

Spotlights on Recent JACS Publications

■ RESTRICTED ROTATION INDUCES FLUORESCENCE IN ARSENIC-CONTAINING DYES

Fluorogenic molecules, in which fluorescence is activated upon interaction or reaction with a specific protein or biomolecule, are commonly used to monitor biological events in cells, tissues, and even in animals. Bis-arsenicals, one class of fluorogenic molecules that fluoresce when bound to four juxtaposed cysteine residues, are used as dyes to label discrete protein structures in live cells. However, an incomplete understanding of why these molecules fluoresce upon protein binding prevents their broader application by making it difficult to identify where the four cysteine residues should be introduced to ensure the brightest signal.

Through calculations and experiments, Allison Walker, Paul Rablen, and Alanna Schepartz show that the bis-arsenical dye ReAsH, which stands for resorufin arsenical hairpin binder, fluoresces upon cysteine binding because the bound protein limits rotation around the bond between the arsenic and the aromatic fluorophore, thereby disfavoring electron-transfer events that quench fluorescence (DOI: [10.1021/jacs.6b03422](https://doi.org/10.1021/jacs.6b03422)).

The results show that ReAsH fluorescence is conformation-restricted and depends on the relative orientation of the chromophore and the arsenic chelate. By shedding new light on how ReAsH fluorescence can be regulated, the reported work offers guidelines for the design of new bis-arsenicals with lower background fluorescence and the identification of ideal dye-binding sites in proteins.

Melissae Fellet, Ph.D.

■ A (MAGNETICALLY) ATTRACTIVE STRATEGY FOR OPTICS

Materials that can undergo large and rapid changes in their physical properties in response to external stimuli, such as temperature, light, humidity, and pH, have become increasingly interesting research subjects due to the large number of potential applications. In a new Perspective, Mingsheng Wang and Yadong Yin highlight recent advances in one particular niche of this field: magnetically responsive nanostructures with optical properties that can be tuned with small shifts in an applied magnetic field (DOI: [10.1021/jacs.6b02346](https://doi.org/10.1021/jacs.6b02346)).

The researchers discuss various types of magnetic nanoparticles, including spherical superparamagnetic magnetite nanocrystal clusters, iron or magnetite nanorods with a protective silica layer, and gold nanorods made “artificially magnetic” by attaching them to magnetite nanorods. By varying the magnetic field’s direction and strength, these materials can assemble into ordered arrays with highly adjustable properties: photonic crystals whose color can be tuned within the visible light spectrum, liquid crystals that can change the direction of light polarization, and plasmonic materials whose resonance can be precisely and reversibly adjusted.

Though this technology faces several hurdles before its widespread use, such as limited understanding of the magnetic building blocks’ self-assembly and the scalability of synthesizing these materials, the authors suggest that these unusual

nanostructures could find use in color displays, anti-counterfeiting devices, and a variety of other applications.

Christen Brownlee

■ IN A NEW MULTIVALENT SYSTEM, COMPLEXITY YIELDS SIMPLICITY

In nature, many biomolecular systems are capable of numerous non-covalent and highly specific interactions that compete with one another. Conversely, synthetic supramolecular systems typically achieve specificity and uniformity by having a small number of assembly pathways so as to minimize competition between different non-covalent interactions. The tradeoff for a simplified system, however, is a limited ability to adapt and respond differently to various stimuli.

In a new report, researchers led by E. W. Meijer describe a molecular system with multiple modes of interaction that can nevertheless be guided into the formation of a single structure using specific ligand binding (DOI: [10.1021/jacs.6b03421](https://doi.org/10.1021/jacs.6b03421)). Thus, despite the apparent increase in complexity, the system becomes simpler. With help from a computational model, the team rationalizes the behavior of a self-assembling molecule that is functionalized with three self-complementary motifs and is capable of yielding two different structures, with the ratio of the structures determined by the concentration of an added complementary ligand. The ratio can be modified to a point where either type of structure is formed almost exclusively. This work is a step toward more adaptive and “life-like” synthetic systems.

Christine Herman, Ph.D.

■ GOLD NANOCCLUSERS SHINE SIGNIFICANTLY BRIGHTER LIGHT

In electrochemiluminescent reactions, intermediates produced when reactants are stimulated by electricity give off light as they relax to less excited states. Electrochemiluminescence (ECL), which is often caused by multi-step charge-transfer reactions, has been proposed for a variety of applications, including immunoassays and sensing. However, limited interaction between the radical intermediates and competing side reactions lead to low efficiency, hampering researchers’ ability to harness this phenomenon for practical use.

In a new study, Gangli Wang and co-workers report a way to dramatically enhance ECL in one particular system by covalently attaching the co-reactant *N,N*-diethylethylenediamine onto suitable gold clusters (DOI: [10.1021/jacs.6b03037](https://doi.org/10.1021/jacs.6b03037)). By putting these two key players in close proximity, the researchers solve the problem of charge transfer between reactants during the lifetime of the generated radical intermediates.

Experiments show that this simple design that works under ambient conditions enhances ECL efficiency multifold compared to standard ECL reactions that use ruthenium complexes. Additionally, gold clusters emit light in the near-infrared range, making them potentially suitable for cell and tissue imaging due

Published: May 27, 2016

to the low autofluorescence and tissue transparency window at these wavelengths. The authors suggest that this strategy of attaching coreactants onto gold clusters is generalizable for other nanomaterials, opening up new ways to increase the efficiency of other ECL reactions.

Christen Brownlee

■ SMALL SYNTHETIC REPLICATOR DRIVES A REACTION-DIFFUSION FRONT

In some chemical and biological systems, stationary patterns and propagating fronts can form spontaneously—a natural phenomenon that has intrigued scientists for decades. It is well known that addition of an autocatalyst to a homogeneous unstirred solution can produce a concentration gradient, creating a propagating reaction–diffusion front that spreads autonomously through the medium. To date, the autocatalytic potential of replicators has been explored in reaction–diffusion environments only using systems based on DNA and RNA

Now, researchers led by Douglas Philp describe a molecular replicating system that can generate and sustain a propagating reaction–diffusion front within a microsyringe (DOI: [10.1021/jacs.6b03372](https://doi.org/10.1021/jacs.6b03372)). In this proof-of-principle study, the team uses NMR and UV–vis spectroscopy to perform kinetic studies, confirming that the replicator forms efficiently and is highly diastereoselective.

The researchers find that the replication process leads to dramatic changes in the sample's optical properties, as evidenced by a change in the color of fluorescence from yellow to blue. When researchers add a small amount of the preformed replicator at a specific location within the microsyringe preloaded with reactants, a propagating reaction–diffusion front is initiated. This reaction format opens up the possibility of exploring networks of replicators under conditions that lie outside the constraints of well-stirred batch reactors.

Christine Herman, Ph.D.

■ METHOXYARENE CROSS-COUPLING: IT'S ALKYL'S TURN NOW

Cross-coupling reactions using methoxyarene substrates via C–O bond activation have surfaced as an attractive alternative strategy for C–C bond formation. Compared to aryl halides, the anisole derivatives are generally less expensive and more stable, but the scope of their coupling partners needs to be expanded further.

The alkylation of methoxyarenes, for example, previously only demonstrated with carbon nucleophiles without β -hydrogens, has been made much more broadly compatible. Mamoru Tobiosu, Naoto Chatani, and co-authors report nickel-catalyzed cross-coupling of methoxyarenes with alkyl Grignard reagents (DOI: [10.1021/jacs.6b03253](https://doi.org/10.1021/jacs.6b03253)). This transformation enables the direct attachment of alkyl groups, including those containing β -hydrogens, to ipso carbons of methoxyarenes.

As the first widely applicable alkylation method for methoxyarenes, this study has provided a convenient approach to arene functionalization. The method may be especially useful in natural product synthesis and modification, considering the abundance of the methoxyaryl motif in biological systems. The researchers have also uncovered a dramatic counterion effect on the reactivity of alkylmagnesium halides, an important consideration when developing catalytic reactions using Grignard reagents.

Xin Su, Ph.D.