Title: Engineering Functional Nanomaterials for Biophotonics and Nanomedicine Applications

Abstract:

To date, functional nanomaterials have been commonly synthesized and applied for various biomedical applications such as sensing, imaging, drug delivery, and tissue engineering due to their unique optical, electronic, and biocompatible property. In this PhD work, two types of nanomaterials have been engineered, characterized, and studied for biophotonic sensing and nanodrug delivery therapy, namely, 2D nanomaterials and triboelectric nanogenerator (TENG). The engineered solutions presented in the thesis aims at addressing the current limitations in optical biosensors and self-powered skin patch drug delivery devices. In the first part of thesis, we studied the physical and optical property of a series two-dimensional (2D) nanomaterials such as molybdenum disulfide, tungsten disulfide, and molybdenum diselenide, etc., to develop and optimize next generation of plasmonic biosensors with sensitivity as high as 100 Deg/RIU. Upon coating these 2D nanomaterials on the surface of gold sensing chip, the detection sensitivity was discovered to increase by at least 2 folds due to the high refractive index up to ~4.7. Through modeling and experimental studies, a 300% increment in the detection sensitivity was achieved by using the engineered 2D nanomaterials-based plasmonic biosensor when compared to traditional devices. In addition, we showed that 1-2 orders of magnitude enhancement could be achieved in the phase-sensing mode that supports real-time submolecular detection in our designed nanoplasmonic sensor.

In the second part of the work, we designed and studied the triboelectric nanogenerator (TENG) in creating a miniaturized self-powered drug delivery device for transdermal patch application. TENG system can effectively convert various mechanical energies into electricity. TENG has many advantages such as large output of power, low cost, simple fabrication and high conversion efficiency. Our prepared TENG was able to power the transdermal patch we designed. The designed TENG-based transdermal patch composed of a conductive and nanoporous polymer and the drugs embedded in the polymer matrix were released upon receiving electric-stimuli externally. Such mechanism can allow one to achieve precise control in programming the drug delivery profile by tailoring the appropriate TENG action time. More importantly, we showed that the TENG-based transdermal patch system can be effectively used to deliver the desired drug concentration to the ex vivo porcine skin. The drug delivery efficiency in dermis was noted to improve by at least 50% when compared with the absence of TENG triggered reaction.

In conclusion, this PhD work has generated reliable and emerging engineering solutions to overcome challenges we faced in the current healthcare diagnostic and therapeutic technology especially in the areas of SPR sensors and skin patch drug delivery devices. Such solutions can be further integrated into other sensing and drug delivery systems for personalized treatment applications.

Publication:

Journal

[1] **Ouyang, Q.**, Feng, X., Kuang, S., Song, P., Yang, G., Yang, C., Chien, Y.H., Chan, K.K., Yoon, H.S., Liedberg, B.G., Zhu, G., Wang, Z., Yong, K.T. Self-powered wearable transdermal delivery systems based on triboelectric nanogenerator. 2018. (**Preparation**)

[2] **Ouyang, Q.**, Zeng, S., Jiang, L., Qu, J., Dinh, X.Q., Qian, J., He, S., Coquet, P. and Yong, K.T. Two-dimensional transition metal dichalcogenide enhanced phase-sensitive plasmonic biosensors: theoretical insight. *The Journal of Physical Chemistry C*, 2017, 121(11), pp.6282-6289.

[3] **Ouyang, Q.**, Zeng, S., Jiang, L., Hong, L., Xu, G., Dinh, X.Q., Qian, J., He, S., Qu, J., Coquet, P. and Yong, K.T. Sensitivity enhancement of transition metal dichalcogenides/silicon nanostructure-based surface plasmon resonance biosensor. *Scientific reports*, 2016, 6, p.28190.

[4] Lin, G.,* **Ouyang, Q.,*** Hu, R., Ding, Z., Tian, J., Yin, F., Xu, G., Chen, Q., Wang, X. and Yong, K.T. In vivo toxicity assessment of non-cadmium quantum dots in BALB/c mice. *Nanomedicine: Nanotechnology, Biology and Medicine*, 2015, 11(2), pp.341-350. (***Contributed equally**)

[5] Sreekanth, K.V.,* Dong, W.,* **Ouyang, Q.,*** Sreejith, S., Mohamed ElKabbash, Chwee Teck Lim，C.T., Strangi, G., Yong, K.T., Simpson, R.E., Singh, R. Femtomole biosensitivity using nanoporous silver-stibnite plasmonics. 2018. (***Contributed equally. Submitted**)

[6] Sreekanth, K.V., **Ouyang, Q.**, Han, S., Yong, K.T., Singh, R., Giant enhancement in Goos-Hänchen shift at the singular phase of a nanophotonic cavity. 2018. *Applied Physics Letters,* 112(16), 161109.

[7] Yuan, Y., Yu, X., **Ouyang, Q.**, Shao, Y., Song, J., Qu, J. and Yong, K.T. Highly anisotropic black phosphorous-graphene hybrid architecture for ultrassensitive plasmonic biosensing: Theoretical insight. *2D Materials*, 2018, 5(2), p.025015.

[8] Jiang, L., Zeng, S., **Ouyang, Q.**, Dinh, X.Q., Coquet, P., Qu, J., He, S. and Yong, K.T. Graphene‐TMDC‐graphene hybrid plasmonic metasurface for enhanced biosensing: a theoretical analysis. *Physica status solidi (a)*, 2017, 214(12).

[9] Yuan, Y., Yu, X., **Ouyang, Q.**, Peng, X., Soehartono, A.M., Shao, Y., Dinh, X.Q., Song, J., Qu, J., Yong, K.T. Promising phase-sensitive plasmonic biosensing device: antimonene-graphene hybrid architectures. 2018. (**Submitted**)

[10] Jiang, L., Zeng, S., Xu, Z., **Ouyang, Q.**, Zhang, D.H., Chong, P.H.J., Coquet, P., He, S. and Yong, K.T., 2017. Multifunctional hyperbolic nanogroove metasurface for submolecular detection. *Small*, 13 (30). pp 1700600

[11] Hong, L., Cheung, T.L., Rao, N., **Ouyang, Q.**, Wang, Y., Zeng, S., Yang, C., Cuong, D., Chong, P.H.J., Liu, L., Law, W.C. and Yong, K.T., Millifluidic synthesis of cadmium sulfide nanoparticles and their application in bioimaging. *RSC Advances*, 2017, 7(58), pp.36819-36832.

[12] Wu, Q., Lin, Y., Wo, F., Yuan, Y., **Ouyang, Q.**, Song, J., Qu, J. and Yong, K.T. Novel magnetic‐luminescent janus nanoparticles for cell labeling and tumor photothermal therapy. *Small*, 2017, 13 (39). pp 1701129

[13] Hu, R., Yang, C., Wang, Y., Lin, G., Qin, W., **Ouyang, Q.**, Law, W.C., Nguyen, Q.T., Yoon, H.S., Wang, X. and Yong, K.T. Aggregation-induced emission (AIE) dye loaded polymer nanoparticles for gene silencing in pancreatic cancer and their in vitro and in vivo biocompatibility evaluation. *NanoResearch*, 2015, 8 (5), pp.1563-1576.

Conference

[14] **Ouyang, Q.**, Panwar, N., Zeng, S., Wang, X., Jiang, L., Dinh, X.Q., Tay, B.K., Coquet, P. and Yong, K.T. Monolayer WS_2 enhanced high sensitivity plasmonic biosensor based on phase modulation. *Conference on Lasers and Electro-Optics (CLEO), IEEE*, 2017. pp 1-2.
[15] **Ouyang, Q.**, Zeng, S., Dinh, X. Q., Coquet, P., & Yong, K. T. Sensitivity enhancement of MoS_2 nanosheet based surface plasmon resonance biosensor. *Procedia engineering*, 2