Engineering the Surface of Nanodiamonds for Applications in Quantum Biosensing

Filip Steiner[1,2], Jakub Čopák[1,2], Michal Gulka[1], Petr Cígler[1,*]
[1]*Institute of Organic Chemistry and Biochemistry, of the CAS, Prague, Czechia*
[2]*Department of Physical and Macromolecular Chemistry, Faculty of Science, Charles University, Prague, Czechia*
[*]*petr.cigler@uochb.cas.cz*

Nanodiamonds (NDs) with nitrogen-vacancy (NV) centers can serve as precise, target-specific, and localized quantum probes [1]. This capability arises from the quantum mechanical interactions between the NV electron spin and its environment, which can be subsequently detected optically. For their use in a range of applications, the ND surface modification is required. The most common surface modification is the oxidation of the ND surface. However, amination and azidation of the NDs are of interest as they provide wide possibilities for further functionalization tailored for quantum biosensing. For instance, strain-promoted [3+2] azide-alkyne cycloaddition (SPAAC) would provide a critical advancement in bioorthogonal chemistry, enabling the formation of triazole rings without the need for a metal catalyst [2].

In this work, we compared different strategies for ND surface amination and azidation, and we demonstrate a successful SPAAC covalent conjugation of modified oligonucleotides with azidated NDs. To prepare aminated NDs, we studied and optimized a high-temperature amination with ammonia gas [3]. The resulting NDs show excellent colloidal stability and contain a high load of amino groups on the surface. Azidated NDs were synthesized by nucleophilic substitution of brominated NDs [4] and by decarboxylative azidation [5] for comparison. We show that the nucleophilic substitution of brominated NDs is a valuable alternative for decarboxylative azidation. Further, we optimized the reaction conditions for conjugations of NDs with oligonucleotides modified by dibenzocyclooctyne (DBCO) or bicyclononyne (BCN) as clickable groups. We showed that the number of attached oligonucleotides can be tuned by the reaction conditions and by the selection of clickable groups.

Acknowledgement
The work was supported by the Czech Science Foundation project No. 23-04876S, the Ministry of Education, Youth, and Sports of the Czech Republic (project No. CZ.02.01.01/00/22_008/0004558, co-funded by the European Union), the European Union project C-QuENS (Grant No. 101135359), the Czech Academy of Sciences – Strategy AV21 – Research program VP29 (to P.C.), TACR project Nr. TH90010001 (QuantERA – ERA-NET Cofund, project EXTRASENS), and Horizon project No 101086142 (FLORIN).

References
[1] Zhang T. et al.: ACS Sens., 2077-2107 (2021)
[2] Bertozzi C. R. et. Al.: J. Am. Chem. Soc., 15046–15047 (2004)
[3] Laube C. et al.: Mater. Chem. Front., 2527-2540 (2007)
[4] Kennedy Z. et al., Langmuir, 2790-2798 (2017)
[5] Melendrez C. et al.: Phys. Chem. Lett., 1147-1158 (2022)