Technology Offer

Nanographene-based dyes as high performance probes for super-resolution microscopy

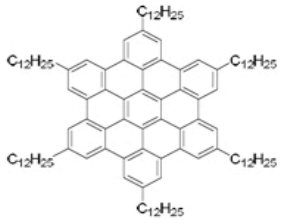
Ref.-No.: MI 0903-5658-LC; MI 0903-5658-LC; MI 0903-5658-LC

Background

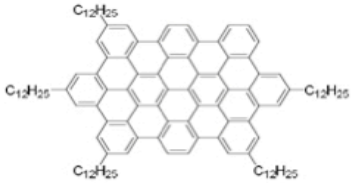
Todays standard codon optimization procedures, that are implemented in software tools such as GeneOptimizer, JCat, Optimizer, Synthetic Gene Designer, Codon Optimization OnLine (COOL) and EuGene, are based on codon adaptation to biases seen in highly expressed genes. This purely heuristic approach does not provide a deeper understanding of the underlying processes and does not answer the question of optimality in a context-dependent and mechanistic manner. As a consequence, these heuristic methods repeatedly cause unexpected or suboptimal outcomes, which triggered the search for further heuristic covariates such as length of genes, GC3 content and more complex mRNA sequence motifs as well as mRNA secondary structure. A codon-specific elongation model (COSEM), that is based on the question how codon bias affects protein expression in combination with a deep understanding of protein synthesis, offers new opportunities to overcome the limitations of the heuristic approaches.

Technology

Here nanographene structures are introduced as a new class of fluorophores for super-resolution fluorescent microscopy that overcome the limitations described above. These nanographene structures are large polycyclic aromatic hydrocarbons obtained by means of organic "bottom-up" synthesis methods. They perform like hybrids of organic dyes and QDs. They have excellent environment-independent blinking properties, emit high photon numbers, display high photostability, possess low toxicity, have a molecular size below 2 nm, and have narrow excitation and emission spectra. These features make nanographenes ideal candidates for SMLM. but also for STED microscopy.

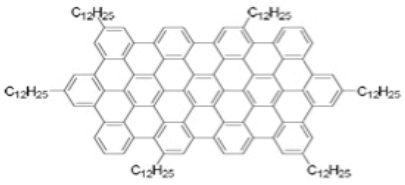


DBOV

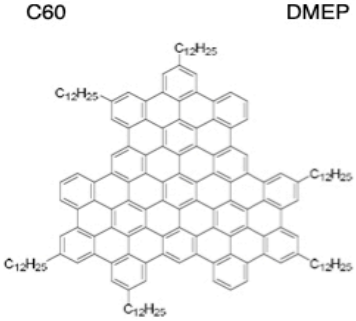


C60

DMEP



C78



C96

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Dye	Excitation maximum (nm)	Emission maximum (nm)	Extinction ($M^{-1}cm^{-1}$)	Quantum yield	Detected photons/ switching event	Duty cycle (x 10^{-4})	Blinking time (ms)
Alexa 647	650	665	239,000	0.33	3438	2.1	65
DBOV	610	614	70, 000	0.79	5570[a]	4.7[a]	108[a]
C60	412	701	22,000	0.1	4960[a]	1.2[a]	79[a]
DMEP	466	518	51,000		6164		102
C78	310	513	54,000	0.02	5740[b]	2.7[b]	83[b]
C96	491	650	61,000	0.01	5020[b]	1.7[b]	94[b]

[a] in air; [b] in polystyrene

The “bottom-up” method allows the synthesis of nanographenes with well-defined absorption and emission spectra due to their precise chemical structure, enables the introduction of various functional groups for binding to specific ligands, reacting to specific target molecules or allowing water solubility.

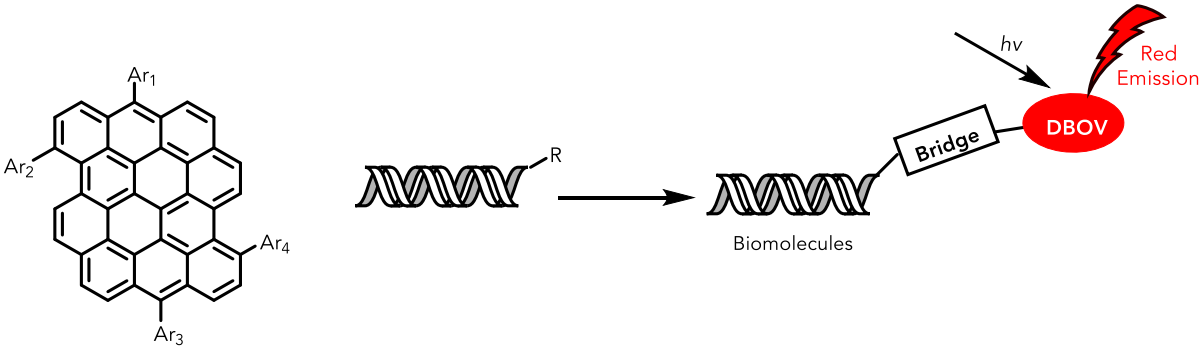

Figure 2.: Biolinkable GQDs - one Ar-group is a clickable functional group, the others can be water-soluble functional groups.

In particular DBOV-Mes has very narrow absorption and emission spectra compared to commonly used organic dyes while being water soluble, making this nanographene ideal for multi-color imaging
COSEM can naturally be adapted to alternative target organisms based on their tRNA pools for exploratory analyses. The full algorithm can then be trained and validated for these new organisms with a dataset of measured protein expression levels.

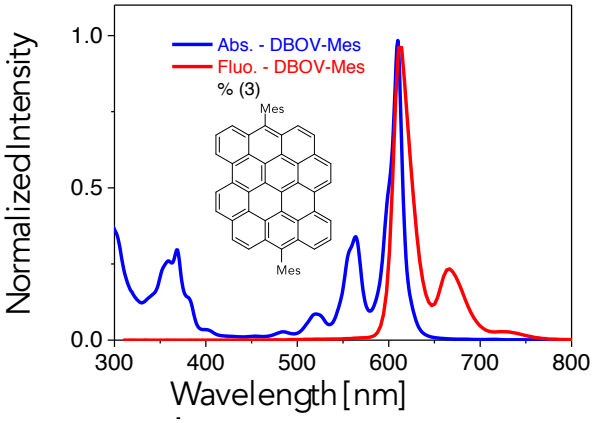

Figure 3. Absorption and emission and chemical structure of DBVO-Mes

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Patent Information

- MI0903-5658: "Use of a substituted or unsubstituted polycyclic aromatic hydro-carbon compounds for high-resolution microscopy", EP priority application filed in October 2018, PCT application filed in October 2019.
- MI0903-5696: "Hydrophilic and particularly water soluble DBOV-derivatives", EP priority application filed in October 2018, PCT application filed in October 2019.
- MI0903-5692: "Novel fluorescent pyrene derivatives, methods for preparing the same, and uses thereo", EP priority application filed in September 2018, PCT application filed in September 2019.

Literature

X. Liu, S-Y Chen, Q. Chen, X. Yao, M. Gelléri, S. Ritz, S. Kumar, C. Cremer, K. Landfester, K. Müllen, S. Parekh, A. Narita, M. Bonn: "Nanographenes: ultrastable, switchable, and bright probes for super-resolution microscopy", Angewandte Chemie, Published online 28 October 2019, https://doi.org/10.1002/ange.201909220

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