University of Missouri-Columbia
Department of Chemistry
Organic Cume, May 5, 2007
Dr. Rainer Glaser

Solution-Based Molecular Recognition

Leading Reference

Differential receptor arrays and assays for solution-based molecular recognition.
Wright, A. T.; Anslyn, E. V. *Chem. Soc. Rev.* **2006**, *35*, 14–28.

Question 1. Differential Sensor Arrays. Arrays of derivatized beads are created to simultaneously identify multiple analytes. (20 points)

(a) The beads are derivatized with "sensor molecules" and two sensor molecules are listed below. Briefly state what the each molecule "senses" and how this sensing is accomplished ("big picture" responses suffice). (8 points)

Fluorescein
Boronic ester

(b) Differential sensor arrays employ "CCDs" for the analysis. Explain what "CCD" stands for and what a CCD does (i.e. what data are measured?). (6 points)

"CCD" stands for:
What a CCD measures:

(c) Differential sensor arrays can be used to perform "indicator displacement assays" (IDA). Briefly explain the idea of the IDA and feel free to exemplify if you wish. (6 points)

Question 2. Molecular Imprinting. (20 points)

From the review: "As an initial demonstration of MIPs within sensor arrays, Mirsky used a simple spreader-bar approach for the development of differential sensors. In this case thiol modified purines and pyrimidines (spreader-bar molecules) were coadsorbed onto a gold surface with dodecanethiol (matrix molecule). Self-assembled monolayers (SAMs) formed having significant differential reactivity towards a number of nucleic acids: adenine, cytosine, thymine, uracil, caffeine, and uric acid. The primary detection method was measurement of the capacitive current. Five different spreader-bar molecules were employed in the development of the array: 6-mercaptopurine (ASH), 2-amino-6-purinethiol (GSH), 4-amino-2-mercaptopyrimidine (CSH), 4-hydroxy-5-methyl-2-mercaptopyrimidine (TSH), & 4-hydroxy-2-mercaptopyrimidine (USH)."

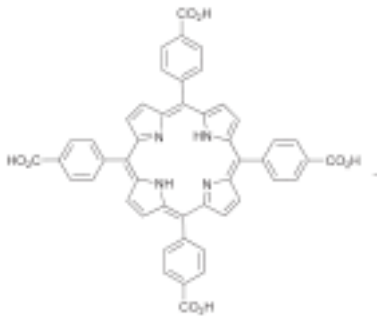
(a) Draw <u>two</u> of the **spreader-bar molecules** employed in the array. (6 points)

(b) Draw a **cartoon of a SAM** that contains one type of spreader-bar molecule. (8 points)

(c) Explain what is being measured in the analysis, that is, explain the sentence "The primary detection method was measurement of the **capacitive current**." (6 points)

Question 3. Porphyrin Fluorescent Surface Protein Receptors. (20 points)

From the review: "Hamilton has created a sensor array for the detection of multiple proteins using tetraphenylporphyrins (TPP). These porphyrins have large hydro-phobic surface areas that are excellent for protein recognition. Derivatization of the TPP periphery with various _____ resulted in a library with receptors encompassing differing charges, size, hydrophobicity, and symmetry well-suited to the recognition of proteins with various surface characteristics. The TPP derivatives also are highly fluorescent making signal detection and pattern development facile."



(a) About the "blank": What kinds of molecules are used to derivatize the TPP periphery? (4 points)

(b) Using concepts and terminology of **intermolecular bonding** explain the statement "porphyrins have large hydrophobic surface areas" and state how this property is used in protein recognition. (8 points)

(c) The measurement is based on "fluorescence quenching". What is being measured, for which chromophore(s), and how is the measured quantity influenced by the presence of analyte? (8 points)

Question 4. Microtiter Plate Arrays. (20 points)

Sometimes the quantitative measurement is not linear with analyte concentration. In such cases, one can resort to so-called "traffic light signalling systems". Fig. 12 shows such an application based on the measurement of the fluorescence and the phosphorescence of indicators dispersed in water soluble thin films of poly(ethylene glycol) on the bottom of MTP wells.

Explain how the determination is made as to whether any given well is "green" or "red". Do the colors "green" and "red" have anything to do with the indicator's color and, if so, what is that connection?

[Concept knowledge is sought, quantitative knowledge is not expected.]

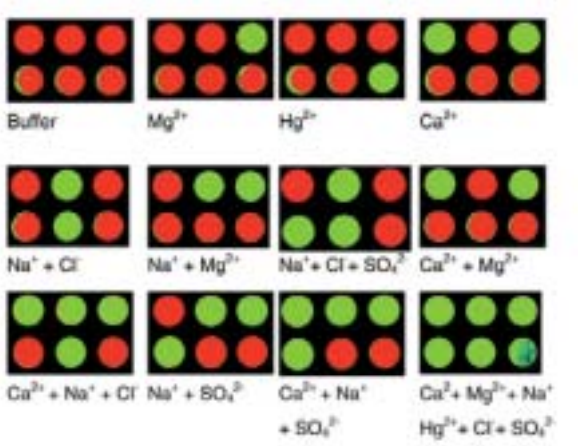
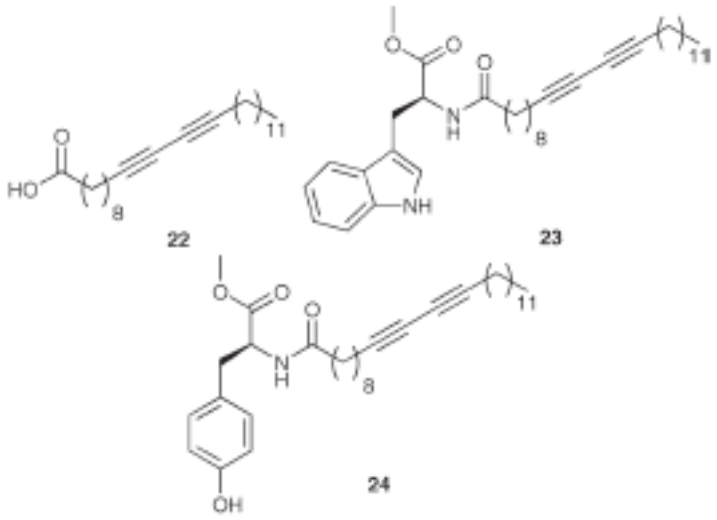


Fig. 12 Traffic light patterns for various ions and ion mixtures. Green indicates the presence of an ion, and red indicates the lack of an ion. Reprinted with permission from Wolfbeis *et al.*,[26] *Analyst*, 2002, 127, 201. © 2002 The Royal Society of Chemistry.

Question 5. Synthetic Biomolecule Assays. (20 points)

From the Review (adapted): "An example of synthetic biomolecules in arrays was completed by Basu. In this study two liposomes were prepared by polymerization of **22** (95 mol%) and either **23** or **24** (5 mol%). These liposomes change color from red to blue when bound to an analyte. Using this rather simple two sensor array, lipopolysaccharides (LPS) from various Gram negative bacteria were discriminated."



(a) Draw any **trimer** formed by trimerization of two molecules **22** and one molecule **23**. (10 points)

(b) Draw a **cartoon of the liposome** formed by the co-polymer of **22** and **23**. (Draw the cartoon any way you like. Anything that makes sense and described the essential architecture of the liposome will receive credit.) (10 points)