemistry determines its reactivity and how a molecule interacts under physiological conditions, including its interaction with various receptors in animal bodies (see Figure 3). An exciting class of in silico tools has now appeared to analyse both the 2D and 3D structure of a given molecule and provide a broad range of molecular descriptors as numerical readouts. These numerical databases can be analysed with various modeling programs with a range of clustering and prediction protocols plugged into the platform. These sophisticated tools can be used to design drug molecules, screen large databases of drugs based on a molecular backbone or understand the molecular mechanisms of how therapeutic molecules interact with receptors at a granular level. Such artificial intelligence (AI)-based suites are currently being used to develop molecular templates that will help synthesise drugs with precise characteristics and tunable affinity toward a receptor of choice. Moreover, in collaboration with leading experts in the field, I am currently working toward the simulation of functionalized nanoparticulate surfaces with further probation of how the surface of engineered nanoparticles interacts with various glycoproteins, including gut mucin. The obtained data will be crucial toward designing nanotherapeutic agents with tailor-made properties and prioritise the functional groups for grafting on nanoparticles to facilitate cellular delivery of pharmaceutics and genetic materials.

Figure 3: Various quantitative structure-activity relationship tools are now used to analyse the structure of therapeutically relevant molecules based on a dataset of molecular descriptors. Such studies can provide an in-depth understanding of which molecular attributes contribute to the studied effect with a thorough comprehension of the mechanisms driving such phenomena (representative image). Photo: Sourav Bhattacharjee.