Self-Driven Multistep Quantum Dot Synthesis Enabled by Autonomous Robotic Experimentation in Flow

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Identifying the optimal formulation of emerging inorganic lead halide perovskite quantum dots (LHP QDs) with their vast colloidal synthesis universe and multiple synthesis/postsynthesis processing parameters is a challenging undertaking for material- and time-intensive, batch synthesis strategies. Herein, a modular microfluidic synthesis strategy, integrated with an artificial intelligence (AI)-guided decision-making agent for intelligent navigation through the complex colloidal synthesis universe of LHP QDs with 10 individually controlled synthesis parameters and an accessible parameter space exceeding $2 \times 10^5$, is introduced. Utilizing the developed autonomous microfluidic experimentation strategy within a global learning framework, the optimal formulation of LHP QDs is rapidly identified through a two-step colloidal synthesis and postsynthesis halide exchange reaction, for 10 different emission colors in less than 40 min per desired peak emission energy. Using two in-series microfluidic reactors enables continuous bandgap engineering of LHP QDs via in-line halide exchange reactions without the need for an intermediate washing step. Using an inert gas within a three-phase flow format enabes successful, self-synchronized continuous delivery of halide salt precursor into moving droplets containing LHP QDs, resulting in accelerated closed-loop formulation optimization and end-to-end continuous manufacturing of LHP QDs with desired optoelectronic properties.

Inorganic lead halide perovskite (LHP) quantum dots (QDs) have recently emerged as a promising class of semiconducting materials for next-generation, solution-processed optoelectronic devices. For example, inorganic LHPs have surpassed the performance of conventional IV–VI QDs in photovoltaic devices. The prominence of LHPs among other semiconductor nanocrystals is mainly attributed to their high photoluminescence quantum yield (PLQY), high defect tolerance, facile bandgap tunability, and narrow emission linewidth. The ease of peak emission bandgap tuning (1.7–3.1 eV) makes inorganic LHP QDs a versatile material for widespread applications ranging from solar cells (1.77 eV), light-emitting diodes (blue 2.7 eV, green 2.39 eV, and red 1.88 eV) and various photocatalytic reactions. The peak emission energy of cesium lead halide QDs (CsPbX₃, X = Cl, Br, I) can be readily tuned by varying i) QD size using the quantum confinement effect; ii) ligand composition; iii) the chemical composition of the QD through anion and/or cation exchange; and iv) the precursor halide content. Despite producing high-quality monodispersed CsPbX₃ QDs, hot-injection synthetic routes impose major challenges from large-scale manufacturing and reproducibility perspectives. Hot-injection colloidal synthesis requires operating at high temperatures (>150 °C), which increases the overall energy costs and necessitates specific reactor design modifications to ensure homogenous, uniform heat distribution across the reactor. Furthermore, manual, flask-based colloidal syntheses are notorious for their lack of reproducibility (batch-to-batch variation and operator error), and difficulty of integration with material diagnostic probes. Room-temperature colloidal synthesis (e.g., ligand-assisted reprecipitation strategy) and post-synthesis halide exchange reactions of CsPbBr₃ QDs are considered attractive alternatives to the hot-injection synthesis strategy for facile and precise bandgap engineering of LHP QDs. QD purification normally involves washing steps that consist of antisolvent addition followed by centrifugation, aliquot disposal, and fresh solvent addition. Moreover, washing and the subsequent redispersal of LHP QDs in fresh solvent disrupts the surface ligands, leading to ligand detachment, surface defects (lowering the PLQY), and reduced colloidal stability of the LHP QDs. Removal of the intermediate washing step of halide exchange reactions can enable end-to-end continuous manufacturing of inorganic LHP QDs and accelerate their adoption by chemical and energy technologies.

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Microfluidic material synthesis strategies with their modular nature, have recently been demonstrated as a reliable and precise tool for accelerated exploration of multivariable synthesis and processing of LHPs, while overcoming the mass and heat transport limitations imposed by flask-based synthesis methods.13,20,24,31–33 The superior heat and mass transfer rates and capability of integration with real-time in situ material diagnostic probes and artificial intelligence (AI)-based experiment selection strategies make microscale flow synthesis techniques an ideal approach for accelerated fundamental and applied studies of inorganic LHP QDs with tunable nucleation and growth kinetics.31,33–38

Multiphase microfluidic reactors, including two- and three-phase flow configurations (gas–liquid, liquid–liquid, or gas–liquid–liquid)—in contrast to single-phase flow formats with their unwanted axial dispersions—have been demonstrated to provide a narrow QD size distribution.39–41 The reduced size dispersity of the in-flow synthesized LHPs using multiphase flow reactors compared with single-phase flow format can be attributed to the enhanced mixing rates achieved through the axisymmetric recirculation patterns formed within the moving droplets.42,43 Utilizing perfluorinated oil (PFO) as the continuous phase, that preferentially wets the microchannel walls, prevents the reactive phase from contacting the microchannel walls, thereby avoiding fouling.44

Considering the envisioned end-to-end manufacturing of inorganic LHP QDs, modular flow reactors are required to achieve continuous, in-series synthesis of CsPbBr3 QDs followed by in-line halide exchange reactions without an intermediate QD washing step. Despite the advantages of using a liquid–liquid two-phase flow in colloidal nanomaterials syntheses, it offers a very narrow operational window for passively synchronized in-line precursor addition (injection) into moving reactive droplets. Introduction of an inert gas as the third phase into a liquid–liquid segmented flow has been demonstrated to enable successful self-synchronization of in-line precursor addition into the flowing droplets, and significantly expands the accessible operation envelope of the flow reactor beyond liquid–liquid segmented flow, without reactor fouling.44 The inert gas phase acts as a cushion for the newly added chemical precursor into the microchannel and automatically synchronizes the precursor injection with the position of the moving reactive droplet. This unique characteristic can be attributed to the change in the three-phase surface force balance (comparing with a two-phase organic solvent—PFO system),45–47 which enables multistep sequential synthesis and processing within microfluidic reactors.44,48 Using a three-phase flow format allows the sequential in-line addition of the halide salt precursor into the as-synthesized CsPbBr3 QDs in a moving droplet (i.e., telescoped reactions) and circumvent the need for an off-line intermediate washing step (workup), thereby intensifying the QD manufacturing process as a result.

The complex and multivariable nature of the synthesis and optimization of LHP QDs make the discovery and search for the optimal LHP QD product a daunting undertaking.29 For example, the output properties of CsPbX3 QDs—peak emission energy, $E_p$ (1.9–3.1 eV), and full-width-at-half-maximum (FWHM < 200 meV)—synthesized via a two-step synthesis of CsPbBr3 QDs followed by an in-series halide exchange reaction can be tuned by a wide range of input parameters, including: i) starting precursors concentration, ii) starting precursors volumetric injection ratio, iii) amount and (type) of surface ligands present in the synthesis and exchange of CsPbX3 QDs, and iv) halide salt concentration and composition. Automated experimentation methods alone may improve the rate in which a material space may be navigated; however, the disjointed experiment selection and conduction cycle reduces the efficiency in which the reaction conditions may be optimized. Generally, experimentation strategies with high reliance on user guidance and operation, require increased time commitment and level of expertise. Recent advances in AI, including deep neural networks (DNN) and reinforcement learning, for rapid chemical space exploration,49–61 provide an exciting opportunity to reshape the development and on-demand manufacturing of colloidal nanomaterials. Consequently, a number of self-optimizing microfluidic reactors have been developed to take advantage of continuous material exploration in a low chemical consumption system.31,36–38 AI-based experimentation strategies may provide the tools necessary to efficiently explore the expanding parameter spaces.

The self-optimizing fluidic studies frequently apply either established optimization methods, such as Stable Noisy Optimization by Branch and Fit,62 or recently re-emerged Gaussian process regression-based modeling (e.g., Kriging),36,63 are often placed in tandem with techniques that use decision making under uncertainty in a closed-loop fashion, such as the case of many recent efforts in the use of Bayesian Optimization (BO) for autonomous materials development.64 In recent work, we demonstrated the use of ensemble neural networks (ENN) for application in a fully self-optimizing fluidic system.31 While the most effective AI algorithm is problem-dependent, ENN-based experimentation methods have shown their potential in navigating large reaction spaces from a position of no prior knowledge as well as with archived data as a starting position to achieve a specific objective.

Increasing the number of input parameters in a reaction space greatly inflates the degree of difficulty in system outputs tuning and optimization. With every added parameter, the size of the accessible reaction space increases exponentially. Thus, as material syntheses become more complicated (e.g., multistep synthesis), the synthesis space becomes arduous to explore and control through manual experiment selection strategies. This is often referred to as the Curse of Dimensionality. For example, the eight input parameters of the two-step synthesis and postprocessing anion exchange reaction of CsPbBr3 QDs present a parameter space of $\approx 2 \times 10^7$ possible combinations (calculated based on the number of independent input parameters, precursor concentration range, and the minimum accurate precursor concentration increment feasible by the fluid delivery system).

In this work, we develop an AI-guided LHP QD synthesis approach for autonomous end-to-end manufacturing of inorganic LHP QDs (Figure 1a). Autonomous operation of an interconnected network of flow-based modules enables in-house generation of large set of in situ spectroscopic data in real time for data mining and intelligent experiment selection. The modular and reconfigurable microfluidic reactors operated using three-phase (gas–liquid–liquid) flow format enable controlled in-flow synthesis of CsPbBr3 QDs followed by a rapid halide exchange reaction without an intermediate washing step (Figure 1b). We leverage the high-throughput and time- and material-efficient nature of the developed autonomous robotic
QD synthesizer for rapid exploration of the vast colloidal synthesis universe of LHP QDs with eight independent input and two output parameters using an AI-guided decision-making strategy within a global learning framework. Using an active learning strategy, we utilize the self-driving modular QD synthesizer for rapid, autonomous formulation exploration of high-quality CsPbX₃ QDs at any desired $E_P$ with a minimized FWHM. We then demonstrate the reconfigurability of the developed LHP QD synthesizer from rapid formulation discovery to end-to-end continuous manufacturing with the desired optoelectronic properties using the results of the global learning experiments as prior knowledge. Furthermore, the developed autonomous LHP QD synthesis strategy utilizes its prior knowledge to mitigate the batch-to-batch variation issue observed in conventional flask-based syntheses of LHP QDs at minimal cost (waste generation).

The developed AI-guided microfluidic material synthesizer with two in-series flow reactors is shown in Figure 2. The hardware of the automated modular platform includes: i) 3 precursor formulation modules with 10 individually controlled input streams producing 3 on-demand formulated precursors ($P_1$, $P_2$, and $P_3$) (Table 1). The individually controlled input streams are represented in the ENN model as nondimensionalized flow rates $X_1$–$X_8$ (Table 2, Supporting Information); ii) Two microfluidic reactors for in-flow synthesis of CsPbBr₃ QDs (microreactor 1) followed by an in-line halide exchange reaction (microreactor 2); and iii) an online spectral characterization module (photoluminescence [PL] spectroscopy). The operation sequence of the modular QD synthesizer is controlled by a custom-developed process automation code (LabVIEW). The rapid formulation optimization and intelligent exploration of LHP QD synthesis space with their massive parameter space (8 independent input parameters and 2 outputs) was achieved via a knowledge transfer strategy through a global learning step (100 experiments with a maximum variance [MV] decision policy), followed by an AI-guided decision-making step using an exploitation (EPLT) decision policy.

Microreactor 1 is where the cesium lead (CsPb) and bromine Br precursors react in flow and form CsPbBr₃ QDs within the reactive phase droplets moving along the flow direction. The halide exchange reaction of the as-synthesized CsPbBr₃ QDs takes place in microreactor 2—without any interruption in the

Figure 1. a) Schematic illustration of the concept of AI-guided QD synthesis in flow. b) Schematic illustration of the on-demand continuous manufacturing of inorganic LHP QDs enabled by an AI-guided modular microfluidic reactor.
workflow—via a passive, self-synchronized addition of a specific volume of zinc halide precursor ($\text{ZnX}_2$, $X = \text{Cl}$ or $\text{I}$) into the train of moving droplets, containing CsPbBr$_3$ QDs. As discussed previously, the presence of the gas droplets within the three-phase flow format utilized in this work, enables facile in-line addition of the zinc halide precursor into the moving droplets without the need for any complex active synchronization techniques.

The composition and concentration of the main precursors, including $P_1$:CsPb, $P_2$:Br, and $P_3$:ZnX$_2$ during each experimental iteration of the AI-guided optimization campaign is selected by the decision-making policy. The autonomously selected compositions are then automatically formulated in flow, before injection into the microreactors, using three formulation modules, shown in Figure 2. $P_1$ and $P_2$ represent the CsPb and Br precursors with tunable concentrations and different amount of oleic acid (OA), respectively. $P_3$ represents the zinc halide precursor with a specific halide (Cl or I), OA, and oleylamine (OAm) composition set by the AI-guided decision-making algorithm.

Formation of a uniform and controlled three-phase flow in microreactor 1 is crucial for continuous operation of the automated platform during the global learning and optimization campaigns. A custom-designed, five-port fluidic junction was machined in polyether ether ketone (PEEK) to minimize the contact time of $P_1$ and $P_2$ precursors before segmentation with the inert carrier phase, PFO, and argon gas. Thus, the CsPbBr$_3$ QDs were formed after segmentation within the reactive phase droplets in microreactor 1.

The optical properties of the LHP QDs synthesized in the modular microfluidic platform are monitored in real-time at
the outlet of microreactor 2 using the custom-developed flow cell. Utilizing the flow cell module, the PL spectra of the autonomously synthesized LHP QDs at each iteration (i.e., AI-selected experimental condition) are obtained and processed automatically to obtain the $E_p$ and FWHM of the in-flow synthesized LHP QDs.

To ensure reliable and consistent injection of the zinc halide precursor into the moving droplets containing as-synthesized CsPbBr$_3$ QDs, we sought to characterize the uniformity and stability of the three-phase flow using the custom-developed five-port fluidic junction, before and after the secondary in-line injection port, via in situ UV–vis absorption spectroscopy. For the three-phase flow characterization experiments, we used toluene (the reactive phase solvent) mixed with Sudan blue (for visualization), PFO, and argon. The light absorption intensity difference of each fluid at 400 nm was utilized to identify the boundaries and length of each phase in both microreactors before and after in-line injection (Figure 3a, Figure S1 and S2, Supporting Information). Droplet length disparity can be quantified by examining the variation in the amount of time it takes for each phase to pass the flow cell port, $\Delta t$ (Figure 3a). Figure 3b shows the consistency and uniformity of the preinjection three-phase flow over a 15 min period. The light absorbance time series at 400 nm, from the flow cell placed after the in-line injection port, were also used to quantify the reliability of the in-line zinc halide precursor injection module, where larger volumetric injection ratios, $P_3/(P_1 + P_2)$, resulted in longer postinjection droplets which is directly indicated by the increase in $\Delta t$ (Figure 3c). Figure 3d shows a series of absorbance time series for different $P_3/(P_1 + P_2)$ ratios, illustrating that the secondary precursor injection, for the set of flow rates chosen, resulted in precise self-synchronized injection into the moving droplets and a uniform postinjection train of droplets over a wide range of secondary injection volumetric ratios $P_3/(P_1 + P_2)$ (up to four times the original droplet volume). The post-/pre-injection $\Delta t$ ratio of the reactive phase ($\Delta t_2/\Delta t_1$) as a function of $P_3/(P_1 + P_2)$ is shown in Figure 3e. The nonlinear behavior of $(\Delta t_2/\Delta t_1)$ versus $P_3/(P_1 + P_2)$ shown in Figure 3e can be attributed to the following: i) difference in the reactive phase mixture density before and after in-line halide precursor addition, ii) different droplet velocities before and after the in-line precursor injection, and iii) gas phase compressibility. Figure 3f shows

Figure 3. a) Bright-field three-phase flow image (top) of dyed-toluene, PFO, and argon, along with its in situ obtained absorbance time series at 400 nm (bottom). b) Preinjection absorbance time-series plot at different time intervals showing the uniformity of the three-phase flow over the span of 15 min. Postinjection absorbance time-series plot at different volumetric precursor ratios, $P_3/(P_1 + P_2)$, for c) single and d) multiple unit cells (toluene + PFO + argon). e) Post-/pre-injection droplet length ratio as a function of $P_3/(P_1 + P_2)$. f) $\Delta t$, a droplet length proxy, at different instances over the span of 15 min.
the reliability of the self-synchronized secondary injection, for a $P_3/(P_1 + P_2) = 1$, over the span of 15 min. The consequent experiments were conducted with the secondary injection ratio, $P_3/(P_1 + P_2) = 1$, to eliminate any mixing variability across different reaction conditions due to the variation in droplet length.\[33,42,43\] It should also be noted that, as previously reported in the literature, reliable and uniform three-phase flow formation and the subsequent in-line injection can be achieved by minimizing the PFO and maximizing the gas (argon) ratio with respect to the total flow rate.\[44\] Furthermore, once the setup reaches steady state at each experimental condition, the three-phase flow and droplet sizes stabilize and remain that way during the continuous flow synthesis of LHP QDs until varying the experimental conditions or consuming all precursors loaded in the syringes. The duration of continuous flow synthesis of the LHP QDs in the multistage microfluidic platform depends on the volume of the precursor syringes loaded on the syringe pumps. By adding an automated precursor refilling module, the continuous flow synthesis of the LHP QDs in the developed platform can be significantly extended (\(>24\) h).\[31\]

Following the characterization of the three-phase flow behavior within the modular microfluidic platform, in the second set of experiments, we investigated the in-flow reaction time of the halide exchange reaction (microreactor 2) using the as-synthesized CsPbBr\(_3\) QDs (microreactor 1). The knowledge of halide exchange reaction time is important to ensure the in situ spectral characterization of the LHP QDs is conducted after completion of the halide exchange reactions. Figure 4a,b shows the temporal PL spectra evolution of the iodide and chloride exchange reactions in flow, respectively. Both halide exchange reactions reached completion (i.e., terminal $E_P$) relatively quickly at about 20 s (Figure 4c), while the FWHM values of both reactions took longer to equilibrate (Figure 4d). As shown in Figure 4d, the halide exchange reaction time is \(\approx60\) s, which is longer than our previous report using washed CsPbBr\(_3\) QDs; where the equilibrium time for both iodide and chloride exchange reactions were 40 s and 10–50 s, respectively.\[20\] The slowed halide exchange kinetics when using as-synthesized CsPbBr\(_3\) QDs compared with the washed QDs can be attributed to the presence of unreacted salts and ligands in the solution.

Following the reaction time studies of the in-series LHP QD synthesis and halide exchange reactions, a residence time of 80 s was used for all subsequent halide exchange reactions to ensure reaction completion before in situ spectral characterization (Figure 4). Next, we employed the modular microfluidic platform for systematic studies of the in-series LHP QD synthesis and halide exchange reactions by varying the concentration of the starting CsPb precursor from 9 to 51 mM. Figure 5 shows the PL spectra of the in-flow halide-exchanged QDs for different zinc halide ($P_3$) concentrations ($C_3$). As shown in Figure 5, lower CsPb and Br precursor concentrations resulted in a higher $E_P$ shift for all $C_3$ values, irrespective of the exchanged halide. The limits of halide exchange reactions on tuning $E_P$ was found to be 1.9 and 2.9 eV for iodide and chloride exchange reactions, respectively.

The second set of in-series halide exchange experiments were conducted to explore the effect of varying $P_1/P_2$ ratio on the

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**Figure 4.** In-line halide exchange reaction time studies. In situ obtained PL spectra of LHP QDs from microreactor 2 at different residence times for a) iodide and b) chloride exchange reactions, using the as-synthesized CsPbBr\(_3\) QDs in-series. $P_1$ and $P_2$ had concentrations of 51 mM, and $P_3$ (for both ZnCl\(_2\) and ZnI\(_2\) exchange studies) had a concentration of 42.5 mM. The flow rates of the reactive phase ($P_1 + P_2$), PFO, argon, and $P_3$ were 250, 50, 500, and 250 $\mu$L min$^{-1}$, respectively. c) Peak emission energy ($E_P$) and d) FWHM of iodide and chloride exchange reactions in flow as a function of residence time.
optoelectronic properties of colloidal CsPbX₃ QDs. The experiments were divided into four main groups, where $P_1/P_2$ value was varied, while maintaining the concentration of the CsPb precursor constant at 9, 20, 30, and 51 mM. Figure 6 shows the effect of varying $P_1/P_2$ ratio along with $C_s$ on $E_P$ for both iodide and chloride exchange reactions. The first notable observation is that higher $P_1/P_2$ values are more resistant to halide exchange. Higher $P_1/P_2$ values correspond to more available CsPbBr₃ QDs in the solution for the subsequent in-line halide exchange reactions, resulting in a faster depletion of the available halide anions and earlier termination of the $E_P$ shift. Another distinct behavior observed is that both iodide and chloride exchange reactions exhibited the same overall trend with increasing $C_s$. However, $C_s$ values required for the chloride exchange reactions were 25% of the iodide exchange reactions. This difference can be attributed to the more facile halide exchange reactions of CsPbBr₃ QDs with chloride than iodide anions. Using lower concentrations of the zinc chloride precursor can enhance the bandgap tunability, and thereby unveil the halide exchange mechanism, as previously observed in the literature.[20]

Following the development and characterization of the three-phase flow format and the self-synchronized, in-line addition of the zinc halide precursor into the moving droplets, an AI-guided decision-making strategy (i.e., autonomous experiment...
selection) was developed and integrated with the modular microfluidic platform for the simultaneous optimization of $E_P$, and FWHM of CsPbX$_3$ QDs. In contrast to other closed-loop, autonomous campaigns that use techniques such as BO, the strategy used here considered the problem of efficiently learning about multistep LHP QD synthesis in general, while performing target optimizations over several optimization episodes, each with different objectives.

Common to each episode were several ground-truth observable and a priori unknown responses, viewed as functions over the colloidal synthesis space. These unknown ground-truth response functions were modeled using ENN models, each representing all response functions. The ENN models comprised 500 randomly structured cascade forward neural networks. Throughout the campaign, based on a limited set of observed data obtained during the campaign, models in the ensemble are trained, and the aggregate of models are used to define summary statistics of the models’ predictions of the responses. Such summary statistics include an expected value of the responses as a function of synthesis inputs, as well as an uncertainty quantification of these predicted values.

In each optimization episode, a target set of responses are defined, resulting in a scalar objective function $z(x)$ which measures how close the ground-truth responses achieve the targeted values. As with the response function, the objective function is a priori unknown, but model predictions and uncertainties can be similarly obtained from the ENN. These predictions and uncertainties can be used within an AI-guided, closed loop decision-making campaign to efficiently learn the optimal synthesis conditions that yield the desired target responses. The algorithms and methods used in the data processing and experiment selection are adapted from our previous work. 

Within the popular and traditional BO framework, decision-making policies attempt to generally balance learning about the objective function of interest (exploration) with focusing on regions in synthesis space that appear promising (EPLT). This balance between exploration and EPLT is generally stuck under the assumption that a BO campaign will be performed once—so that decisions are made to effectively go from little or no prior knowledge to the best understanding possible of the optimal regions within a limited amount of data. In contrast, the problem studied here considers a balance in which the general knowledge gained through exploration can be amortized over several optimization episodes with dynamic targets. In this sense, such decision making is more in line with non-BO techniques, such as more general active learning methods or episodic reinforcement learning.

The strategy used here is to initially invest in the general, global learning of the various response functions before the optimization of the synthesis parameters for any particular target responses. This first phase of the global learning is done using the MV decision-making policy, which selects, at any particular time, the synthesis conditions corresponding to the output function values of the objective function $z(x)$ with the largest uncertainty for a preselected target peak emission energy ($E_P = 2.2$ and 2.65 eV for iodide and chloride exchange reactions, respectively). Using a closed-loop, active learning policy such as MV potentially offers an advantage over traditional and nonsequential experimental design such as Latin hypercube sampling (LHS) by continuously updating and evaluating regions of the sample space where there is less confidence in the model prediction, thereby offering more efficient allocation of sampling resources. In addition, the complexity of the posterior predictions made by the neural networks used in the ENN may be more amenable to the sequential design—it is not clear that information gained by the NNs about the response from a data point transfers only “locally,” as in the case of nonparametric models such as Gaussian processes. As such, space-filling designs such as LHS may prove an inefficient allocation for fitting an ENN model.

The autonomous robotic experimentation is conducted on an automated modular, microfluidic platform (Figure 2) which controls precursor delivery and in situ spectral sampling. Integrated data processing algorithms extract relevant PL spectra and optical properties from the continuously reacting three-phase flow system in real-time for subsequent analysis. The AI-guided optimization was conducted by first performing 100 experiments for each halide exchange system (i.e., ZnI$_2$ and ZnCl$_2$), each using the MV policy. These exploratory experiments provide a baseline structure for the ENN model to effectively represent the multivariable colloidal synthesis space of CsPbX$_3$ QDs.

Before conducting the autonomous LHP QD formulation optimization experiments, we used the ENN model constructed from the 200 collected experimental data points (i.e., the surrogate model) to simulate the multistep LHP QD synthesis universe. Figure 7 shows a representative 2D surface response of the output parameters ($E_P$ and FWHM) of the ENN model for both the iodide (Figure 7a,c) and chloride (Figure 7b,d) reaction exchanges. The surface plots represent the change in $E_P$ (Figure 7a, b) and FWHM (Figure 7c,d) as a function of $X_1$ and $X_6$ for specific $X_1$, $X_6$, and $X_7$ values; $X_1$, $X_6$, and $X_7$ were held at a constant value (0.5) for all of the simulated outputs. Figure 7 shows a snapshot into the multivariable synthesis space of CsPbBr$_8$X$_{12−6}$ (X: Cl or I) QDs, which further highlights the importance of AI-guided microfluidic material synthesis strategies for accelerated parameter space mapping, formulation optimization, and manufacturing of solution-processed (nano)materials. A similar trend for peak emission energy shift was observed for both chloride (bandgap increase) and iodide (bandgap decrease) exchange reactions across different $X_1$, $X_6$, and $X_7$ combinations (Figure 7a,b). As expected, increasing $X_6$ (i.e., increasing halide salt concentration) resulted in increased peak emission energy shift. $X_1$ exhibits a weak effect on $E_P$, where larger $X_1$ values resulted in a slight increase in peak emission energy shift. This observed phenomenon can be explained by considering that $X_1$ represents the amount of injected CsPb precursor as a compliment to the Br precursor (S1, Supporting Information), where higher $X_1$ values correspond to lower free Br$^-$ in the solution, and thereby less available Br$^-$ that exploits the halide exchange reaction. FWHM, on the other hand, exhibits more dynamic trends with regards to all five independent variables shown in Figure 7c,d. Figure 7c shows the complex, nonlinear nature of FWHM evolution of in-line iodide exchange reactions with respect to $X_1$ and $X_6$. Higher $X_1$ values result in larger FWHM, whereas lower $X_1$ and higher $X_6$ produce iodide-exchanged LHP QDs with lower FWHM. According to Figure 7c, the best iodide-exchanged LHP QDs can be obtained with a moderate level of Br$^-$ (the lowest FWHM of each hyperbolic plot were located...
at $X_4 = 0.4–0.6$), while minimizing amount of the participating CsPb species (minimum $X_1$ and $X_3$). Figure 7d shows the FWHM evolution of LHP QDs during the chloride exchange reactions in flow. The correlation between $X_6$ and FWHM offers the most distinctive and consistent correlation for FWHM of chloride-exchanged LHP QDs, where higher $X_6$ values correspond to lower FWHM values of chloride-exchanged QDs in flow. In addition, increasing $X_2$ and $X_8$ results in larger FWHM values. Based on Figure 7d, the lowest FWHM for chloride-exchanged LHP QDs can be obtained with $X_1$ values closer to 1, while minimizing both $X_2$ and $X_8$.

After this initial phase of the closed-loop global learning of the response functions, various optimization episodes were carried out. In each episode, the pure EPLT policy is used, selecting, at each iteration of the closed-loop LHP QD formulation discovery, the synthesis conditions predicted to minimize the objective function $z(x)$. Specifically, using the developed library of archived experimental conditions as prior knowledge, 10 optimization campaigns were conducted with the EPLT policy on varying target emission colors, shown in Figure 8a,b for iodide and chloride exchange reactions, respectively. For all target peak emission energy values, the AI-guided microfluidic synthesis platform was able to reach $E_p$ within 5 meV after only 5 experiments (~40 min).

The developed AI-guided experiment selection approach integrated with the modular microfluidic QD synthesis platform allowed for the rapid formulation optimization of an 8D colloidal synthesis space of CsPbX$_3$ QDs without user guidance and within a moderate number of experiments: 10 optimized LHP QD products (i.e., 10 target emission colors) were autonomously identified using 250 total experiments (200 global learning experiment and 5 EPLT experiments for each target $E_p$). The strategy of mixed exploration and EPLT used in this study enabled efficient isolation of optimal synthesis conditions and the production of precisely

![Figure 7. Five-dimensional visualization of the synthesis universe of LHP QDs obtained using an ENN model trained on the in-house generated experimental data.](image-url)
The developed smart (i.e., AI-guided) LHP QD synthesizer in this work will accelerate adoption of the emerging concept of smart modular material manufacturing in energy and chemical industries through seamless integration of discovery, synthesis optimization, and end-to-end material manufacturing stages. The autonomous QD synthesis strategy integrated with the modular microfluidic reactors provides an all-in-one platform capable of autonomous learning, optimization, and on-demand manufacturing of LHP QDs with optoelectronic properties.

Figure 8. Sample output values of the AI-guided LHP QD optimization algorithm using an EPLT decision policy and 100 data points from the global learning stage (global learning, knowledge transfer) for a) iodide and b) chloride exchange reactions. c) On-demand, wheel of color demonstration of UV-illuminated, optimized halide-exchanged LHP QD droplets synthesized in flow using the AI-guided decision-making strategy under uncertainty. d) In situ obtained PL spectra of the 10 in-flow optimized CsPbX3 (X = Cl, Br, I) QDs.

The autonomous robotic experimentation platform can accelerate development of solution-processable materials and unlock broader access to more complex material spaces.

tuned colloidal LHP QDs on-demand (Figure 8c,d). Figure 8c shows fluorescence images of 10 different in-flow optimized LHP QDs (under UV illumination) using the autonomous robotic experimentation platform. The PL spectra of the in-flow optimized LHP QDs are shown in Figure 8d (also see Figure S4, Supporting Information). Further implications of the developed autonomous robotic experimentation platform can accelerate development of solution-processable materials and unlock broader access to more complex material spaces.
precisely tuned for applications in next-generation photonic devices, lighting/displays, and organic synthesis (photocatalysis). The autonomous modular QD manufacturing strategy can result in a paradigm shift in the development and manufacturing of colloidal nanomaterials, while promoting energy and environmental sustainability.

Experimental Section

Materials: All chemicals were used as received. Lead (II) oxide (>99.9%, trace metal basis), cesium hydroxide solution (50 wt% in H2O > 99.9%, trace metal basis), tetracyclammonium bromide (98%), oleic acid (90%, technical grade), zinc iodide (>98%), zinc chloride (>98%), methyl acetate (99%, extra pure), and toluene were purchased from Sigma-Aldrich. Oleylamine (>50.0%, GC) was purchased from TCI Chemicals. PFO (Galden HT200) was purchased from Solvay.

CsPb Precursor: The CsPb precursor was prepared using a slightly modified synthesis protocol reported in the literature. Briefly, lead (II) oxide (1.38 mmol, 310 mg), OA (2 mL), and cesium hydroxide solution (121 μL) were added to an 8 mL septa vial. The vial was inserted into an oil bath at 160 °C for 30 min. The resultant cesium-lead olate precursor was then diluted to 60 mM with toluene (1 mL of CsPb precursor with 10.47 mL of toluene). Then the 60 mM CsPb precursor solution was diluted to the desired concentration with toluene/OA solution (Tol:OA, 6:1 volumetric ratio).

Br Precursor: The Br precursor was prepared by adding tetracyclammonium bromide (TOAB) to toluene/OA solution (Tol:OA, 6:1 volumetric ratio) where the amount of TOAB was determined based on the desired concentration. For example, for a 15 mM Br precursor, 0.27 mmol of TOAB and 2.571 mL of OA were added to 15.429 mL of toluene in an 8 mL septa vial.

Zinc Halide Precursor: The highest concentration used in this study for both iodide and chloride exchange reactions was 45 mM. Toluene (30.857 mL), OA (2.571 mL), and OAm (2.571) were added to a 40 mL septa vial along with the desired amount of ZnX2 (X = Cl or I), depending on the desired concentration. All zinc halide precursor solutions were prepared in open air and without any heating. The solutions were sonicated to dissolve the salts.

Modular Microfluidic Platform: The modular microfluidic platform consisted of 10 automated syringe pumps (3 Fusion 4000, and 4 Harvard PHA-ULTRA) loaded with stainless steel syringes (six 50 mL and four 20 mL, Harvard apparatus) for controlled liquid delivery and an automated mass flow controller (MFC, Bronkhorst, EL-FLOW Select) for controlled gas delivery to the microreactors. Three-phase flow in microreactor 1 was formed by delivering the reactive phase (P1 and P2), PFO, and argon into the custom-machined five-port PEEK junction. Fluorinated ethylene propylene (FEP) tubing (500 μm inner diameter, ID, 45 cm long) was used to connect all single-phase streams from syringe pumps and MFC to the formulation modules of both microreactors. The toluene and OA streams were mixed with CsPb (P1) and Br (P2) precursors in a PEEK cross junction (IDEX Health & Sciences) was used to mix the zinc halide precursor, toluene, OA, and OAm (P3) on demand. The halide precursor was passively injected into the train of moving reactive phase droplets containing CsPbBr3 QDs using a PEEK T-junction (IDEX Health & Sciences). Microrreactors 1 and 2 were constructed using 90 cm of 750 μm ID FEP tubing. The total flow rates of the reactive phase (P1 + P2), PFO, argon, and the secondary injection port (P3) were 250, 50, 300, and 250 μL min⁻¹ respectively.

Spectral Monitoring Module: The in situ spectral characterization of the in-flow synthesized LHP QDs was conducted using a custom-machined flow cell module (90° configuration) connected to a fiber-coupled miniature UV–vis spectrometer (Flame UV–vis spectrometer, Ocean Insight) and a fiber-coupled UV LED (365 nm, Thorlabs). An integration time of 12 ms was used for all in situ PL spectral measurements.

Three-Phase Flow Stability Studies: The stability and uniformity of the three-phase flow were characterized utilizing the absorption intensity difference of each phase at 400 nm. A custom-machined flow cell module (180° configuration) connected to a fiber-coupled deuterium-halogen lamp (Ocean Insight) and a fiber-coupled miniature UV–vis spectrometer (Flame UV–vis spectrometer, Ocean Insight) were used to monitor the absorption intensity time series of each phase passing through the flow cell module. The absorption intensity time-series plots shown in Figure 3 were constructed by considering the absorption intensity values over 4.5 s at 400 nm with an integration time of 10 ms.

Neural Network Modeling and Decision-Making Policies: The ENN model used is an ensemble of 500 randomly structured cascade forward, artificial neural networks. The AI-guided exploration of the colloidal synthesis parameter space of in-series synthesis and halide exchange reactions of LHP QDs was adapted from Epps et al.,[20,26] where the ENN was trained on E, and FWHM, and the predictions are passed through a quality metric objective function (z), shown in the following equation.

\[ z(x) = 0.9 \left( \frac{|E_p(x) - E_{P,up}(x)|}{1.2} \right) + 0.1 \frac{FWHM(x)}{0.4} \]  

where \( E_p \) is the in situ measured peak emission energy, \( E_{P,up} \) is the target peak emission and FWHM is the in situ measured PL FWHM, and \( x \) is the synthesis input conditions. The constants 0.9 and 0.1 are the weights assigned to \( E_p \) and FWHM, respectively, based on their relative importance as optimized outputs. 1.2 was selected based on the maximum possible \( E_p \) difference (1.9–3.1 eV), and 0.4 (400 meV) exemplifies the maximum FWHM of a polydispersed LHP QD solution. Each NN model in the ensemble defines a prediction of the three objectives, and hence of the objective function \( z(x) \), where we denote the \( i \)th model’s prediction of the objective function as \( z_i(x) \). From the ensemble of such models \( z_i \) and their corresponding posterior weighting \( p_i \), we therefore can obtain summary statistics, such as the expected value of the objective function

\[ z(x) = \sum_i p_i z_i(x) \]  

and the variance

\[ \sigma^2(x) = \sum_i p_i (z_i(x))^2 - z(x)^2 \]  

This variance function measures a level of uncertainty associated to the prediction of ground truth objective function \( z(x) \) by the expected value \( z(x) \).

An active-learning, closed-loop experimental campaign was conducted by selecting the next experiment to perform using a decision-making policy. One policy used was the MV decision-making policy, which selects the input with largest associated uncertainty in the predicted objective function value: \( x_{\text{rand}} = \arg \max_i \sigma^2(x) \). The pure EPLT policy was also used, selecting the next experiment by the one predicted to yield the minimal objective \( x_{\text{rand}} = \arg \max_x \mathcal{z}(x) \). Both the ENN model and policies are reported fully in prior work.[31]

Optimization Runs Precursor Preparation: The concentration of the precursors used for the AI-guided CsPbX3 (X = Cl, Br, I) QD synthesis runs were lower than those used for the systematic screening studies to provide the ENN a larger operating window. The concentrations of the starting CsPb and Br precursors were 15 mM. The concentration of the starting zinc iodide and zinc chloride salts was 10 and 7.5 mM, respectively. The ligand-to-solvent ratios used for these runs were identical to those mentioned in the precursors preparation sections earlier. The OA and OAm syringes had a Tol:OA/OAm ratio of 2:1.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.
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Conflict of Interest

The authors declare no conflict of interest.

Keywords

accelerated materials development, continuous manufacturing, lead halide perovskites, microfluidics, quantum dots

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