Cucurbit[*n*]uril-Immobilized Sensor Arrays for Indicator-Displacement Assays of Small Bioactive Metabolites

Chunting Zhong [1,2]**, Changming Hu** [1]**, Ravi Kumar** [1,2]**, Vanessa Trouillet** [2,3]**, Frank Biedermann** [1,]*** and Michael Hirtz** [1,2,]*****

[1] Institute of Nanotechnology (INT), Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany; chunting.zhong@partner.kit.edu (C.Z.); changming.hu@partner.kit.edu (C.H.); ravi.kumar@kit.edu (R.K.)

[2] Karlsruhe Nano Micro Facility (KNMF), Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany; vanessa.trouillet@kit.edu

[3] Institute of Applied Materials (IAM), Karlsruhe Institute of Technology (KIT), Hermann-von-Helmholtz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany

* Correspondence: frank.biedermann@kit.edu (F.B.); michael.hirtz@kit.edu (M.H.)

Abstract: The patterned immobilization of chemosensors into nano-/microarrays has often boosted application in diagnostics and environmental sensing applications. While this is a standard approach for biosensors, e.g. with antibodies, other proteins and DNA, arraying is not yet adopted widely for supramolecular chemosensors which are still predominantly used in solution systems. Here we introduce the patterned immobilization of cucurbit[*n*]urils (CB*n*).[1,2] into multiplexed microarrays and elucidate their prospects for advancement of surface-bound indicator-displacement assays (IDA) to detect small molecule analytes.[3,4] The microarrays were generated by microchannel cantilever spotting (μCS) of functionalized CB*n* and subsequent self-assembly of corresponding indicator dyes from solution. Enhanced sensitivity of surface-bound microarrays was established in demonstrations with small bioactive metabolites (spermine, amantadine, and cadaverine) compared to bulk assays. Furthermore, integration of the CB*n*/indicator microarrays into microfluidic channels provides an efficient way for real-time monitoring of the sensing process, allows easier handling and reduces need in analyte volume. The concept was further extended to differential sensing of analytes on diplex or multiplex CB*n*/indicator microarrays, opening-up a route to multi-component sensing of small molecule analytes in complex liquids.[5]

Keywords: host-guest; indicator-displacement assays; microarrays; microchannel cantilever spotting; chemosensors

Reference

1. Biedermann, F.; Nau, W.N. *Angew. Chem. Int. Ed.*, **2014**, *53*, 5694–5699.
2. Hu, C.; Grimm, L.; Prabodh, A.; Baksi, A.; Siennicka, A.; Levkin, P.A.; Kappes, M.M.; Biedermann, F. *Chem. Sci.*, **2020**, *11*, 11142.
3. Atwater, J.; Mattes, D.S.; Streit, B.; Kninski, C.B.; Loeffler, F.F.; Breitling, F.; Fuchs, H.; Hirtz, M. *Adv. Mater.*, **2018**, *30,* 1801632.
4. Dadfar, S.M.M.; Sekula-Neuner, S.; Bog, U.; Trouillet, V.; Hirtz, M. *Small*, **2018**, *14*, 1800131.
5. Zhong, C.; Hu, C.; Kumar, R.; Trouillet, V.; Biedermann, F.; Hirtz, M. *ACS Appl. Nano Mater.*, **2021**.