

FEEDBACK-CONTROLLED AUTOMATED NANOPARTICLE SYNTHESIS

Cross-Reference to Related Application

[0001] This application claims the benefit of priority of Singapore Patent Application
5 No. 10202103565Q, filed 7 April 2021, the content of it being hereby incorporated by
reference in its entirety for all purposes.

Technical Field

[0002] The present disclosure relates to a system operable to synthesize nanoparticles.
10 The present disclosure also relates to a method of synthesizing nanoparticles using the
system.

Background

[0003] Nanoparticle synthesis in a wet chemistry laboratory setting began several
15 decades ago. While years of research may have given rise to a variety of approaches to
make nanoparticles of various shapes and sizes, the process of synthesizing
nanoparticles remains highly experiential to date. Despite best efforts, nanoparticle
sizes and shapes may vary significantly from batch to batch even for experienced
chemists. The inconsistency arises from nuanced changes of experimental parameters
20 and handling processes under human operation, including but not limited to changes in
reagent concentration and timing of reagent addition. As a result, reproducibility and
success rates are susceptible to being undesirably low. In turn, scalable production of
nanoparticles remains challenging to realize, which further limits the downstream
development of nanomaterial-based platforms for translational applications.

25 [0004] Observably, majority of studies conducted tend to be focused on converting
reactions from batch process into continuous flow system. Some of these studies may
use a “one-pot” system, static reaction system, utilize in-line/online sampling without
changing the composition of reaction mixture during the entire synthesis, while other
include sophisticated artificial intelligence and machine learning for materials
30 discovery. Unfortunately, these traditional systems cannot work for synthesis of shape-
controlled metal nanoparticles.

[0005] There is thus a need to provide for a solution that addresses one or more of the limitations mentioned above. The solution should at least provide for a method of synthesizing nanoparticles with high yield, scalability, with ongoing size and shape tunability as the synthesis of nanoparticles progresses.

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Summary

[0006] In a first aspect, there is provided for a system operable to synthesize nanoparticles, the system comprising:

a robotic module comprising:

a temperature controller;

one or more dispensers operable to dispense different reagents; and

an extraction device;

10 a reaction vessel configured to receive the different reagents from the one or more dispensers to form a reaction mixture from which the nanoparticles are synthesized; and

a process control module operably coupled to the robotic module and a spectroscopy module, wherein the process control module configures:

15 the extraction device to withdraw a sample of the reaction mixture at an interval as the reaction mixture progresses and to transfer the sample into one or more cuvettes of the spectroscopy module, and

the spectroscopy module to generate spectral data based on an optical property of the sample and from the spectral data identify a condition
20 which serves as a feedback to the process control module to configure:

the temperature controller to change or maintain temperature of the reaction mixture as the reaction mixture progresses,

the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed
25 into the reaction mixture as the reaction mixture progresses, and

the extraction device to change or maintain the interval for withdrawing further samples of the reaction mixture to provide the feedback continuously to have the process control module configure the temperature controller, the one or more dispensers,

and the extraction device, in aforesaid manner until synthesis of the nanoparticles in the reaction mixture is completed.

[0007] In another aspect, there is provided a method of synthesizing nanoparticles using the system described in various embodiments of the first aspect, the method comprising:

providing a reaction mixture from which the nanoparticles are synthesized in a reaction vessel;

5 having a process control module configure an extraction device to withdraw a sample of the reaction mixture at an interval as the reaction mixture progresses and to transfer the sample into one or more cuvettes of a spectroscopy module;

generating spectral data from the spectroscopy module based on an optical property of the sample;

10 identifying from the spectral data a condition which serves as a feedback to the process control module; and

having the process control module, based on the feedback, configure:

a temperature controller to change or maintain temperature of the reaction mixture as the reaction mixture progresses,

15 the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction mixture as the reaction mixture progresses, and

the extraction device to change or maintain the interval for withdrawing further samples of the reaction mixture to provide the feedback continuously to have the process control module configure the temperature controller, the one or more dispensers, and the extraction device, in aforesaid manner until synthesis of the nanoparticles in the reaction mixture is completed.

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25 **Brief Description of the Drawings**

[0008] The drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the present disclosure. In the following description, various embodiments of the present disclosure are described with reference to the following drawings, in which:

30 [0009] FIG. 1A shows the extinction spectrum of Ag nanocubes.

[0010] FIG. 1B is a photo image of the present system.

[0011] FIG. 1C shows the temporal evolution of plasmon resonance modes as a function of reaction time.

5 [0012] FIG. 2 is a digital screenshot of the “Robosoft” software interface of the process control module of the present system.

[0013] FIG. 3 shows SEM images of Ag nanocubes. The right image is a x10 magnification of the left image.

10 [0014] FIG. 4 shows a comparison of the extinction spectra for hand-synthesized Ag nanocubes (left plot) and Ag nanocubes synthesized from the present system (right plot).

[0015] FIG. 5 shows the extinction spectra for five sets of Ag nanocubes synthesis reaction produced by the present system and method operated via a single user.

[0016] FIG. 6A shows the solutions of the reaction mixture collected over the course of synthesis of Ag nanocubes using the present system.

15 [0017] FIG. 6B shows an extinction spectrum corresponding to the samples shown in left image of FIG. 6A.

[0018] FIG. 6C shows an extinction spectrum corresponding to the samples shown in center image of FIG. 6A.

20 [0019] FIG. 6D shows an extinction spectrum corresponding to the samples shown in right image of FIG. 6A.

[0020] FIG. 7 shows various scanning electron microscopy (SEM) images for characterizing the samples collected during synthesis via the present system and method.

25 [0021] FIG. 8 shows the growth process (via particle size) of Ag nanocubes synthesized from the present system and method.

[0022] FIG. 9 is a plot of the time-dependent evolution of the various localized surface plasmon resonance modes.

30 [0023] FIG. 10 shows the time-dependent changes in the position of mode 1 and nanocube size (left plot) and the linear fit of variations of mode 1 against particle size (right plot).

[0024] FIG. 11 shows the kinetics of nanocube growth, tracked using the change in peak position of mode 1 (left plot), and using nanocube sizes derived from SEM measurements (right plot).

5 [0025] FIG. 12 shows correlation of the size and purity of Ag nanocubes with their extinction spectra. Top row shows the SEM images of the Ag nanocubes and the corresponding extinction spectra are shown in the second row. The size and size distribution of the individual samples are also indicated.

[0026] FIG. 13 shows the relationship between the spectral positions of modes 1, 2 (left and right plots, respectively) and Ag nanocube sizes.

10 [0027] FIG. 14 shows the relationship between the full width at half maximum (FWHM) of modes 1, 2 (left and right plots, respectively) and purity of Ag nanocubes synthesized.

[0028] FIG. 15 is a plot of the intensity ratio of mode 2/mode 1 against nanocube purity.

15 [0029] FIG. 16 is an image of different tubes of Ag nanocubes manually synthesized by four operators experienced with Ag nanocubes synthesis.

[0030] FIG. 17 shows corresponding extinction spectra of the four reactions of Ag nanocubes synthesized manually by four operators in FIG. 16.

[0031] FIG. 18 shows corresponding SEM images for the Ag nanocubes of FIG. 16.

20 [0032] FIG. 19 shows the reaction time-dependent evolution of the plasmon resonance modes 2 (left plot) and 4 (right plot), and their correlation with growth in sizes of the Ag nanocubes.

[0033] FIG. 20 shows large cubic crystals with poor shape uniformity (left SEM image) near start of synthesis reaction (6 mins) and cubic crystals with highly uniformed shape (right SEM image) at 15 mins into the reaction of the present method.

25 [0034] FIG. 21 is a SEM image showing silver nanoparticles synthesized by a traditional method where silver nitrate (example of a metal precursor) and PVP (example of a polymeric precursor) are introduced into at fixed intervals (compared to present system and method which involves a feedback loop to continuously adjust the interval at which the metal precursor and polymeric precursor are introduced as reaction progress). As can be seen in the SEM image and inset, a mixture of nanocubes and nanorods are formed. Meanwhile, the present system and method renders consistent
30 nanocubes instead of such a mixture.

[0035] FIG. 22 shows the silver nanocubes synthesized from the present system and method. In this example, as can be seen in the plot, 3 rounds of silver nitrate were introduced at 2 min, 3 min and 8 min as reaction progresses. The solution was heated for 5 more minutes after the last round of injection. The SEM image (bottom image is a magnification of the top image) shows the resultant silver nanocubes with a highly uniform shape and highly uniform size distribution 74 ± 5 nm.

Detailed Description

[0036] The following detailed description refers to the accompanying drawings that show, by way of illustration, specific details and embodiments in which the present disclosure may be practised.

[0037] Features that are described in the context of an embodiment may correspondingly be applicable to the same or similar features in the other embodiments. Features that are described in the context of an embodiment may correspondingly be applicable to the other embodiments, even if not explicitly described in these other embodiments. Furthermore, additions and/or combinations and/or alternatives as described for a feature in the context of an embodiment may correspondingly be applicable to the same or similar feature in the other embodiments.

[0038] The present disclosure relates to a system operable to synthesize nanoparticles and a method of synthesizing nanoparticles using the system. Details of various embodiments of the present system and method, and advantages associated with the various embodiments are now described below. Where the embodiments and/or advantages have been described in the examples section further hereinbelow, they shall not be iterated for brevity.

[0039] In the present disclosure, there is provided a system operable to synthesize nanoparticles. In various embodiments, the system includes a robotic module comprising a temperature controller. In various embodiments, the system includes one or more dispensers operable to dispense different reagents. In various embodiments, the system includes an extraction device. In various embodiments, the system includes a reaction vessel configured to receive the different reagents from the one or more dispensers to form a reaction mixture from which the nanoparticles are synthesized. In

various embodiments, the system includes a process control module operably coupled to the robotic module and a spectroscopy module.

[0040] In various embodiments, the process control module configures (i) the extraction device to withdraw a sample of the reaction mixture at an interval as the reaction mixture progresses and to transfer the sample into one or more cuvettes of the spectroscopy module, and (ii) the spectroscopy module to generate spectral data based on an optical property of the sample and from the spectral data identify a condition which serves as a feedback to the process control module to configure (a) the temperature controller to change or maintain temperature of the reaction mixture as the reaction mixture progresses, (b) the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction mixture as the reaction mixture progresses, and (c) the extraction device to change or maintain the interval for withdrawing further samples of the reaction mixture to provide the feedback continuously to have the process control module configure the temperature controller, the one or more dispensers, and the extraction device, in aforesaid manner until synthesis of the nanoparticles in the reaction mixture is completed.

[0041] In various embodiments, the robotic module may further comprise a heating stage for a heating vessel to be arranged thereon. The heating stage may comprise a heating element. The heating element may be operably coupled to the temperature controller to adjust heat provided from the heating element to the reaction mixture.

[0042] In various embodiments, the heating vessel may house an oil bath. The heating vessel may be any suitable container to house an oil bath and for the reaction vessel to be placed in the oil bath. The reaction vessel can be any suitable flask (e.g. a round-bottom flask) having an opening to receive the one or more reagents dispensed from the one or more dispensers. The heating vessel may be wrapped with an insulating material that minimizes heat exchange out of the oil bath. The insulating material may be an aluminium foil as a non-limiting example (see FIG. 1B).

[0043] In various embodiments, the robotic module comprises a rotatably adjustable receptacle to position the reaction vessel in the heating vessel. In other words, the receptacle is able to move the reaction vessel vertically and horizontally, and maintain

the reaction vessel in an upright position that prevents any spillage from the reaction vessel.

[0044] In various embodiments, the one or more dispenser may comprise one dispenser to dispense a solvent, one dispenser to dispense a polymeric precursor, and one
5 dispenser to dispense a metal precursor. Examples of the solvent, polymeric precursor and metal precursor are already described in the examples section and shall not be reiterated for brevity. The solvent can be an organic solvent. The solvent can be used to dissolve the polymeric precursor and/or the metal precursor.

[0045] In various embodiments, there may be one dispenser for dispensing the solvent,
10 which is operable to dispense the solvent into the one or more cuvettes.

[0046] In various embodiments, the extraction device may comprise a suction pump connected to a tube, and the extraction device is operably coupled to a fan which is operable to dry the tube. The extraction device may be operated to have the tube submerged into a reaction mixture residing in the reaction vessel so as to withdraw a
15 portion (i.e. a sample) of the reaction mixture into the tube. The suction pump provides the suction required to withdraw a portion of the reaction into the tube. The extraction device may then be operated to have the tube dispensed the withdrawn portion of reaction mixture into the one or more cuvettes, thereby transferring the sample from the reaction vessel into the one or more cuvettes for characterizing and/or identifying the
20 nanoparticles' synthesis progress and/or contents in the reaction vessel. The suction pump may be operated to reverse suction, i.e. pump/deliver the reaction mixture from the tube into the one or more cuvettes.

[0047] In various embodiments, the spectroscopy module may comprise a rack to house the one or more cuvettes, a light source configured to project light toward the one or
25 more cuvettes, a detector configured to receive light projected through the sample in the one or more cuvettes, and a data acquisition module operably coupled to the process control module. In various embodiments, the data acquisition module converts light received by the detector into spectral data. Any data acquisition module capable of aforesaid operation may be used in the system.

[0048] In various embodiments, the process control module may be operable to have
30 each of the one or more dispensers dispense the different reagents in a dropwise or single-shot manner.

[0049] Also, as can be seen in FIG. 1B, the system can have two reaction vessels. In such non-limiting embodiments, the functions of the dispensers and pump(s) may remain the same as described in various embodiments of the first aspect, i.e. to help dispense one or more reagents into the reaction vessel or to draw liquids (e.g. the reaction mixture) from the reaction vessel for optical measurements. The two vessels may be aligned parallel to the one or more dispensings, to allow the one or more dispenser to introduce the reagents (e.g. polymeric precursor, solvent, metal precursor) into the reaction vessels and draw samples thereafter for measurements. The initiation, progression, and termination of the reaction remains identical and/or similar to a one vessel setup.

[0050] At the start of the reaction, one dispenser may dispense the polymeric precursor (e.g. PVP) into one vessel, followed by the other vessel. Next, one dispenser may dispense the metal precursor (e.g. AgNO_3) into one vessel, followed by the other vessel.

[0051] The system can be operated such that there is enough time interval for both reactions to proceed concurrently, and enable liquid samples to be drawn out in between the addition of various reagents. Due to the configuration of the two-vessel system, the reaction of one vessel should finish before the other vessel. In such non-limiting embodiments, the computer interface may allow separate control over the two reactions, with the optical characterization from each vessel showing up independently.

[0052] The present disclosure also provides for a method of synthesizing nanoparticles using the system described in various embodiments of the first aspect. Embodiments and advantages described for the system of the first aspect can be analogously valid for the present method subsequently described herein, and vice versa. As the various embodiments and advantages have already been described above and examples demonstrated herein, they shall not be iterated for brevity.

[0053] The method includes providing a reaction mixture from which the nanoparticles are synthesized in a reaction vessel. The method includes having a process control module configure an extraction device to withdraw a sample of the reaction mixture at an interval as the reaction mixture progresses and to transfer the sample into one or more cuvettes of a spectroscopy module. The method includes generating spectral data from the spectroscopy module based on an optical property of the sample. The method includes identifying from the spectral data a condition which serves as a feedback to

the process control module, and having the process control module, based on the feedback, configure (a) a temperature controller to change or maintain temperature of the reaction mixture as the reaction mixture progresses, (b) the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction mixture as the reaction mixture progresses, and (c) the extraction device to change or maintain the interval for withdrawing further samples of the reaction mixture to provide the feedback continuously to have the process control module configure the temperature controller, the one or more dispensers, and the extraction device, in aforesaid manner until synthesis of the nanoparticles in the reaction mixture is completed.

[0054] In various embodiments, prior to providing the reaction mixture, the method may further comprise providing an oil bath in a heating vessel and having a robotic module operably configure a rotatably adjustable receptacle to position the reaction vessel in the heating vessel.

[0055] In various embodiments, wherein prior to providing the reaction mixture, the method may further comprise heating the oil bath to 150°C to 250°C, 150°C to 200°C, 200°C to 250°C, 170°C to 210°C, etc.

[0056] In various embodiments, providing the reaction mixture may comprise operating the one or more dispensers to dispense each different reagent at one or more specified times into the reaction vessel, wherein operating the one or more dispensers comprises having one dispenser to dispense a solvent, having one dispenser to dispense a polymeric precursor, and having one dispenser to dispense a metal precursor.

[0057] In various embodiments, having the one dispenser to dispense the polymeric precursor may comprise dissolving the polymeric precursor in an organic solvent. The organic solvent for dissolving polymeric precursor can be the same for dissolving the metal precursor.

[0058] In various embodiments, operating the one or more dispensers to dispense the different reagents may comprises adding the polymeric precursor before adding the metal precursor but after loading the solvent into the reaction vessel. Advantageously, this step helps to heat up the solvent before the reaction begins. Nevertheless, the sequence of adding the reagents is not restricted to such a step. For example, the metal precursor may first be added into the reaction vessel.

[0059] In various embodiments, having the process control module configure the extraction device to withdraw the sample may comprise operating a suction pump to withdraw a sample of the reaction mixture via a tube positioned in reaction vessel and having the suction pump deliver the sample into the one or more cuvettes, and operating
5 a fan coupled to the extraction device to dry the tube after the extraction device delivers the sample.

[0060] In various embodiments, generating spectral data from the spectroscopy module based on an optical property of the sample may comprise projecting a light toward the one or more cuvettes, having a detector configured to receive the light projected through
10 the sample in the one or more cuvettes, and having a data acquisition module convert the light received by the detector into spectral data.

[0061] In various embodiments, having the process control module, based on the feedback, configure the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction
15 mixture as the reaction mixture progresses may comprise having the process control module configure each of the one or more dispensers to dispense the different reagents in a dropwise or single-shot manner.

[0062] In various embodiments, the optical property may comprise or may be a color of the sample.

[0063] In various embodiments, identifying from the spectral data the condition which serves as the feedback to the process control module may comprise identifying a first wavelength and/or a second wavelength which correspond to a first peak and/or a second peak in the spectral data, respectively, and/or identifying any change in the first wavelength and/or second wavelength from the further samples as the reaction mixture
25 progresses to determine completion of synthesis of the nanoparticles in the reaction mixture.

[0064] Understandably, the method described above can be applied for the two-vessel system.

[0065] The word “substantially” does not exclude “completely” e.g. a composition
30 which is “substantially free” from Y may be completely free from Y. Where necessary, the word “substantially” may be omitted from the definition of the present disclosure.

[0066] In the context of various embodiments, the articles “a”, “an” and “the” as used with regard to a feature or element include a reference to one or more of the features or elements.

[0067] In the context of various embodiments, the term “about” or “approximately” as applied to a numeric value encompasses the exact value and a reasonable variance.

[0068] As used herein, the term “and/or” includes any and all combinations of one or more of the associated listed items.

[0069] Unless specified otherwise, the terms "comprising" and "comprise", and grammatical variants thereof, are intended to represent "open" or "inclusive" language such that they include recited elements but also permit inclusion of additional, unrecited elements.

Examples

[0070] The present disclosure relates to a system and method of synthesizing nanoparticles. The system and method may involve a feedback-controlled automated nanoparticle synthesis setup. The feedback-controlled automated nanoparticle synthesis system setup is capable of performing on-demand nanoparticle synthesis with minimal human involvement.

[0071] The present system and method of nanoparticle synthesis are demonstrated hereinbelow via synthesis of silver (Ag) nanocubes as a non-limiting example. Ag nanoparticles are used as a non-limiting example, because Ag nanoparticles tend to be in commercial demand, i.e. the compound annual growth rate in demand of Ag nanoparticles is projected to grow 13% between 2018 and 2024, with demand coming from the electronics, healthcare, textile and even food industries. Ag nanocubes tend to stand out among the various types of Ag nanoparticles due to its excellent optoelectronic properties, capable of achieving intense electromagnetic field confinements around their sharp edges and vertices. However, the synthesis of Ag nanocubes appears challenging, as it may require precisely timed and alternate addition of two reagents, AgNO₃ and poly(vinylpyrrolidone) (PVP), into a reaction vessel over the course of approximately 20 minutes. Any fluctuation in reagent volume added or addition interval may easily affect the synthesis process, e.g. leading to low yields of Ag nanocubes. However, the present system and method are able to circumvent such a

limitation. The present system and method are also applicable for other types of nanoparticles

[0072] The present system and method are described in further details, by way of non-limiting examples, as set forth below.

5 **[0073] Example 1: Introductory Discussion on Present System and Method**

[0074] The present method of synthesizing nanoparticles can include monitoring dipolar resonance (see FIG. 1A, Mode 1) and quadrupolar resonance (see FIG. 1A, Mode 2) of optical spectra of synthesized nanoparticles during the reaction.

[0075] As an example, Mode 1 for silver nanoparticles is an initial peak which forms
10 at around 400 nm, and subsequently undergoes continuous redshift to around 750 nm at the end of the reaction. Mode 2 peak occurs after occurrence of Mode 1 peak at around 420 nm, which also undergoes continuous redshift to around 560 nm at the end of the reaction. By monitoring the change in the wavelengths of Mode 1 and/or Mode 2 and adjusting the reaction parameters towards the desired wavelength(s) of Mode 1
15 and/or Mode 2, desired nanoparticles (e.g. nano-spheres, nanocubes) can be obtained. For example, the variation in the desired wavelength(s) of Mode 1 and/or Mode 2 for different synthesized batches is around ± 10 nm.

[0076] Monitoring of the nanoparticle synthesis can be carried out manually, or more preferably, using a feedback-controlled automated nanoparticle synthesis system.

20 **[0077]** The present nanoparticle synthesis system can include (a) robotic platform (i.e. a robotic module) including one or more reagent dispensers (for brevity termed “dispenser”) and/or a temperature controller, (b) a reaction vessel where reagents are dispensed into and where the synthesis takes place for a period of time, and (c) a process control module (for brevity termed “processor”) communicatively coupled to the
25 robotic platform and a spectroscopy module and configured to control the robotic platform by changing amount, frequency and/or absolute time at which reagents are dispensed into, and/or temperature of the reaction vessel to tune the properties of synthesized nanoparticles based on one or more obtained optical spectra of the synthesized nanoparticles in the reaction vessel.

30 **[0078]** The present method of synthesizing nanoparticles using the nanoparticle synthesis system can include communicatively coupling a process control module to a robotic module and a spectroscopy module wherein the process control module is

configured to control the robotic platform by changing amount, frequency and/or absolute time at which reagents are dispensed into, and/or temperature of a reaction vessel to tune the properties of synthesized nanoparticles based on one or more obtained optical spectra of the synthesized nanoparticles in the reaction vessel.

5 [0079] The nanoparticles may have at least a property (e.g. physical, including shape and size, or chemical) that changes (reproducibly) with at least an optical property. Changes in the optical property can be identified through one or more changes in the obtained spectrum.

[0080] The nanoparticles may be metal nanostructures (e.g. silver/gold, nanocubes/nano-octahedra/truncated nanocubes/nano-cuboctahedra/truncated nano-octahedra/nanowires/nano-spheres). The nanoparticles may also be nanowires. The nanoparticles may have a particle size (e.g. diameter for nano-sphere/edge length for other nanostructures mentioned above) of from 40 nm to 400 nm. For example, nanoparticles shaped as nanocubes may have an edge length in the range of 40 nm to 15 130 nm, nanoparticles shaped as nano-octahedra may have an edge length in the range of 200 nm to 400 nm.

[0081] The size distribution in a batch of nanoparticles synthesized from the present method and system is advantageously $\pm 10\%$. For example, if the desired size is 40 nm, the present system and method are able to synthesize nanoparticles with a size 20 distribution of around 40 ± 4 nm.

[0082] As mentioned above, the present system and method involve a process control module. The process control module may include a software to enable dynamic tracking of the optical properties of the nanoparticles, establishing how nanoparticles form and grow in the setup. Through the process control module and having such a software, the 25 composition of the reagents, and hence, the reaction mixture, may be changed during the synthesis process. For example, the process control module may obtain one or more optical spectra of synthesized nanoparticles through the spectroscopy module, determine from the one or more optical spectra whether the properties of the synthesized nanoparticles are acceptable, and control the robotic module to increase, 30 maintain, decrease or terminate reagent dispensing, the frequency and/or absolute time of dispensing reagent, and/or temperature.

[0083] Advantageously, the present nanoparticle synthesis system and method are that the amount, frequency and/or absolute time at which reagents are dispensed can be varied precisely during the reaction process and hence, the reactions can be terminated precisely such that the reactions are configured to reach completion without any reagents wastage.

[0084] The feedback-controlled automated nanoparticle synthesis system can include a software to control the type of liquid dispensing, position of the pump for liquid dispensing, the interval of liquid dispensing, and drawing and mixing of samples. From several rounds of investigations, the Ag precursor may need to be added in 0.5 ml aliquots every minute and the PVP precursor may need to be added in 0.25 ml aliquots, for example at an interval ranging from 5 s to 90 s, for synthesis of Ag nanocubes. That is to say, the PVP precursor may be added, as a non-limiting example, every 5 s. Such interval may range from 5 s to 90 s, 10 s to 90 s, 20 s to 90 s, 30 s to 90 s, 40 s to 90 s, 50 s to 90 s, 60 s to 90 s, 70 s to 90 s, 80 s to 90 s, etc. Such interval may be varied as the reaction progresses. The reaction occurs at 190°C, using 1,5-pentanediol as the reaction solvent in a round bottom flask.

[0085] To create a feedback loop, a continuous reaction monitoring system was developed by using a pump to withdraw reaction mixtures at regular intervals for absorbance measurements. During the synthesis process, the color of the reaction mixture may undergo a series of changes. Such changes may correspond to characteristic emergence and shifts of absorption peaks, which can be measured using the halogen lamp and optical fiber. The absorbance measurements may be recorded on the software of the process control module, and every measurement can be completed in less than 1 s. The process control module, via the software, can then be programmed to terminate the addition of the precursors based on the peak position measured from the samples. Another automated motion controller may be installed to remove the reaction vessel from the oil bath upon reaction termination.

[0086] Traditional systems are neither suitable nor configured to prepare and synthesize Ag nanoparticles, especially for a complex experimental process such as Ag nanocubes. Instead, using the present system and method, an improved yield of 95% for Ag nanocubes with average edge lengths of 116 ± 3 nm was achieved. Such improved higher yield also means that post-synthetic purification steps can be

significantly shortened, by doing away with the need for multiple rounds of vacuum filtration to remove other impurities based on size differences. In addition, the monodispersity of the particle sizes are significantly improved with a standard deviation of less than 3% about the mean. Both the improved high yields and superior size distribution arises from the capability of the present system and method to introduce reagents accurately at the right time without stopping the synthesis reaction, and stopping the reaction on-demand.

[0087] In addition, the present system and method demonstrate the capability of synthesizing Ag nanocubes with edge lengths ranging from about 45 nm to 140 nm.

The growth of Ag nanocubes is a continuous process, which begins from small crystalline seeds of about 30 nm and subsequently grows into cubic nanoparticles. This information was unknown prior to the development of the present system. With the system, aforesaid capability of stopping the reaction at targeted reaction times, based on the appearance of the absorption spectrum, is developed. Both the continuous size tunability and capability to stop reaction to achieve targeted nanocube sizes as demonstrated in the present system and method are not achieved in any traditional systems and method.

[0088] Example 2A: A Non-Limiting Example of the Present System and its Operation

[0089] As can be seen in FIG. 1B (a non-limiting example of the present system), four reagent dispensers (e.g. four liquid dispensing pumps) for reagent/liquid dispensing, sampling, and mixing can be configured. There is also one reaction vessel holder (e.g. reaction flask holder) to control reaction vessel position, height, and rotation. There is a computer-controlled temperature control module to maintain the temperature for nanoparticle synthesis. There is a spectroscopy module (e.g. UV-vis spectrometer using halogen lamp as light source) and optical fiber for signal collection. The system can also include a 30-cuvette track for online sample measurements, one fan to blow dry sampling pump/needle, one power supply to power the system, and one computer (e.g. configured as part of the process control module) to control the entire setup (not shown in picture).

[0090] The computer, as part of the process control module, can be used to operate all movements on the system through a customized LabVIEW-based software, nicknamed Robosoft (see FIG. 2).

[0091] The system can have four pumps. The four pumps can be operable to provide
5 for (i) a timed one-shot addition of AgNO_3 precursor (Ag) – described as pump B, (ii) a timed addition of poly(vinylpyrrolidone) precursor (PVP) – described as pump A, (iii) a timed drawing of reaction mixture and liquid mixing for absorbance measurements – described as pump C, and (iv) addition of solvent for diluting reaction mixture – described as pump D.

10 **[0092] Example 2B: Non-Limiting Example of Present Method**

[0093] Steps for the synthesis of silver nanoparticles are described as follows.

[0094] A typical reaction begins with the powering up of the system and launching of Robosoft software of the process control module (see FIG. 2).

15 [0095] The heating and stirring process on the temperature-controlled setup was started.

[0096] The temperature of the oil bath was ramped up to a preset temperature in the range of 170 - 210°C.

[0097] PVP precursors dissolved in 1,5-pentanediol (PD, 0.01 to 1 g/mL) was loaded into pump A by using the Robosoft interface. The PVP precursor used may have a
20 molecular weight ranging from 10 kg/mol to 1300 kg/mol, 10 kg/mol to 55 kg/mol, 55 kg/mol to 1300 kg/mol, etc. As an example, the PVP used may be 55 kg/mol. Apart from PVP precursor, other polymeric precursor suitable may be used. For the solvent, ethylene glycol and/or diethylene glycol can be used instead of PD. The solvent can be an organic solvent.

25 [0098] Ag precursors dissolved in PD (0.01 to 1 g/mL) was loaded into pump B by using the Robosoft interface. The solvent (e.g. an organic solvent) for dissolving the polymeric precursor can be used to dissolve the metal precursor as well. Non-limiting example of Ag precursors can also include silver trifluoroacetate, for example, to render silver nanocubes. Other suitable silver precursors, which render silver nanocubes, can
30 be used. Other than Ag precursors, the metal precursor can include gold precursors to synthesize gold nanocubes. A non-limiting example can be gold (III) chloride, which

was used to synthesize gold nanocubes using the present system and method. Other suitable gold precursors, which render gold nanocubes, can be used.

[0099] Round-bottomed flasks are mounted onto the reaction flask holders.

[00100] The cuvette rack was loaded with cuvettes.

5 [00101] Pump D can be filled with solvent (e.g. ethanol) during this time through the Robosoft interface.

[00102] The reaction flask with the PD solvent was lowered into the oil bath to kickstart the nanoparticle synthesis process.

10 [00103] Once the temperature stabilized, the reaction begins by pressing the 'Start Process' button on Robosoft.

[00104] Robosoft software of the process control module was used to monitor the UV-vis spectrum until the target resonance peak appears.

[00105] The Robosoft software prompts a if user would like to fill the cuvettes with ethanol, and the number of cuvettes to be filled.

15 [00106] The use can key in the number of cuvettes to be filled.

[00107] After the previous step, the reaction begins with the introduction of PVP precursors (0.25 mL aliquots added, for example, at an interval ranging from 5 s to 90 s). That is to say, the PVP precursor may be added, as a non-limiting example, every 5 s. Such interval may range from 5 s to 90 s, 10 s to 90 s, 20 s to 90 s, 30 s to 90 s, 40 s to 90 s, 50 s to 90 s, 60 s to 90 s, 70 s to 90 s, 80 s to 90 s, etc. Such interval may be varied as the reaction progresses.

[00108] After addition of the first PVP aliquot, pump C was operated to draw 0.1 mL of the reaction mixture.

25 [00109] The reaction mixture can be introduced to the first cuvette on the cuvette rack for UV-vis measurements.

[00110] The reaction mixture can be mixed with ethanol using pump C, through repeated liquid dispensing and drawing.

[00111] The entire process takes approximately 10 s, including the UV-vis measurements.

30 [00112] After addition of the second PVP aliquot, pump B can introduce 0.5 mL of Ag precursors at, for example, at an interval ranging from 30 s to 120 s, 40 s to 120 s, 50

s to 120 s, 60 s to 120 s, 70 s to 120 s, 80 s to 120 s, 90 s to 120 s, 100 s to 120 s, 110 s to 120 s. Such interval may be varied as the reaction progresses.

[00113] The steps from introducing the reaction mixture to the first cuvette for UV-vis measurements to addition of the second PVP aliquot can be repeated over the course of
5 reaction until either the target cycle or target resonance peak position is attained.

[00114] The Robosoft interface can be configured to prompt user to remove the reaction flask from the oil bath, and to introduce a new reaction flask into the oil bath to start a new round of nanoparticle synthesis.

10 **[00115] Example 2C: Configuration/Operation of the Process Control Module (“Robosoft”)**

[00116] The process control module, having the software “Robosoft”, operably configures:

[00117] (i) the positions of all four pumps, ensuring liquid precursors and reaction mixtures can be accurately introduced and withdrawn.

15 [00118] (ii) the positions of the flask holder, to achieve precise heating and positioning of the flask relative to the pumps.

[00119] (iii) number of reaction cycles, which enable continuous precursor addition for the synthesis of nanocubes, cuboctahedra, and octahedra (which require different cycles).

20 [00120] (iv) number of UV-vis measurements to perform, even after target wavelength is attained. Alternatively, precursor addition can stop but the UV-vis sampling measurements can continue (via the ‘Stop Mixing’ button). In this instance, sampling intervals can also be customized (via the ‘Sample every x s’ button). This allows continuous UV-vis data collection under a variety of experimental conditions, and
25 samples can also be collected for subsequent SEM measurements. This set of data allows reconstruction of the kinetics of various experimental conditions and sample the complex reaction space for nanoparticle formation.

[00121] (v) heating temperature and stirring speed of the temperature-controlled heating setup.

30 [00122] (vi) type of reagents, volume of reagents introduced and the interval of addition, which enable synthesis of multiple types of nanoparticles.

[00123] (vii) position precision of pump down to mm-scale, allowing precursors to be added right into the center of the stirring vortex for efficient liquid mixing. In contrast, manual addition is often challenging to control, and sometimes precursors slide down the sides of the reaction flask. Poorer precision might affect reaction outcome.

5 [00124] (viii) height of the flask relative to oil bath can also be controlled to the mm-scale accurately using the Robosoft. Again, this is challenging to achieve with a manual setup. From several runs, it was observed that the height affects different reaction rates. The height may affect the amount of contact between the solvent (e.g. PD) in reaction vessel (in this instance the flask) and the oil bath. A lower height may confer greater
10 contact, which may in turn render better heat transfer and faster reaction rates. Nevertheless, nanocubes can still be produced at various heights.

[00125] Additionally, the process control module, having the software “Robosoft”, can be operably configured to perform automatic spectral analysis, determining the peak positions in real time using algorithmic fitting. For every spectrum generated, the
15 spectrum may first be smoothed using Savitzky-Golay algorithm with a polynomial order of 3, followed by Gaussian peak fitting. If the peak position is below the target position specified by user, reaction continues. If the peak position hits the target position, the process control module (e.g. through the Robosoft software) prompt users if the reaction should be stopped.

20 [00126] **Example 3: Results and Discussion**

[00127] The examples above demonstrated successful synthesis of Ag nanocubes as a proof-of-concept using the automated feedback-controlled nanoparticle synthesis system (FIG. 3). Synthesis of Ag nanocubes was selected because this is one of the most challenging nanoparticle to synthesize via automation, requiring constant
25 precursor additions, and at different volumes. Traditional methods, and even synthesis of Ag nanocubes, do not allow or have significant synthesis difficulty using flow chemistry (a continuous system) to achieve automation.

[00128] Using the present system and method, improved high yields of more than 95% for Ag nanocubes with average edge lengths of 116 ± 3 nm were obtained. Such
30 excellent yield signifies that post-synthetic purification steps can be significantly shortened, by doing away with the need for multiple rounds of vacuum filtration to remove other impurities based on size differences. In addition, the particle sizes are also

highly monodisperse, with a standard deviation of less than 3% about the mean. Both the high yields and superior size distribution arises from the capability of the present system and method to introduce reagents accurately at the right time, and stopping the reaction on-demand. The standard extinction spectrum of Ag nanocubes is shown in
5 FIG. 1A, exhibiting 6 localized surface plasmon resonances (LSPR) (labeled as different modes in the spectrum).

[00129] A comparison of Ag nanocubes synthesized through the present system and human operators was also carried out in the research laboratory, so as to demonstrate the challenge in achieving consistent batch-to-batch output through the manual
10 synthesis as compared to the advantage of streamlining batch-to-batch quality of the nanocubes synthesized by the present system and method. The group of participants in the manual synthesis includes experts who are very familiar with nanocube synthesis.

[00130] From FIG. 4, it can be seen that hand-synthesized Ag nanocubes give rise to a multitude of extinction spectra (left plot), indicating different sizes and qualities of Ag
15 nanocubes made by 5 different users. On the other hand, the five batches of Ag nanocubes synthesized using the present system and method exhibited highly consistent extinction spectra (right plot). All five spectra overlap with each other, indicating that the Ag nanocubes exhibit similar sizes and sharpness. The batch-to-batch variation is evidently larger in the group of expert users (hand-synthesized batch) when compared
20 against the Ag nanocubes made by the present system.

[00131] The superior performance of the present system and method was further demonstrated by requesting a single expert user to perform five sets of reactions to synthesize Ag nanocubes using the present system (FIG. 5). It was observed that manual
25 synthesis gave rise to large fluctuations in the extinction spectra of the synthesized products. This fluctuation indicates clear differences in terms of nanocube purity, nanocube size, and the nanocube's size distribution.

[00132] The setup of the present system advantageously allows collection of a series of samples over the course of the Ag nanocube synthesis process. This is unprecedented and enables us to gain new insights on the kinetics of nanocube formation (FIG. 6A to
30 6D). During the synthesis reaction, it can be seen that the reaction mixture undergoes a series of color changes, from transparent to light yellow to green. The green color also becomes increasingly opaque, and continues to change to beige before finally ending at

a reddish clay color. These color changes also generate corresponding changes in the extinction spectra of the various samples. An initial peak forms at around 400 nm, which undergoes continuous redshift to around 650 nm at the end of the reaction (mode 1 in FIG. 1A). At the same time, the number of localized surface plasmon resonances increases from a single resonance mode to six resonance modes over this period of time. After their spectral emergence, these resonances undergo continuous redshifts as the reaction progresses.

[00133] In addition to characterizing the extinction spectra, we also performed SEM characterization of all the samples isolated from the reaction (FIG. 7). Formation of cube-like nanoparticles was observed as early as 6 mins into the reaction, and the cubes continue to grow until the end of the reaction, at which point the cube grows to an average edge length of 115 ± 5 nm. Such information/observation appears difficult or impossible with traditional synthesis systems and methods. While the color changes are often seen during the reaction process, traditional systems and methods do not demonstrate isolation of the samples and performed comprehensive characterization of these samples during synthesis of the nanoparticles. Because of such in-depth characterization while the synthesis progress, new information regarding the formation and growth kinetics of Ag nanocubes (FIG. 8) can be established. As shown in FIG. 8, the formation and growth of Ag nanocubes follow a sigmoidal growth process.

[00134] More importantly, the use of localized surface plasmon resonances as a rapid and robust approach to monitor the growth of Ag nanocubes has been demonstrated (FIG. 9). Peak positions of all the extinction spectra are extracted from FIG. 5 and plotted against reaction time. From FIG. 9, clear changes in the peak positions of all resonance modes in the extinction spectra can be observed over time. However, to serve as a feedback loop and inform users of the nanocube size at any point in time, there needs to be a correlation between peak shifts and nanocube sizes which the present system and method are able to establish/demonstrate. To examine this correlation, the time-dependent changes in peak positions and nanocube sizes were plotted in the same graph for mode 1 (FIG. 10 left plot).

[00135] FIG. 10 shows that mode 1 changes synchronously with the growth of Ag nanocubes over the course reaction (left plot). The time-dependent variation between peak position and nanocube sizes overlap well. This relationship is further confirmed

through a linear fit in the plot of peak position against particle size, yielding a high linearity value of 0.994 (FIG. 10 right plot).

[00136] Mode 1 is also an ideal candidate to track the formation and growth of Ag nanocubes because it is the first mode to appear in the extinction spectrum, and the largest number of datapoints can be derived from this mode. To further demonstrate the feasibility of the present system and method, the experiments were repeated 4 times, extracting the peak positions of mode 1 and nanocube sizes from the samples collected (FIG. 11).

[00137] The trends in FIG. 11 are consistent with earlier experiments, demonstrating a sigmoidal formation process for Ag nanocubes. This process is characterized by a slower initial incubation period, followed by increased growth rate, before tapering off. The initial incubation period may involve time required for seed nucleation from metallic salt precursors, as well as the etching of twinned seeds before supersaturation is achieved. Thereafter, the growth of single crystalline seeds into nanocubes experiences a rapid size increase process. Once the cubes reach around 100 nm in edge length, the growth process slows down. The reaction conditions are no longer favorable for the rapid and sustained growth of nanocubes.

[00138] It is noted that the present method advantageously enables the formation of nanocubes with sizes ranging from about 40 nm to about 140 nm, using a single set of reaction conditions. The experimental observations to this point involve one set of reaction conditions. The results are promising, demonstrating scalable production of nanocubes (~35 mg per batch or even more than 50 mg per batch) in high yields. The highest achievable purity is more than 95% (example in FIG. 3). This is based on counting 500 particles, and determining the percentage of cubes within this 500 particles. Randomized counting process involving different human analysts is carried out to remove any potential bias.

[00139] The present system and method provide opportunities for the exploration of the multidimensional chemical reactivity space, because various experimental parameters can now be investigated without having to worry about human-related errors that may easily render any study invalid. The present system and method can be expected to uncover ways to synthesize nanoparticles of different shapes and sizes that may be difficult or not possible in traditional systems and methods.

[00140] The present system and method are compatible with use of artificial intelligence to boost materials discovery in the laboratory. Such discovery can directly enable scalable and targeted production of various nanoparticles quickly, arising from the integration of automation with artificial intelligence.

5 [00141] In-depth structure-to-property analyses by investigating both electron microscopic and optical data, collected from 50 reactions, were further carried out. By correlating the electron microscopic characterization of the Ag nanocubes with their extinction spectra, we demonstrate how the extinction spectra can be used to gauge the purity of the Ag nanocubes (FIG. 12). As mentioned in earlier discussion, successful
10 synthesis of Ag nanocubes give rise to multiple well-defined localized surface plasmon resonances (FIG. 1A, FIG. 12, first 3 panels). With decreasing purity (less than 80%), automated spectral peak identification becomes less accurate and lesser peaks are detected, where peak finding function is performed using Origin software. In the situation of a failed reaction, the extinction spectrum becomes broad and featureless
15 (FIG. 12, rightmost image).

[00142] For the 50 batches of reactions, focus was placed on nanocube sizes in the range of 110 – 140 nm. Nanocubes in this size range are most widely employed for diverse applications. In FIG. 13, the positions of modes 1 and 2 against the nanocube sizes were plotted (left and right plots, respectively). Mode 1 corresponds to the dipolar resonance and mode 2 corresponds to the quadrupolar resonance. Both plasmon
20 resonances exhibit a linear correlation with nanocube sizes. As the nanocube size increases from 110 nm to 140 nm, mode 1 redshifts from ~620 nm to ~750 nm whereas mode 2 redshifts from ~500 nm to ~560 nm. This trend enables both plasmon resonances to serve as an indicator of nanocube size.

25 [00143] The FWHM of both modes 1 and 2 can be employed to gauge the purity of Ag nanocubes synthesized, is also demonstrated (FIG. 14 – left and right plots, respectively). FWHM are obtained by a Gaussian fit of the respective plasmon resonance in the Origin software. It was observed that increasing Ag nanocube purity decreases the FWHM of modes 1 and 2, i.e. the resonances become narrower. For mode
30 1, the FWHM decreases from ~290 nm to ~230 nm as the purity increases from 60 % to > 90 %. For mode 2, the FWHM decreases from ~170 nm to ~105 nm as the purity increases from 60 % to > 90 %.

[00144] In addition to FWHM, the intensity ratio between modes 1 and 2 can be used to predict the purity of the Ag nanocubes synthesized was highlighted (FIG. 15). The mode 2/mode 1 ratio increases from ~1.05 to ~1.25 as the purity of the Ag nanocubes increases from 60 % to > 90 %. Experimentally, mode 2 becomes significantly more pronounced and sharper for high purity Ag nanocubes relative to mode 1, as shown in Figures 4 and 13. Both FWHM and mode 2/mode 1 ratio can be used in conjunction with each other to achieve greater predictive accuracies over the purity of the Ag nanocubes.

[00145] **Example 4: Commercial and Potential Applications**

[00146] The present system and method provides for scalable production of various nanoparticles, including Ag nanoparticles of different shapes and sizes, and other metallic nanoparticles such as gold (Au). The nanoparticles synthesized exhibited consistently narrow size distribution across different batches, and can be easily prepared using the present system on demand. The system's and method's scalability allows us to create a variety of downstream nanoparticle-based platforms with potential applications in sensing and diagnostics, energy generation, and anti-wetting surfaces. Given the high market demand for Ag nanoparticles, it is expected that the high-quality Ag nanoparticles produced by the present system and method stand out against existing Ag nanoparticles in the market, rapidly gain traction and appeal among global users. The present method provides not just high yields, but also high quantity (e.g. more than 50 mg per pot), ongoing size and shape tunability of the nanoparticles as synthesis reaction progresses.

[00147] While the present disclosure has been particularly shown and described with reference to specific embodiments, it should be understood by those skilled in the art that various changes in form and detail may be made therein without departing from the spirit and scope of the present disclosure as defined by the appended claims. The scope of the present disclosure is thus indicated by the appended claims and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced.

CLAIMS

1. A system operable to synthesize nanoparticles, the system comprising:
 - a robotic module comprising:
 - a temperature controller;
 - one or more dispensers operable to dispense different reagents; and
 - an extraction device;
 - a reaction vessel configured to receive the different reagents directly from the one or more dispensers to form a reaction mixture from which the nanoparticles are synthesized; and
 - a process control module operably coupled to the robotic module and a spectroscopy module, wherein the process control module configures:
 - the extraction device to withdraw a sample of the reaction mixture from the reaction vessel at an interval as the reaction mixture progresses and to transfer the sample into one or more cuvettes of the spectroscopy module, and
 - the spectroscopy module to generate spectral data based on an optical property of the sample and from the spectral data identify a condition which serves as a feedback to the process control module to configure:
 - the temperature controller to change or maintain temperature of the reaction mixture as the reaction mixture progresses,
 - the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction mixture as the reaction mixture progresses, and
 - the extraction device to change or maintain the interval for withdrawing further samples of the reaction mixture to provide the feedback continuously to have the process control module configure the temperature controller, the one or more dispensers, and the extraction device, in aforesaid manner until synthesis of the nanoparticles in the reaction mixture is completed.

2. The system of claim 1, wherein the robotic module further comprises a heating stage for a heating vessel to be arranged thereon, wherein the heating stage comprises a heating element, wherein the heating element is operably coupled to the temperature controller to adjust heat provided from the heating element to the reaction mixture.
3. The system of claim 2, wherein the heating vessel houses an oil bath.
4. The system of any one of claims 1 to 3, wherein the robotic module comprises a rotatably adjustable receptacle to position the reaction vessel in the heating vessel.
5. The system of any one of claims 1 to 4, wherein the one or more dispenser comprises:
 - one dispenser to dispense a solvent;
 - one dispenser to dispense a polymeric precursor; and
 - one dispenser to dispense a metal precursor.
6. The system of claim 5, wherein the one dispenser for dispensing the solvent is operable to dispense the solvent into the one or more cuvettes.
7. The system of any one of claims 1 to 6, wherein the extraction device comprises a suction pump connected to a tube, and the extraction device is operably coupled to a fan which is operable to dry the tube.
8. The system of any one of claims 1 to 7, wherein the spectroscopy module comprises:
 - a rack to house the one or more cuvettes;
 - a light source configured to project light toward the one or more cuvettes;
 - a detector configured to received light projected through the sample in the one or more cuvettes; and
 - a data acquisition module operably coupled to the process control module, wherein the data acquisition module converts light received by the detector into spectral data.

9. The system of any one of claims 1 to 8, wherein the process control module is operable to have each of the one or more dispensers dispense the different reagents in a dropwise or single-shot manner.

10. A method of synthesizing nanoparticles using the system of any one of claims 1 to 9, the method comprising:

- providing a reaction mixture from which the nanoparticles are synthesized directly in the reaction vessel;

- having the process control module configure the extraction device to withdraw a sample of the reaction mixture from the reaction vessel at an interval as the reaction mixture progresses and to transfer the sample into one or more cuvettes of the spectroscopy module;

- generating spectral data from the spectroscopy module based on an optical property of the sample;

- identifying from the spectral data a condition which serves as a feedback to the process control module; and

- having the process control module, based on the feedback, configure:

- the temperature controller to change or maintain temperature of the reaction mixture as the reaction mixture progresses,

- the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction mixture as the reaction mixture progresses, and

- the extraction device to change or maintain the interval for withdrawing further samples of the reaction mixture to provide the feedback continuously to have the process control module configure the temperature controller, the one or more dispensers, and the extraction device, in aforesaid manner until synthesis of the nanoparticles in the reaction mixture is completed.

11. The method of claim 10, wherein prior to providing the reaction mixture, further comprises providing the oil bath in a heating vessel and having the robotic module operably configure a rotatably adjustable receptacle to position the reaction vessel in the heating vessel.

12. The method of claim 11, wherein prior to providing the reaction mixture, further comprises heating the oil bath to 150°C to 250°C.

13. The method of any one of claims 10 to 12, wherein providing the reaction mixture comprises operating the one or more dispensers to dispense each different reagent at one or more specified times directly into the reaction vessel, wherein operating the one or more dispensers comprises:

having one dispenser to dispense a solvent;

having one dispenser to dispense a polymeric precursor; and

having one dispenser to dispense a metal precursor.

14. The method of claim 13, wherein having the one dispenser to dispense the polymeric precursor comprises dissolving the polymeric precursor in an organic solvent.

15. The method of claim 13 or 14, wherein operating the one or more dispensers to dispense the different reagents comprises:

adding the polymeric precursor before adding the metal precursor but after loading the solvent into the reaction vessel.

16. The method of any one claims 10 to 15, wherein having the process control module configure the extraction device to withdraw the sample comprises:

operating the suction pump to withdraw a sample of the reaction mixture via a tube positioned in reaction vessel and having the suction pump deliver the sample into the one or more cuvettes; and

operating the fan coupled to the extraction device to dry the tube after the extraction device delivers the sample.

17. The method of any one of claims 10 to 16, wherein generating spectral data from the spectroscopy module based on an optical property of the sample comprises:

projecting a light toward the one or more cuvettes;

having the detector configured to receive the light projected through the sample in the one or more cuvettes; and

having the data acquisition module convert the light received by the detector into spectral data.

18. The method of any one of claims 10 to 17, wherein having the process control module, based on the feedback, configure the one or more dispensers to change or maintain a frequency and/or time and/or an amount of each different reagent dispensed into the reaction mixture as the reaction mixture progresses comprises:

having the process control module configure each of the one or more dispensers to dispense the different reagents in a dropwise or single-shot manner.

19. The method of any one of claims 10 to 18, wherein the optical property comprises color of the sample.

20. The method of any one of claims 10 to 19, wherein identifying from the spectral data the condition which serves as the feedback to the process control module comprises:

identifying a first wavelength and/or a second wavelength which correspond to a first peak and/or a second peak in the spectral data, respectively; and/or

identifying any change in the first wavelength and/or second wavelength from the further samples as the reaction mixture progresses to determine completion of synthesis of the nanoparticles in the reaction mixture.