A UNIVERSAL PARTICLE ENCODING ARCHITECTURE

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ABSTRACT

Polymer microparticles with unique, decodable identities are versatile information carriers with a small footprint. Widespread incorporation into industrial processes, however, is limited by a tradeoff between encoding density, scalability and decoding robustness in diverse physicochemical environments. We report the rational design of an encoding strategy that combines spatial patterning of rare-earth upconversion nanocrystals (UCNs) and portable CCD-based decoding to distinguish particles synthesized via flow lithography. This architecture exhibits large, exponentially scalable encoding capacities (>10^6), an ultralow decoding false alarm rate (<10^{-9}), the ability to manipulate particles via applied magnetic fields, and dramatic insensitivity to both particle chemistry and harsh processing conditions.

KEYWORDS: Flow lithography, encoding, Multiplex, microparticle

INTRODUCTION

Encoded microparticles are attractive as information carriers due to small size and an ability to serve as scaffolds for functional payloads like molecular sensors [1-9]. However, satisfying the exacting specifications of industrial functions like anti-counterfeiting, massively parallelized bioassays or forensic labeling has proven elusive. Unique encoding of single units within information-intensive processes like pharmaceutical packaging entails encoding capacities of 10^5-10^{12} and high-throughput particle synthesis, out of reach for many current systems [1-3]. Exposure to harsh environments requires thermal insensitivity, biocompatibility and/or chemical resistance. Simple, portable decoding equipment avoids crippling implementation complexity, yet must retain the capability for low-error readout in the presence of confounding factors (e.g. complex background, obscurants, noise). Here, we employ a rational multiscale design strategy to engineer a robust encoding method for compatibility with high-throughput particle synthesis and portable CCD-based decoding. The resulting architecture exhibits dramatic insensitivity to particle chemistry – enabling tuning of encoding capacity and decoding error rate independently of particle material properties – as well as the capacity for straightforward magnetic manipulation. We demonstrate quantitatively predictable decoding of both temperature-resistant and biocompatible particles in challenging, realistic environments. With single-particle encoding capacities in excess of 1 million and error rates of less than 1 part per billion (ppb), we expand the practically accessible number of codes for applications like forensic product labeling and multiplexed bioassays by orders of magnitude. Extending the use of encoded particles to a broad and evolving range of previously unexplored industrial applications, we also introduce a novel procedure to produce covert, durable anti-counterfeiting labels with practically unlimited encoding capacity from small sets of uniquely encoded particles.

THEORY

We generate unique particle barcodes by micropatterning spectrally distinct upconversion nanocrystals (UCNs). This intuitive coding motif scales exponentially as C^S, where C is the number of distinguishable spectral signatures (UCN 'colors') and S is the number of spatial features (microparticle 'stripes'). Thus, a modest number of colors may be coupled with a similarly modest number of stripes to yield considerable encoding capacities that scale rapidly with mere incremental changes to either quantity. To implement this approach, we use a versatile, high-performance stop-flow lithography (SFL) technique for synthesizing chemically anisotropic particles [2]. In a semicontinuous process, multiple coflowing laminar streams – each containing a single optically active UCN moiety or probe molecule – are convected into a microchannel formed from polydimethylsiloxane (PDMS), stopped and photopolymerized in place via mask-patterned ultraviolet light (365 nm) to form barcoded particles at a rate of 18000 particles/hr, which are then displaced when flow resumes (Fig. 1A).

EXPERIMENTAL

PUA particles were synthesized using stop-flow lithography (SFL) as described previously [2]. Briefly, photomasks were designed using AUTOCAD 2011 and printed with a high-resolution printer at CAD Art Services (Bandon, OR). The mask was placed in the field-stop of the microscope (Zeiss Axio Observer, Zeiss) before synthesis. PUA pre-polymer mixture consisting of 150 mg of UCNs in 300 µL of PUA prepolymer solution (90 % [v/v] PUA (MINS-311RM, Minuta Technology), 10 % [v/v] Darocur 1173). The microfluidic channel was loaded with the composite monomer solution, aligned on the microscope stage, and subjected to a pressure-driven flow. In every synthesis cycle, monomer flow was halted (300 ms) and particles were photo-polymerized in the device using UV light (Lumen 200, Prior Scientific) filtered through a dichroic filter set (11000v3-UV, Chroma Technology Corp., 365 nm, 100 ms exposure time). The polymerized particles were then flowed into a collection tube (500 ms). Synthesis occurred at a rate of ~5 particles/s. After synthesis, PUA particles were rinsed 8 times with ethanol/PEG200 (1/1(v/v)) and stored in ethanol.

RESULTS AND DISCUSSION

We reported a novel particle encoding strategy by utilizing spatial patterning of rare-earth-doped upconverting nanocrystals (UCNs) via flow lithography (Figure 1) and demonstrated applications in anti-counterfeiting and biosensing (Figures 3-4). A series of multiple colored UCNs were rationally synthesized by changing the dopant ratio with high reproducibility (Figure 2a-d), and then successfully integrated into hydrophilic/hydrophobic polymeric particles to give a distinctive encoding capability. Our coding motif scales exponentially as CP where C is the 'number of UCNs colors' and P "number of positions" or stripes on the particle. We demonstrate thus far $>10^6$ codes and a very low false decoding rate ($<10^{-9}$) (Figure 2e). We generated encoded particles in a predictive manner with high reproducibility and provided robust encoding/decoding capability in biological approaches as well as in a variety of harsh industrial processing conditions. We provided a wide range of practical applications including multiplexed bioassays (Figure 3a), covert anti-counterfeit encoding on a variety of substrates (Figure 4), and durable labeling of high temperature cast objects (>250 °C). Furthermore, encoded particles were read out using a portable iPhone decoder (Figure 4). UCNs absorb low energy near infrared (NIR) light (980 nm) and emit in the visible spectrum - this is crucial for imaging them when embedded covertly in complex media. Lastly, the rare-earth dopant of UCNs permitted manipulation of encoded particles via applied magnetic fields. Our novel encoding architecture paves the path to virtually unlimited coding capability that can integrated into industrial processes and later scanned on site with an iPhone.

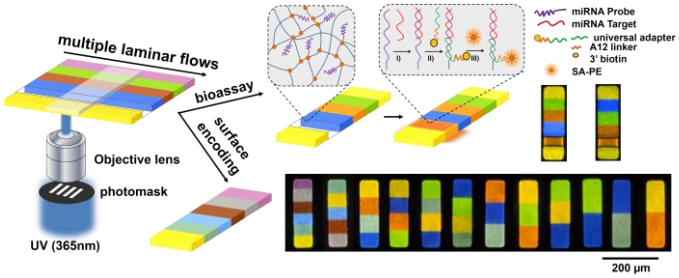

Figure 1: Schematic of encoded particle generation for bioassay and industrial surface encoding application.

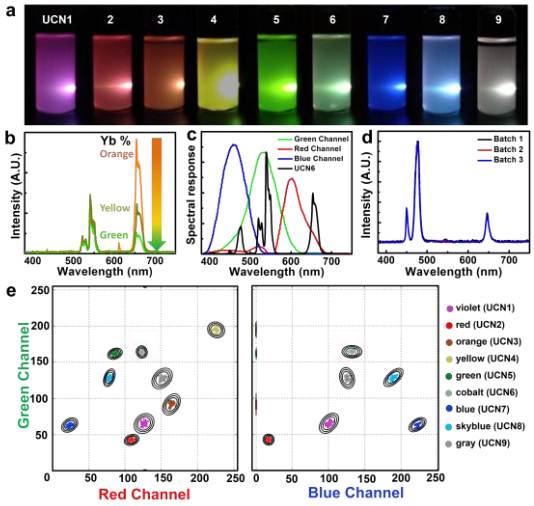

Figure 2: (a) Fluorescence images of UCNs suspensions in cyclohexane with 980 nm NIR excitation. (b) Fluorescence emission spectra change upon the dopant concentration change. (c) Output color prediction through the convolution of UCNs emission signal with CCD spectral response. (d) Reproducibility of UCNs synthesis. (e) RGB scatter plots of encoded particles representing distinctive emission color distribution (black ellipses around each color cluster represent three, four and five-sigma contours derived from fitting a Gaussian mixture model).

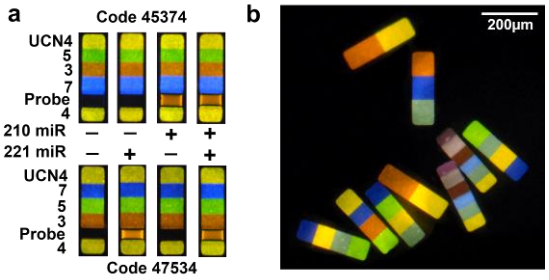

Figure 3: Fluorescence images of (a) multiplexed miRNA bioassay and (b) surface encoding of pharmaceutical blister pack.

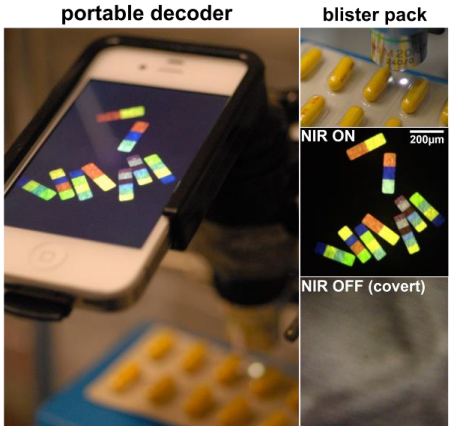

Figure 4: (left) Code calling using portable decoder and (right) covert feature of encoded particles on pharmaceutical blister pack.

CONCLUSION

The exceptional performance of our architecture in practical settings represents a significant step toward widespread use in challenging, high-value applications. The mere ability to tune particle material properties without impacting encoding performance unlocks a vast potential for immediate in-line integration of encoded particles into complex manufacturing processes or even consumer products. With modest expansion of the available color palette or number of stripes per particle, for which no foreseeable impediment exists, single-particle encoding capacities will skyrocket. The flexible architecture immensely expands the scope of what is possible for encoded particles, promising to accelerate incorporation into a broadening range of modern industrial processes.

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