AUTONOMOUS EXPERIMENTAL DESIGN SYSTEM FOR AUTOMATED MATERIAL ANALYSIS

Abstract: Embodiments generally relate to an autonomous system and method for automated material analysis. In some embodiments, the system comprises: at least one processor; memory that is accessible to the processor or processors; a user interface to receive input parameters for automated material testing; and a material testing interface to allow the processor or processors to communicate with a robotic material testing system. The program code of the system comprises an experimental design module configured to automatically design the execution of an experiment based on the received input parameters. The experimental design module transmits execution instructions to the robotic material testing system via the material testing interface.
"Autonomous experimental design system for automated material analysis"

Technical Field

[0001] Embodiments relate generally to systems for automated material analysis. Some embodiments particularly relate to systems employing autonomous experimental design for conducting the automated material analysis.

Background

[0002] Materials discovery is a time consuming and costly endeavour, which, when combined with validation and quality assurance tasks, often results in misalignments between research and development cycles and manufacturing cycles. This undermines the competitive advantage that new materials and technologies bring, as they are unable to be utilised in current or next-generation products.

[0003] Further, human input into experimental design has limitations. If the need for human input into experimental design can be minimised, then this may limit inherent human bias in certain experimental testing procedures. In some instances, expert "intuition" can be counterproductive, through the dismissal of material or chemical candidates without testing, for a variety reasons which may include: unfamiliarity with the chemistry, time constraints, financial constraints or personal arrogance or ignorance.

[0004] It is desired to address or ameliorate one or more shortcomings or disadvantages of prior experimental design or execution techniques, or to at least provide a useful alternative thereto.

[0005] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.
In this specification, a statement that an element may be "at least one of a list of options is to be understood that the element may be any one of the listed options, or may be any combination of two or more of the listed options.

Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present disclosure as it existed before the priority date of each claim of this application.

Summary

Some embodiments relate to an autonomous experimental design system for automated material analysis, the system comprising:

at least one processor;

memory accessible to the at least one processor and storing executable program code;

a user interface to receive input parameters for the automated material analysis; and

a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

wherein the program code comprises an experimental design module configured to automatically design execution of an experiment based on received input parameters as part of the automated material analysis and to transmit execution instructions to the robotic material testing system via the material testing interface.

The system may further comprise the robotic material testing system. The robotic material testing system may comprise an electrochemical testing system.
The experimental design module may be configured to query a data store for past experimental data that is relevant to a planned experiment and to design execution of the planned experiment based at least in part on data returned by the query.

The planned experiment may comprise a material discovery experiment and the program code comprises a material discovery module configured to control execution of the material discovery experiment.

Designing execution of the experiment by the experimental design module may comprise determining whether to conduct a computer simulation of at least part of the experiment or to conduct a simulated test as a pre-cursor to the experiment.

The experimental design module may comprise a plurality of experiment planning sub-modules, each of which is configured to plan a specific type of experiment.

The program code may further comprise a plurality of material analysis modules, each of which is configured to interface with the robotic material testing system to control execution of a specific type of experiment.

The experiment may comprise one of:

- an alternative molecule searching experiment;
- a material discovery experiment;
- a material operational window determination experiment; and
- a critical concentration determination experiment.

The experiment may be a first type of material analysis experiment and the experimental design module may be configured to automatically design execution of a second experiment of a second type of material analysis experiment that is of a
different type from the first type. The second experiment may be designed to be conducted based on data received from conduct of the first experiment. The first type of experiment may be a critical concentration determination experiment, for example. The second type of experiment may be an operational window determination experiment, for example.

[0017] The experiment may be a first type of material analysis experiment and the experimental design module may be configured to automatically design execution of a second experiment of the first type of material analysis experiment based on data received from conduct of the first experiment.

[0018] The experimental design module may be configured to receive experimental results from the robotic material testing system via the material testing interface and to store the experimental results in a data store accessible to the experimental design module.

[0019] Some embodiments relate to an autonomous experimental design system for automated material analysis, the system comprising:

- at least one processor;

- memory accessible to the at least one processor and storing executable program code;

- a user interface to receive input parameters for the automated material analysis; and

- a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

wherein the program code comprises a material discovery module configured to cooperate with an experimental design module to automatically design a material discovery experiment based on received input parameters and to transmit execution
instructions to the robotic material testing system via the material testing interface for
performing the material discovery experiment.

[0020] Some embodiments relate to an autonomous experimental design system for
automated material analysis, the system comprising:

at least one processor;

memory accessible to the at least one processor and storing executable
program code;

a user interface to receive input parameters for the automated material
analysis; and

a material testing interface to allow the at least one processor to communicate
with a robotic material testing system;

wherein the program code comprises a critical concentration determination
module configured cooperate with an experimental design module to automatically
design a critical concentration determination experiment based on received input
parameters and to transmit execution instructions to the robotic material testing system
via the material testing interface for performing the critical concentration determination
experiment.

[0021] The system may further comprise an alternative molecule searching module
configured to cooperate with the material discovery module for design of a material
discovery experiment. The alternative molecule searching module may be configured to
receive a molecule specification from the material discovery module and to search for
alternative molecules having features that at least satisfy the molecule specification.

[0022] The alternative molecule searching module may be further configured to rank
molecules identified in the search based on quantitative structure-activity relationship
(QSAR) descriptors identified in the search.
[0023] The experimental design module may be configured to design an in silico
experiment as part of designing a material discovery experiment.

[0024] The critical concentration determination module may be further configured to
process received results of the critical concentration determination experiment using a
defined metric of worth to identify best test results from conduct of the critical
concentration determination experiment. The critical concentration determination
module may be configured to cooperate with the experimental design module to design
a new critical concentration determination experiment to probe an immediate region
around one or more of the best test results to validate previous test results or determine
a new best test result.

[0025] Some embodiments relate to an autonomous experimental design system for
automated material analysis, the system comprising:

- at least one processor;

- memory accessible to the at least one processor and storing executable
  program code;

- a user interface to receive input parameters for the automated material
  analysis; and

- a material testing interface to allow the at least one processor to communicate
  with a robotic material testing system;

wherein the program code comprises an operational window determination
module configured cooperate with an experimental design module to automatically
design an operational window determination experiment based on received input
parameters and to transmit execution instructions to the robotic material testing system
via the material testing interface for performing the operational window determination
experiment.
Some embodiments relate to an autonomous experimental design system for automated material analysis, the system comprising:

- at least one processor;
- memory accessible to the at least one processor and storing executable program code;
- a user interface to receive input parameters for the automated material analysis; and
- a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

wherein the program code is configured to:

- generate a chemical property hypothesis based on at least one data source relating to chemical properties,

- design at least one experiment to test the chemical property hypothesis using an experimental design module,

- transmit execution instructions to the robotic material testing system via the material testing interface to test the chemical property hypothesis, and

- based on received results of the testing, validate or invalidate the chemical property hypothesis.

Some embodiments relate to a computer implemented method for automated material analysis, comprising:

- receiving input parameters for the automated material analysis;

- automatically designing execution of an experiment based on received input parameters; and
transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the experiment.

[0028] The receiving, designing and transmitting may be performed by an automated material analysis system that is separate from the robotic material testing system.

[0029] Some embodiments relate to a computer implemented method for automated material discovery, comprising:

   receiving input parameters for the automated material discovery;

   automatically executing a material discovery module configured to cooperate with an experimental design module to automatically design a material discovery experiment based on received input parameters; and

   transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the automated material discovery experiment.

[0030] Some embodiments relate to a computer implemented method for critical concentration determination, comprising:

   receiving input parameters for the critical concentration determination;

   automatically executing a critical concentration determination module configured cooperate with an experimental design module to automatically design a critical concentration determination experiment based on received input parameters; and

   transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the critical concentration determination experiment.
Some embodiments relate to a computer implemented method for operational window determination, comprising:

- receiving input parameters for the operational window determination;

- automatically executing a operational window determination module configured cooperate with an experimental design module to automatically design an operational window determination experiment based on received input parameters; and

- transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the operational window determination experiment.

Some embodiments relate to a computer implemented method for automated material analysis, comprising:

- receiving input parameters for the automated material analysis;

- autonomously generating a chemical property hypothesis based on at least one data source relating to chemical properties;

- autonomously designing at least one experiment to test the chemical property hypothesis using an experimental design module;

- transmitting execution instructions to a robotic material testing system via a material testing interface to test the chemical property hypothesis; and

- based on results of the testing received via the material testing interface, validate or invalidate the chemical property hypothesis.
Brief Description of Drawings

[0033] Embodiments are described in further detail below, by way of example and with reference to the accompanying drawings, in which:

[0034] Figure 1 is a schematic block diagram of a robotic material testing system forming part of some embodiments;

[0035] Figure 2 is a block diagram of a computer system forming part of the robotic material testing system of Figure 1;

[0036] Figure 3 is a block diagram of a system for automated material analysis according to some embodiments;

[0037] Figure 4 is a schematic illustration of interactions between modules of the system of Figure 3;

[0038] Figure 5 is flowchart of a first part of a method of automated experimental design according to some embodiments;

[0039] Figure 6 is flowchart of a second part of a method of automated experimental design according to some embodiments;

[0040] Figure 7 is a flowchart of a method of critical concentration determination according to some embodiments;

[0041] Figure 8A is a plot of test results of an example experiment showing critical inhibitor concentration vs corrosion current;

[0042] Figure 8B is an example plot similar to Figure 8A to illustrate testing to probe an immediate region around a data point to find a critical inhibitor concentration;
[0043] Figure 9 is a schematic illustration of a first testing scenario for determining a critical concentration;

[0044] Figure 10 is a schematic illustration of a second testing scenario for determining a critical concentration;

[0045] Figure 11 is a schematic illustration of a third testing scenario for determining a critical concentration;

[0046] Figure 12 is a flowchart of a first part of a method of operational window determination according to some embodiments;

[0047] Figure 13 is a flowchart of a second part of a method of operational window determination according to some embodiments;

[0048] Figure 14 is a plot of test results of an example experiment showing absolute current density measured in a sample material vs pH value;

[0049] Figure 15 is an example plot similar to Figure 14 to illustrate testing to determine an optimal operational window for the sample material;

[0050] Figure 16 is an illustration of an example hypothesis test;

[0051] Figure 17 is a flowchart of a first part of a method of automated material discovery according to some embodiments;

[0052] Figure 18 is a flowchart of a second part of a method of automated material discovery according to some embodiments;

[0053] Figure 19 is a flowchart of a third part of a method of automated material discovery according to some embodiments;
Figure 20 is an illustration of an example application of a fitness function to test an automatically generated hypothesis;

Figure 21 is a flowchart of a method of simulation applied to automated material discovery according to some embodiments;

Figure 22 is a schematic illustration of an example searching methodology for use in conjunction with automated hypothesis generation;

Figure 23 is a first part of a flowchart of a method of automated alternative molecule searching according to some embodiments;

Figure 24 is a second part of a flowchart of a method of automated alternative molecule searching according to some embodiments;

Figure 25 is a third part of a flowchart of a method of automated alternative molecule searching according to some embodiments; and

Figure 26 is block diagram of a system for material analysis comprising more than one of the robotic material testing systems of Figure 1.

**Detailed Description**

Embodiments relate generally to systems for automated material analysis. Some embodiments particularly relate to systems employing autonomous experimental design for conducting the automated material analysis.

Co-owned International Patent Application No. PCT/AU2015/050834, filed 23 December 2015 and entitled "Electrochemical testing system" (the '834 application), describes an automated high throughput robotic electrochemical testing system. The entire contents of the '834 application is expressly incorporated herein by reference. The present application describes an automated material analysis system that can include the robotic electrochemical testing system described in the '834 application as
one example of a robotic material analysis system that can be used in conjunction with embodiments described herein.

[0063] Figure 1 is a block diagram of a system 10 described in the '834 application. Figure 1 shows generally an electrochemical testing system 10 for testing work pieces or other materials or substances held in a plurality of testing wells, exemplary ones of which are referenced 12, 14 and 16 in this figure. The number of testing wells is only limited by practical consideration, but may comprise at least 5 testing wells, preferably at least 10 testing wells, more preferably at least 50 testing wells and even more preferably at least 100 testing wells. The testing wells 12 to 16 are each capable of holding a work piece, material or substance to be tested and forming a contained volume into which a testing media or electrolyte, such as a suitable fluid or gel, is introduced and brought into contact with the work piece, material or substance.

[0064] The work pieces or materials may include one or more of: intercalating materials, corrosion inhibiting materials, porous materials, technical ceramics, supported or unsupported thin films, foils, membranes or pellicles, proton conducting membranes, biologically active samples, gums, gels, hydrogels, aerogels, xerogels, catalytic materials, as well as catalytic support materials, materials used in the study of artificial photosynthesis, photocatalytic materials, electrochromic materials, switchable or responsive coatings, natural and synthetic rubbers, functional coatings or other relevant types or classes of materials.

[0065] The electrochemical testing system 10 includes a sensing head 18 for securing one or more sensing elements, such as one or more electrodes or ion-selective probes. One or more sensing elements may be adapted to form part of an electrochemical circuit, together with the testing media in each of the testing wells 12 to 16, the work piece itself and a working electrode lead that makes contact with the work piece held within a relevant well. In such an arrangement, the work piece effectively becomes the working electrode of the electrochemical testing system 10. It will be appreciated that not every sensing element need form part of an electrochemical testing circuit. For example, one or more sensors/probes (e.g. pH, spectroscopic, hyperspectral, optical)
may be secured to the sensing head 18 for *in situ* data collection of important and/or complimentary data useful to an experimenter.

[0066] A number of sensing heads each supporting one or more sensing elements may be prepared in advance. The various sensing heads may be interchangeable to facilitate the rapid testing of work pieces.

[0067] At least one sensing head may be adapted to secure one or more non-electrochemical sensing elements to perform non-electrochemical testing and measure one or more non-electrochemical properties such as compositional characteristics of the media and/or work piece (e.g. electrode), such as moisture content, degradation by-products and migrated species.

[0068] For example, the non-electrochemical sensing/analysis elements may include a Raman spectroscopic system/probe or a fibre-optic camera, ion selective electrodes, solid-state physical or chemical sensors, macroscopic imaging systems, microscopic imaging systems, NIR imaging, UV-Vis systems, FTIR systems, general measurement/analysis techniques and other systems considered state-of-the-art. The electrochemical testing system 10 also includes a media delivery system 20 for selectively delivering fluid, gel or other testing media into the testing wells 12 to 16. The media delivery system 20 notably includes exemplary media delivery tubing 22 running between one or more media storage units (not shown) and one or more media delivery output nozzles which will be explained in relation to Figure 5. One or more pump units 24 are provided as part of the media delivery system 20 to selectively cause delivery of the media along the tubing 22 and out of the nozzles. The media delivery system 20 is adapted to handle volumes of liquid in the range of 1 nL to 1 L or above.

[0069] In some embodiments, the media is in a solid form (e.g. solid electrolyte), such as a film or composite material (e.g. ion conducting polymers) The media delivery system is such embodiments preferably comprises a robotic "pick and place" mechanism which transfers pre-cut solid electrolytes into the wells. An alternative mechanism is deliver of the solid electrolyte as a film covering the wells and then
cutting (mechanically or via laser) a proportion of the film above the well, such that the film portion is deposited into the well after cutting. It would be understood that other variations of the delivery of the media would be available to those skilled in the art.

[0070] A programmable controller 26 is configured to control operation of the media delivery system 20 including controlling operation of the pump units 24. As the media delivery system 20 is controlled by the programmable controller 26, it is possible to actively control the dosage and desired chemical delivery for each testing well 12 to 16.

[0071] In various embodiments of the invention, the pump units 24 may be either analogue or digitally controlled and may include but are not limited to syringe pumps, diaphragm pumps, peristaltic pumps, mechanical pumps, impellor pumps, as well as conventional pumping, dosage and metering techniques or solutions.

[0072] Connections between the pump units 24 and the micro-fluidic tubing or other piping is preferably chemically resistant and leak proof.

[0073] Although not depicted in Figure 1, solenoids may also be included in the fluid path 22 to arrest, or redirect media flow when used in conjunction with a manifold suitable for fluid or viscous liquids. Inline mixing chambers may also be included in the fluid path. The nozzles or other outputs from the tubing 22 connected to the pump units may either be terminated individually at the sensing head 18 as shown in Figure 1, or combined together upstream in a fluid path to ensure adequate mixing of solutions, gels or other media. Moreover, whilst Figure 1 depicts the mounting of the nozzles at the sensing head 18, it is also possible to provide a separate media delivery system operating independently of and physically apart from the sensing head 18.

[0074] The electrochemical testing system 10 also includes a motion control system 28 for controlling relative movement of the sensing head 18 and the testing wells 12 to 16 so that one or more sensing elements mounted to the sensing head 18 are selectively brought into contact with testing media held within a selected one of the testing wells 12 to 16 in which a selected work piece to be tested is held. The motion control system
28 may take a number of forms, but in one or more embodiments includes a servo or other drive mechanism 30 for driving one or both of the testing wells 12 to 16 and the sensing head 18 along three orthogonal axes.

[0075] In the embodiment depicted in Figure 1, the servo mechanism 30 includes a servo motor 32 driving a spindle 34 which in turn connects to a ball screw 36. Operation of the servo motor 32 causes rotation of the ball screw 36 about its longitudinal axis. A coupling device 38 interconnects the sensing head 18 and the ball screw 36 so that the rotational movement of the ball screw 36 is translated into linear movement of the coupling device 38. The arrangement depicted in Figure 1 is replicated along X, Y and Z orthogonal axes in order to provide three dimensional movement of the sensing head 18.

[0076] An encoder 40 is coupled to the servo motor 32 and provides a series of pulses to the servo control circuit 42 to enable a determination of the angular position of the spindle 34. In addition, an optical scale 44 converts linear movement of the coupling device 38 in the X, Y or Z axis into pulses to enable the servo control circuit 42 to determine the linear position of the coupling device 38 along each of the three orthogonal axes. The servo motor 32 is controlled by signals from a servo amplifier 46 which is in turn controlled by the servo control circuit.

[0077] The servo mechanism 38 is merely one example of an arrangement for selective positioning of the sensing head with respect to the testing wells. Other embodiments may include a combination of components conventionally used in servo mechanisms, such as transducers, stepper motors, actuators and servos. In some embodiments, relative positioning of the sensing head 18 and the testing wells 12 to 16 may be provided along three or more axes of movement.

[0078] In use, the servo control circuit 42, acting under control of the programmable controller 26, typically causes the sensing head 18 to be positioned over a relevant testing well 12 to 16. The sensing head 18 is then lowered into the relevant testing well, and reagents, fluid or other testing media is dispensed into (or sometimes
aspirated from) the relevant testing well as required. A testing sequence then begins, and after conclusion the sensor head is retracted from the well. The sensor head 18 may then be moved by the servo control circuit 42 to a cleaning station 48 where the sensor head 18 is decontaminated with de-ionised water or any appropriate fluid/solvent/chemical/gas, etc. The electrochemical testing system 10 is then ready to begin the next step.

[0079] A variety of reagents, fluid or other testing media can be dispensed into the testing wells, such as electrolytes, ionic liquids, solvents, stabilisation agents and corrosion inhibitors. Examples of the testing media or electrolyte that may be used are listed in paragraphs 18 to 75 of EP1365463. Examples of electrode materials which may form part of the electrochemical testing system are listed in paragraphs 70 to 94 of that document.

[0080] In some embodiments, individual electrolyte components can be directly deposited into the wells. This is advantageous in regard to reducing contamination, including cross contamination, degradation (e.g. oxidation) and minimising wastage. The open cell structure of the testing wells also facilitates the dosing of highly viscous materials (e.g. ionic liquids) and enables dosing pipes to be heated to facilitate flow.

[0081] Moreover, while it is possible to pre-dispense liquids before testing, the system 10 facilitates on-demand dosing, thus mitigating issues of evaporation during long testing cycles which would typically range from 3 to 7 days.

[0082] To complete the electrochemical circuit which is necessary to perform electrochemical measurements of the work piece, each testing well is electrically addressable and electrically and physically isolated from all other testing wells. This prevents the marring of electrochemical measurements by parasitic or concurrent chemicals/mechanical/electrochemical processes that would occur if testing occurred on a single work piece only.
Utilising individual work pieces rather than a larger approximate sample means that individual manufactured components can also be tested. Some examples of manufactured samples could include: screws, nuts, bolts, washers, metal coupons, enclosures, wire, coils, cylinders, vessels, panelling, bearings, capsules, containers, shielding, etc.

In an exemplary implementation, the electrochemical testing system 10 includes at least one electrochemical measurement instrument, such as a potentiostat 182 for example, having inputs connected to the working electrode and one or more of the sensing elements (in this case both the reference electrode and counter electrode). The potentiostat 182 also includes an output connected to measurement recording apparatus, which in this case is embodied by the programmable controller 26 in conjunction with the database 50 shown in Figure 1.

The potentiostat 182 is one example of a device that can measure the voltage difference between a working electrode and a reference electrode in an electrochemical cell, however a variety of other probes, sensors and instruments can be used to measure a range of electrochemical properties.

To establish an electrical/electronic circuit between one or more instruments, such as the potentiostat 182, a galvanostat, other scientific/analytical measurement instrument(s) or data logging device(s), and a testing board containing the wells 12 to 16, many connections can conveniently be multiplexed into a single connection by circuitry, such as a multiplexer 184, that connects the working electrode of a selected testing well to the electrochemical testing circuit. Conventional multiplexers, relay arrays (for example, reed, mechanical, micro, etc.) or other single switching/shunting technologies can be employed.

In other embodiments, a bus topology network may be used in place of the multiplexer 184 to simplify circuit design. In such a network, each instrument would be connected to a single cable or backbone and individually addressable on that backbone by the programmable controller 26.
[0088] Addressing of the individual testing wells is carried out by the programmable controller 26. The sensors, electrodes and other devices residing within the testing head 18 (as a stand-alone unit, or as part of an interchangeable arrangement) can be directly wired into testing/analytic instrumentation.

[0089] Alternatively, electrical connection to the reference and counter electrodes, pH probe or other attached sensors/probes can occur via multiple single-core or several multi-core cables/wiring to one or more patch panels located near the motion control system 28. Such panels allow for the rapid connection of instrumentation and power sources to sensors, electrodes, probes, motors, light sources or any utilised attachment.

[0090] It is also possible to use wireless or optical transmission in lieu of conductive wiring to achieve the same functionality/connectivity. It is also possible to use a bus connection topology to eliminate the need for electrically individually addressable testing wells. This eliminates the need for a multiplexing system, thus simplifying the system design.

[0091] Operation of the servo mechanism 30, electrical testing apparatus 180, media delivery system 20 and other elements of the electrochemical testing system 10 is achieved by the programmable controller 26. In that regard, data from connected instruments, pumps and ancillary devices is captured by the programmable controller 26 and stored in the data base 50. A graphical user interface 52 is provided to enable an operator to set up a testing routine, control movement of the motion control system, analyse data and provide real time output of events, including error messages and take like actions. Data is stored in the database 50 on a per-experiment basis, with all variables such as inputs, outputs and time stamps recorded in the database 50.

[0092] The graphic user interface 52 enables individual samples to be electronically registered by an operator with a unique sample ID and material ID. In that regard, barcodes, RFID tags or other machine readable identifiers can be applied to individual samples, and read by a manual operable tag/code reader or the like. Calibration or re-zeroing and positioning of the motion control system 28 can also be performed by a
user. The graphic user interface 52 can also enable an operator to specify parameters of media delivery system components such as flow rate, allow manual definition of what volume of which chemical is to be dispensed in any given testing well, enable users a selection of scan settings, testing protocols etc, as well as a variety of other user operable functionality that may be programmed in to the programmable controller 26.

[0093] The programmable controller 26 and graphic user interface 52, as well as various other elements of the electrochemical testing system 10, may be provided by one or more computer systems capable of carrying out the above described functionality. An example of such a computer system is depicted in Figure 2 as computer system 200. The computer system 200 includes one or more processors, such as the processor 202. The computer system may include a display interface 204 that forwards graphics, text and other data from a communication infrastructure 206 or display to a display unit 208. The computer system 200 may also include a main memory 210, preferably random access memory, and may also include a secondary memory 212.

[0094] The secondary memory 212 may include, for example, a hard disc drive 214, or optical disk drive or the like. A removable storage drive 216 reads from and/or writes to the removable storage unit 218 in a well-known manner. The removable storage unit 218 represents an optical disc, CD, DVD or like data storage device.

[0095] The removable storage unit 182 includes a computer usable storage medium including a non-volatile memory having stored therein computer software in the form of a series of instructions to cause the processor 202 to carry out desired functionality. In alternative embodiments, the secondary memory 212 may include other similar means for allowing computer programs or instructions to be loaded into the computer system 200. Such means may include, for example, a removable storage unit 220 and corresponding interface 222.

[0096] The computer system 200 may also include a communications interface 224. The communications interface 224 allows software and data to be transferred between
the computer system 200 and external devices, such as an automated material analysis system 310 (Figure 3). Examples of the communication interface may include a modem, network interface, communications port. Software and data transfer via the communications interface 224 are in the form of signals which may be electro-magnetic, electronic, optical or other signals capable of being received by the communications interface 224. The signals are provided to the communication interface 224 via a communications path 226 such as a wire, cable, fibre optics, phone line, cellular phone link, radio frequency or other communication channel, including the communications bus 54 depicted in Figure 1.

[0097] Computer system 200 is intended to encompass arrangements that are less complex than the computer system 200 as shown in Figure 2, including one or a combination of microcontrollers, microprocessors, digital signal processors or the like.

[0098] Embodiments described herein are primarily concerned with computer-aided systems 300 in which the robotic material testing system (RMTS) 10 assists an automated material analysis system (AMAS) 310 to conduct material analysis experiments. AMAS 310 may form part of computer system 200 or may be separate therefrom. If AMAS 310 is separate from computer system 200, then the two systems are configured to communicate via the communications interface 224 and materials testing interface 335 (Figure 3). RMTS receives materials 305, such as solid and liquid materials for use in the conduct of specific experiments. Particular embodiments relate to a device/system or collection of devices/systems (in hardware and/or software) which enables the automated material analysis system 310 to perform one or more of the following tasks/procedures without human intervention or decision making required (other than some basic equipment and experimental setup parameters): material optimisation through alternative molecule searching; material discovery; operational window determination; and critical concentration determination. These procedures are governed in part by program code modules stored in memory 325 of the automated material analysis system 310.
The computer-aided system 300 comprises the AMAS 310, the RMTS 10, the data store 50 storing robotic experimental test data, a further data store 313 accessible to the AMAS 310 and external data sources 312 and/or external servers 314 (providing cloud computing services, high performance computational resources, accelerated computing services, etc.) accessible to the AMAS 310 over a network 311. Network 311 may include a public or private network or a combination of such networks. Further, a client device 312 may be part of system 300 to allow remote interaction and/or configuration of the AMAS 310.

The AMAS 310 comprises at least one processing device 315 (referenced herein as "processor 315" for convenience) cooperating with suitable user interface components and peripherals 320 to allow user access and configuration. Memory 325 is accessible to the processor 315 and is non-volatile. Memory 325 may not be co-located with processor 315. Memory 325 may include any suitable program code storage medium or media and comprises a series of program code modules to give effect to or underpin the functionality and processes described herein. Such program code modules include an autonomous experimental design module (AEDM) 330, an alternative molecule searching module 340, a material discovery module 350, an operation window determination module 360 and a critical concentration determination module 370. Such code modules further include an interface module 335 to act as a material testing interface in communication with the RMTS 10 directly or over a network connection, for example via a public or private network or a combination of such networks.

In one example application, the AMAS 310 may perform material analysis for the purposes of battery electrolyte formulation optimisation, which includes solving the high dimensional problem of commercial battery electrolyte formulation which may include the following constituent chemical components: solvents, lithium salts, ionic liquids, redox shuttles, scavenger molecules. The optimisation may be weighted towards a specific outcome, for example electrochemical operating window, cell voltage.
In another example application, the AMAS 310 may perform material analysis for the purposes of battery electrode compositional studies, which includes preparing a variety of electrode materials with a graded or varying composition and testing against a fixed electrolyte composition to determine the optimal electrode composition. Subsequent optimisation of the battery electrolyte formulation may yield further performance improvements.

In another example application, the AMAS 310 may perform material analysis for the purposes of anti-corrosion coating formulation, which includes identification of the critical inhibitor concentration and subsequent characterisation towards a wide range of pH environments to establish an operational windows where the corrosion inhibitor at the critical inhibitor concentration will be effective.

In another example application, the AMAS 310 may perform material analysis for the purposes of electrowinning or electroextraction or electrorefining, which includes loading of test pieces into testing wells equipped with non-reactive working electrodes, addition of an appropriate electrolyte; and an electrochemical assessment.

In another example application, the AMAS 310 may perform material analysis for the purposes of electrochemical separation, electrolysis, electrodeposition and anodisation methods which includes solution composition and process condition optimisation.

In another example application, the AMAS 310 may perform material analysis of natural, biological and anthropogenic materials, and derivatives thereof.

In another example application, the AMAS 310 may perform material analysis for the development, discovery and optimisation of any electrochemical device or chemical system containing electrochemically active materials; such as sensing molecules.
In another example application, the AMAS 310 may perform material analysis for aqueous and non-aqueous electrochemistry and electrochemical processes.

In another example application, the AMAS 310 may perform material analysis for primary and secondary batteries.

In another example application, the AMAS 310 may perform material analysis for synthetic photosynthesis systems.

In another example application, the AMAS 310 may perform material analysis for photocatalytic materials.

In another example application, the AMAS 310 may perform material analysis for water splitting units.

In another example application, the AMAS 310 may perform material analysis for functional coatings.

In another example application, the AMAS 310 may perform material analysis for electrochromic materials.

In another example application, the AMAS 310 may perform material analysis for switchable or responsive coatings.

The alternative molecule searching module 340, material discovery module 350, operation window determination module 360 and critical concentration determination module 370 can each be utilised in isolation, or linked and used in combination. The autonomous material analysis architecture outlined in this document (illustrated in Figure 4) operates in a closed loop configuration, using experimental and/or simulation data to automatically validate hypotheses made by the autonomous material analysis system 310. This automatic hypothesis generation and testing, and storage of results in an internal or secure external database (data store 50 or data store 313) can almost eliminate or at least significantly reduce human interactions with the
system by removing the need for intensive oversight in the research and development process.

[0117] The AEDM 330 is configured to automatically interact with each of the other code modules in memory 325 and to design, in conjunction with one or more of the alternative molecule searching module 340, a material discovery module 350, an operational window determination module 360 and a critical concentration determination module 370, one or a series of experiments to be performed by the RMTS 10. The AEDM is configured to source data from various data sources or data stores, such as robotic test data from data store 50, previous (actual or in silico) experimental data from data store 313 or external data sources 312 in order to conduct the design of experiments. Further, AEDM 330 assists in the generation of simulation instructions for transmission to external computing resources for conducting in silico experiments, as shown in relation to Figure 21.

[0118] The alternative molecule searching module 340 is configured to design and control the conduct of experiments for optimising a property of a material. Material or material combination optimisation can be performed by the alternative molecule searching module 340 with respect to one or more of the following non-exhaustive list of example characteristics: efficacy, cost, minimum reduction of required materials, and maximising functionality.

[0119] Materials discovery module 350 is configured to automatically design and control the conduct of experiments for new material discovery. For example, given a known chemical “family” of effective compounds, the materials discovery module 350 is configured to identify and test new potential candidates for similar effectiveness. This can be useful for broadening potential supply chains for certain materials, or substitutional elimination of toxic or undesirable chemicals.

[0120] Operational window determination module 360 is configured to design and control the conduct of experiments for determining an operational window of a particular material, for example in a particular environment. For example, given a
concentration of active chemical component(s), the operational window determination module 360 is configured to determine a safe operational pH range, within which the functional nature of the chemical component(s) is retained.

[0121] Critical concentration determination module 370 is configured to design and control the conduct of experiments for the determination of the minimum concentration of a given chemical component that is required to maintain an important feature, such as chemical functionality.

[0122] While some hardware embodiments may rely on operator/user intervention to load and unload testing samples and solutions, full automation is also possible, for example by employing auxiliary fluid delivery systems and pick and place robotic hardware, or substitutional equivalents.

[0123] High throughput testing methodologies described herein facilitate both rapid materials screening and the capability to reduce evaluation cycles, as robotic technologies can operate 24 hours per day and with no or limited human intervention.

[0124] The concept of autonomous science can be formalised into an architecture of modules or routines, each specifically design to solve an industrially/commercially relevant challenge. In this implementation routines are indicated to operate separately from each other, however modules (or combinations thereof) can be linked together to obtain richer and more holistically relevant results.

[0125] While some embodiments include performing ex-situ experimental testing by the RMTS 10 and importing the data into an AMAS 310, in some embodiments, the RMTS and AMAS 310 form part of the same system and cooperate directly to further the aims of the system 300. Generally, the autonomous experimental design and testing capability of the system 300 can be procedurally situated between the interpretation of results and the experimental setup, and is used to plan new experiments after interrogating previously stored data.
Autonomous experimental design and testing as described herein, and more specifically automated hypothesis generation, relies on the interpretation of existing data which has been already captured/recorded by an external measurement system(s) or device(s), with the subsequent data analysis leading to extracted parameters. Such extracted parameters in an electrochemical context could include corrosion current, corrosion potential, Tafel slopes (anodic and cathodic), polarization resistance, impedance measurements as well as others known to those skilled in the art. Additional information from external data sources or new robotic materials analysis/testing schemes (non-electrochemical) can also be utilised to improve the complexity of the data being considered during decision making. Once extracted and quantified, these variables can then be fed into an iterative testing scheme and one or more new hypotheses subsequently generated and tested, leading to an optimised solution for a given autonomous experimental material analysis routine. The generated hypothesis may broadly relate to chemical properties in material analysis experiments. The chemical properties may comprise the various parameters under which an experiment may be conducted, such as critical concentration of chemical, pH values of environments or other relevant parameters for material analysis experiments.

External data sources 312 can include large databases of molecules and compounds, materials properties, etc. External servers 314 can be tasked for high performance computing to run in silico discovery tasks which are of particular relevance to the materials discovery module 350.

The autonomous experimental design module 330 is core to the present disclosure as it communicates instructions from connected analysis modules 340, 350, 360, 370 and translates them into a series of executable commands sent via interface 335, which are then actioned by the RMTS 10 (at AEDM3), as shown and described in relation to Figures 5 and 6. The functional interactions of the autonomous experimental design module 330 in designing and controlling experimental material analysis are shown in the flowcharts of Figures 5 and 6, starting at AEDM1 in Figure 5 and finishing at AEDM4 in Figure 6. Between AEDM1 and AEDM2 is an operational configuration process that takes various testing parameters and robotic system
parameters into account in the experimental design. Such parameters include RMTS calibration data, sensor data, robotic axis limits, testing well or testing board configuration, fluid pump resolution, fluid pump maximum volume, testing solution concentration, testing well maximum volume and other data, for example. The AEDM2 link follows the operational configuration process and indicates the process link between the flowcharts of Figures 5 and 6 and can feed into other material analysis processes, as shown in Figures 7, 12, 13 and 18, for example.

[0129] In the flowchart of Figure 6, a material testing plan is developed (610). Depending on the specific requirements of the connected modules 340, 350, 360, 370, the testing plan (610) translates the requirements of the connected modules and automatically translates information/instructions into the test parameters. Based on the configuration process of Figure 5 and based on inputs from one or more of the connected modules 340, 350, 360 and 370. Test parameters are stored in an array (620) in memory 325 and then these are translated (630) by the autonomous experimental design module 330 into machine commands for controlling execution of the RMTS 10 and then sent (635) to the RMTS 10 via material testing interface 335. Collected results returned from the RMTS 10 via the interface 335 are stored (640) in a relational database, for example, in data store 313. In some instances, the results of the first experiment may be fed back (650) to one or more of the connected modules 340, 350, 360 and 370 for improving the design/planning of further (second, third or more) experiments for which new experimental instructions (660) can be received to create a new material testing plan (610). Otherwise if all of the testing is finished, the process ends at AEDM4.

[0130] Referring now to Figures 7 to 11, performance of a critical concentration determination routine by critical concentration determination module 370 is shown and described.

[0131] The elucidation of a critical concentration is important in minimising the use of an "active" ingredient in a given commercial formulation. In this example, the AEDM 330 capability is used to plan refinement tests to narrow down the number of
potential tests which require to be executed. The example illustrated with respect to Figure 8A, 8B and Figures 9 to 11 is contextualised to the development of anti-corrosion thin films where minimum loading of the active ingredient is defined as the critical inhibitor concentration. The critical inhibitor concentration is the smallest possible concentration which gives the lowest current density. In this example, the lower the respective values the better, in terms of performance, material utilisation and cost effectiveness. Figure 8A is a plot of an example set of experimental results of testing for corrosion current (current density) across different inhibitor concentrations. Data point 3 is seen to be the best of the initial test results. Figure 8B is similar plot to Figure 8A but shows that further experiments are conducted around data point 3 in order to determine the critical concentration more precisely. This approach is further illustrated schematically in Figure 9.

[0132] The process and functionality executed by the critical concentration determination module 370 is shown in the flowchart of Figure 7, and the parameters/variables are explicitly described in Table 1 below.

[0133] It should be noted that the examples given only consider single variable (ID) optimisation. However, multi-variable optimisation can also be employed according to this disclosure. Such multi-variable optimisation has particular relevance to studying synergistic combinations of materials or for optimising complex multi-component/chemical systems.

[0134] Table 1:

<table>
<thead>
<tr>
<th>#</th>
<th>Rule</th>
<th>Value/Equation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Syringe pump resolution</td>
<td>200 µL</td>
<td>Minimum drop size permitted by tubing diameter and resolution of pump steppers</td>
</tr>
<tr>
<td>(2)</td>
<td>Syringe max volume</td>
<td>60 mL</td>
<td>Default syringe size</td>
</tr>
<tr>
<td>(3)</td>
<td>Testing well max volume</td>
<td>15 mL</td>
<td>Default max well volume in robotic materials analysis system testing plate</td>
</tr>
<tr>
<td>(4)</td>
<td>Min testing solution volume</td>
<td>10 mL</td>
<td>Requires a min of 10 mL using the current (default) robotic materials</td>
</tr>
<tr>
<td></td>
<td>Solution concentration</td>
<td>Varies (M)</td>
<td>Obtained from robotic materials analysis and testing system log file/input settings</td>
</tr>
<tr>
<td>---</td>
<td>------------------------</td>
<td>-----------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>6</td>
<td><strong>Min concentration</strong></td>
<td>((3)-(4))#((1)#(5))</td>
<td>Min concentration limit which could be dispensed into the testing well, as dictated by physical and chemical parameters of the system</td>
</tr>
<tr>
<td>7</td>
<td><strong>Max concentration</strong></td>
<td>((3)-(4))#(5)</td>
<td>Max concentration limit which could be dispensed into the testing well, as dictated by physical and chemical parameters of the system</td>
</tr>
<tr>
<td>8</td>
<td><strong>Range</strong></td>
<td>ln(6)l - ln(7)l</td>
<td>Concentration range available for testing given the solution concentration available</td>
</tr>
<tr>
<td>9</td>
<td><strong>Low fuzzy logic value</strong></td>
<td>l(8) x ((1)x (1/64))</td>
<td>“Low value” if the fineness is set to low, the search algorithm will change the concentration by either increasing or decreasing the next test value by this amount</td>
</tr>
<tr>
<td>10</td>
<td><strong>Medium fuzzy logic value</strong></td>
<td>l(8) x ((1)x (1/32))</td>
<td>“Medium value” if the fineness is set to medium, the search algorithm will change the concentration by either increasing or decreasing the next test value by this amount</td>
</tr>
<tr>
<td>11</td>
<td><strong>High fuzzy logic value</strong></td>
<td>l(8) x ((1)x (1/16))</td>
<td>“High value” if the fineness is set to high, the search algorithm will change the concentration by either increasing or decreasing the next test value by this amount</td>
</tr>
<tr>
<td>12</td>
<td><strong>Convergence cut-off</strong></td>
<td>X % of (8)</td>
<td>If the difference between the trial result and the original is ≤ to (12) the algorithm halts, and the result is recorded</td>
</tr>
<tr>
<td>13</td>
<td><strong>Max number of trials</strong></td>
<td>Y</td>
<td>Default values 20, 40. This is the max number of physical tests at the disposal of the robotic materials analysis/testing system. Should this value be reached testing will halt and the “best” value recorded in the series of tests shall be considered the answer</td>
</tr>
<tr>
<td>14</td>
<td><strong>Number of initial tests</strong></td>
<td>6</td>
<td>Default of 6 initial tests. Arbitrary division of the range by this value, this provides an auto-scalable set of initial tests to begin to map the effect of varying concentration against a metric of worth (15)</td>
</tr>
</tbody>
</table>
While the following serves to illustrate some basic functions and processes of the critical concentration determination module 370 it will be appreciated by those trained in the art that a number of methodologies could be employed to find the critical concentration, which include but are not limited to those listed in Table 2 below.

Table 2:

<table>
<thead>
<tr>
<th>Name</th>
<th>Optimisation type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bi-sectioning method</td>
<td>Single variable (N)</td>
</tr>
<tr>
<td>Golden section</td>
<td>Single variable (N)</td>
</tr>
<tr>
<td>Parabolic interpolation</td>
<td>Single variable (N)</td>
</tr>
<tr>
<td>Brent’s method</td>
<td>Single variable (N)</td>
</tr>
<tr>
<td>One-dimensional search with first derivatives</td>
<td>Single variable (N)</td>
</tr>
<tr>
<td>Steepest descent (and related)</td>
<td>Single variable (N)</td>
</tr>
<tr>
<td>Multivariable regression</td>
<td>Multiple variables (N^2)</td>
</tr>
<tr>
<td>Radial basis</td>
<td>Multiple variables (N^2)</td>
</tr>
<tr>
<td>Parametric model</td>
<td>Multiple variables (N^3)</td>
</tr>
<tr>
<td>Simplex method</td>
<td>Multiple variables (N^3)</td>
</tr>
<tr>
<td>Conjugate gradient (CG)</td>
<td>Multiple variables (N^3)</td>
</tr>
<tr>
<td>Quasi-Newton method(s)</td>
<td>Multiple variables (N^3)</td>
</tr>
<tr>
<td>Davidson-Fletcher-Powell (DFP)</td>
<td>Multiple variables (N^3)</td>
</tr>
<tr>
<td>Broyden-Fletcher-Goldfarb-Shanno (BFGS)</td>
<td>Multiple variables (N^3)</td>
</tr>
</tbody>
</table>

Some of the methodologies listed in Table 2 may not be ideally suited, as they would require a large number of tests to reach convergence, which is less preferred.
[0138] Three distinct scenarios have been identified which the critical concentration
determination module 370 may encounter during testing, which are presented in
Figures 9 to 11:

[0139] Scenario 1 - Figure 9 - \textbf{locating a minimum region} - a testing vector
direction is established after initial testing and proceeds until the minimum value (as
determined by the metric of worth) is reached, this is further determined by
encountering a decrease in the metric of worth with further testing.

[0140] Scenario 2 - Figure 10 - \textbf{locating a plateau region} - this is identical to
scenario 1 until the algorithm detects that 3 sequential tests in the same direction were
measured to be equal or equivalent (according to the convergence cut-off). While it is
possible to increase the number higher than three, it is preferential to identify suitable
candidates with the lowest number of possible experimental tests.

[0141] Scenario 3 - Figure 11 - \textbf{already at a minimum} - after probing the
immediate/adjacent concentrations according to the fineness of the test criteria, both
slightly lower and slightly higher concentrations when compared against the initial
arbitrary trial were found to be worse (according to the metric of worth), no further
tests are necessary, testing loop exits.

[0142] The presented methodology does not address generic limitations of
optimisation/convergence algorithms where it is not possible to ensure the global
minimum has been reached, unless a significantly large number of tests/trials/iterations
have conclusively mapped the profile of the system. Despite this, the application of the
preferred embodiment is for rapid screening to identify candidate materials/systems/etc.
and in the conventional path of material discovery/science further tests to qualify
systems for their given application may be necessitated. It is accepted that this later
stage would overcome any perceived limitations with respect to the
optimisation/convergence algorithms employed throughout. It will be appreciated that
other methodologies known to those trained in the art can also be utilised similarly.
Referring now to Figure 12 and 13, performance by the operational window determination module 360 of an operational window determination routine is shown and describe in further detail.

The operational window determination module 360 determines and/or validates operational windows of materials and material systems. This allows taking materials identified as candidates, and quantifying the conditions in which they would be capable of operating. Due to the inherent nature of materials, for a given chemistry it is highly likely that it can be safely utilised only in an environment which is chemically compatible. A primary example is pH, where certain materials will dissolve or dissociate when exposed to extreme pH values, for example by exposure to extreme pH environments. An example of processes implemented by the operational window determination module 360 in the determination of an operational window is outlined in Figures 12 and 13. Here particular context is given to finding the minimum inhibitor concentration, for example using the process shown in Figure 12, beginning at OW1 and following the process through OW2, and then identifying the pH range in which it will remain active, for example using the process shown in Figure 13 between OW2 and OW3. As an example, Figure 12 illustrates that initial tests are run (by the RMTS 10) to get initial results to which the metric of worth is applied and then used to identify (1240 or 1340) the "best" experimental result from that data set. The RMTS 10 can then be configured (with the help of the AEDM 330) to run a series of follow up experiments (1245 or 1345) to probe the immediate region around the best result to determine an even more optimised result.

Other non-electrochemical parameters or values may be incorporated into the metric of worth, either in isolation or in combination with electrochemically derived data.

The metric of worth to be applied in the initial testing or subsequent testing may be defined as an equation with user defined or automatically provided set of weights corresponding to variables (for example Ecorr, Icorr, Tafel slopes). Solving the metric of worth equation for each physical test yields a number or value which can be
used to rank the relative success of a trial of a physical test within an initial test dataset. The initial test dataset may comprise the values obtained by solving the metric of worth equation for a series of trials of a physical test.

[0147] An exemplary metric of worth could include but is not limited to:

\[
\text{Modified Polarization Resistance (MPR)} = \left( \frac{\beta}{I_{\text{corr}}} \right) + \left( \frac{E_{\text{corr}}}{K \cdot I_{\text{corr}}} \right)
\]

Where \( \beta = \frac{ba \cdot bc}{2.3 \cdot (ba + bc)} \)

[0148] For example, for steel in seawater:

\( ba = 201 \text{ mv/dec}; \ be = 405 \text{ mv/dec}; \ E_{\text{corr}} = -303 \text{ mV}; \ I_{\text{corr}} = 4.97 \mu \text{A}; \ (\beta/I_{\text{corr}}) = 11.75 \Omega; \ [E_{\text{corr}}/(K \cdot I_{\text{corr}})] = 3.05; \) and MPR=14.8\( \Omega \).

[0149] Legend

\( I_{\text{corr}} = \text{corrosion current (experimentally measured)} \)

\( E_{\text{corr}} = \text{corrosion potential (experimentally measured)} \)

\( ba = \text{anodic tafel slope (experimentally measured)} \)

\( be = \text{cathodic tafel slope (experimentally measured)} \)

\( K \) can be varied but typical has a value of 20,000

[0150] Identification of the best test result (1240 or 1340) using metric of worth may comprise the steps of: loading testing data, loading automatic or user defined metrics, utilising the metric of worth equation weights and equation to calculate results based on testing data, and ranking the results obtained to find the best performer from the initial tests.
[0151] Probing the immediate region around the best data point (1245 or 1345) may comprise the steps of: loading and sorting results from initial tests; using the lowest test result set as a new reference point; testing from the new reference point by adding or subtracting low, medium or high values; and running subsequent tests to probe the immediate region around the best data point.

[0152] Similar definitions of the metric of worth, the best test and the probing actions given above are applicable to the flowchart shown in Figure 7.

[0153] The graph in Figure 14 shows a simple relationship between pH and current density, with example (not actual) experimental data points. Idealised global minimums may not exist or may not be readily found, but rather many local minima or higher order saddle points may exist. However, Figures 14 and 15 serve to illustrate the general methodology, where a plot of initial example test results is made for current density vs pH over arbitrary limits: max current 40 μA/cm², pH range 2-14. Subsequent tests results (indicated in Figure 15 as "AS tests") designed and run using the AEDM 330 in conjunction with the RMTS 10 are shown in Figure 15 and can be seen to populate areas of unknown data arising from the initial tests. The arbitrary limits are supplied by the operator and are limited by the physical capabilities of the RMTS 10. For example, pumps have a maximum and minimum dispense volume capacity according to their configuration. Those trained in the state of the art will appreciate that interpolating between sparse data points can distort the true chemical nature, by over- or under-estimating operational windows. This underscores the benefits of the described autonomous material analysis system 310 to appropriately sample and test, rather than relying on interpolated data.

[0154] Figure 15 is a worked example plot of the operational window example experimental tests as described in Figure 13. Here the operational window determination module 360 can identify pH regions where it would be unsafe or ineffective to deploy the material which is being tested, as well as the optimal pH value, pH range and the limits of the effective operational range.
[0155] Referring now to Figures 16 to 19, performance of a materials discovery routine by the materials discovery module 350 is described and shown in further detail. Materials discovery module 350 comprises a hypothesis generation function to generate hypotheses for material discovery that can be tested using the RMTS 10.

[0156] Screening tasks and the identification of substitutional analogues is a time consuming and expensive process. Despite having identified an excellent candidate chemical/material (primary candidate) with desirable functionality in many instances cost, toxicity or availability limit the application of the primary candidate. The materials discovery module 350 may use the primary candidate molecule and other molecule/chemical information and/or statements stored in the internal or external data stores 312 or 313, together with a series of logical hypothesis generation rules stored in the memory 325 (or data store 313) to generate a hypothesis.

[0157] An example of hypothesis generation and testing is outlined in Figure 16. The flowcharts of Figures 17, 18 and 19 illustrate a process flow for material discovery, beginning at MO1 in Figure 17, proceeding through M02 to M03 in Figure 18 and ending at M04 in Figure 19. Given a series of known statements/rules, the hypothesis generation module within the materials discovery module 350 generates a hypothesis suggestion which is then translated through the process shown in Figures 17 and 18, reaching the experimental planning module, which for the purposes of Figure 18, is a part of materials discovery module 350 and treats simulation/modelling as an in silico experiment, and a decision is made to perform a physical test or in silico experiment.

[0158] The in silico experiment may be initiated by the experimental planning module in parallel with or before or after the physical experiments, as illustrated in the flowchart in Figure 18. Within the experimental planning module, the configuration of the RMTS 10 is imported, so that if the chemical is available to the RMTS 10 (i.e. already loaded among materials 305) then it will utilise it and experimentally test the hypothesis. If the chemical is not present in the materials 305 of the RMTS 10, as is often the case, the material discovery module 350 may generate and send to the external servers 314 instructions describing the structure to be simulated, and from this
simulation (once it has been executed) return an indication of whether or not the simulated molecule is likely to be experimentally effective. It should be noted that not all experiments can be assessed or executed in silico.

[0159] The material discovery module can also prompt an operator to load the suggested chemical sample into the RMTS 10. During the next changeover cycle of the RMTS 10, where tested samples/plates are unloaded and fresh samples are reloaded, the operator may be prompted to load the chemical/molecule into one or more testing wells of the RMTS 10 to be experimentally assessed and validated against the simulation results. Regardless of the outcome, be it positive or negative effectiveness, the material discovery module 350 will cause the results to be stored in a secure data store 313 and encoded into one or more rules or statements to be used to refine future hypothesis formulation. Table 3 below describes functional modules and parameters/variables used in the execution of the process illustrated by Figures 17 to 19.

[0160] Table 3

<table>
<thead>
<tr>
<th>#</th>
<th>Variable/module</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Molecule features</td>
<td>Creates machine readable strings which are used to represent the molecule(s)</td>
</tr>
<tr>
<td>(2)</td>
<td>Descriptors</td>
<td>Collates both input and output variables and converts them to descriptors for use by the QSAR module</td>
</tr>
<tr>
<td>(3)</td>
<td>QSAR module</td>
<td>Standard QSAR (quantitative structure-activity relationship) module. This module analyses the relationship between the structural (or other property) configuration of a molecule, which collectively define a molecular specification, in a dataset and predicts the importance of that feature/property to another property i.e. molecular feature or specification on the experimentally determined corrosion inhibition efficacy.</td>
</tr>
<tr>
<td>(4)</td>
<td>NN (neural network) module</td>
<td>Generates neural network weights for the QSAR descriptors</td>
</tr>
<tr>
<td>(5)</td>
<td>Weights</td>
<td>Mathematical weights for each descriptor which passes through the QSAR module</td>
</tr>
<tr>
<td>(6)</td>
<td>Importance ranking module</td>
<td>Applies weights to QSAR descriptors to rank the contribution that each descriptor makes to the activity/function This is done by multiplying the weight</td>
</tr>
</tbody>
</table>
As time progresses and the system 300 evaluates 100's of samples, hypothesis generation rules can become more focused and detailed, with many rules making up future hypotheses, so that honing in on relevant chemistries becomes more effective.

A workflow for autonomous materials discovery through hypothesis generation is provided in Figures 17 to 19, with a worked example of hypothesis functions highlighted in Figure 20. Here fitness functions can be viewed as a general class of equations which typically contain more than one of the following: structural features, descriptors, calculated properties, experimentally measured properties and are either minimised or maximised according to preference of the user or connected module. The PMF while not explicitly a fitness function, is used to compare against the result of FF1, without it, there is no reference point for comparison.

The flowchart of Figure 19 illustrates application of a fitness function such as is given as an example in Figure 20. Here \( \alpha, \beta, \gamma \) are the weights of ranking #1 descriptor through to the ranking #3 descriptor (Figure 18), respectively; PMF is the parent molecule function.

A description of the functionality of the searching module (identified in Figure 18) is shown in Figure 22, with reference to the molecular structures to which the fitness function was applied in Figure 20. As shown in Figure 22, the following methodology as executed by the alternative molecule searching module 340 may be applied to molecule searching:

<table>
<thead>
<tr>
<th></th>
<th>Searching module</th>
<th>Experimental planning module</th>
<th>Fitness function calculation</th>
<th>Iteration comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Searches databases/data sources 312 for molecules which feature high ranking descriptors</td>
<td>This module receives a hypothesis suggestion and determines whether to execute a physical experiment or an in silico experiment</td>
<td>Used to calculate the fitness function which is comprised of a series of weighted variables originating from the QSAR/NN modules</td>
<td>Compares between multiple NN trained models to find a molecule with the greatest fitness function.</td>
</tr>
</tbody>
</table>
[0165] 2210: Given the dataset of available molecules this module will search external/internal databases and data sources for molecules which feature descriptors 1, 2, 3, nth descriptor.

[0166] 2220: Assuming that benzene is the starting molecule then: the hypothesis would postulate that molecules which feature a ranking #1 descriptor would function better than the parent molecule. Similarly, a molecule which features both a ranking #1 and #2 descriptor would function better than the parent of molecule containing only #1 feature. This logic can be repeated multiple times until the system has planned a series of experiments in a RMTS or manual testing regime, using a variety of molecules which feature subtle changes in structure.

[0167] 2230: If successful, the results from the test will be fed back into the NN module and the model will be refined, with new weights assigned accordingly.

[0168] 2240: If unsuccessful, and the original test molecule(s) reveal superior performance when compared with the test molecules, then the NN module will be retrained, and the assigned weights of the ranking #1, #2, #3, nth descriptors will plummet. Consequently, the next most important descriptors will be tested.

[0169] Figure 21 is a more detailed flowchart of a simulation process (SIM1 to SIM2) invoked in the flowchart of Figure 18 as part of the material discovery process performed by the material discovery module 350. The simulation process illustrated in Figure 21 may be carried out by a simulation module (not shown) in conjunction with an external computing resource, such as the external servers 314. The simulation module forms a sub-module of the material discovery module 350. The simulation module defines the simulation parameter space based on received calculation settings and a specified maximum number of calculation and then prepares and sends simulation files and data/directory structures to be used by the external computing resource. The external computing resource may specify a wall time, which refers to the maximum computation time allocated by a job scheduler application running on the computational resource hosted by external servers 314 (e.g. supercomputer,
workstation, high performance computing cluster, cloud service, etc.) for executing the requested simulation.

[0170] Here simulation is defined as (any form of) one or more of: molecular modelling, atomistic modelling, condensed matter physics modelling, quantum chemistry, empirical modelling, molecular dynamics modelling, continuum modelling, computational fluid dynamics, Monte Carlo modelling, Density Functional Theory, and similarly related techniques and fields of academic enquiry.

[0171] The materials discovery module 350, in conjunction with the alternative molecule searching module 340 can be used to seek out molecules with similar chemistry to an already identified candidate molecule/material etc. There are several reasons why an operator may wish to perform this task, which include but are not limited to one or more of the following: identifying alternatives with lower toxicity, seeking cheaper alternatives, identifying alternatives which are already available in commercial quantities, or avoiding materials which originate from geopolitically unstable regions. Figures 23 to 25 illustrate the steps the alternative molecule searching module 340 may take in seeking out molecules with chemistry similar to an already identified candidate molecule/material etc.

[0172] Table 4 below sets out a list of functional modules employed in the alternative material discovery process outlined in Figures 23 to 25.

[0173] Table 4:

<table>
<thead>
<tr>
<th>#</th>
<th>Variable/module</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>Exemplary molecule</td>
<td>The current best candidate</td>
</tr>
<tr>
<td>(2)</td>
<td>Deconstruction module</td>
<td>Breaks down the structure of the exemplary molecule into a series of metrics which can be used for comparison and in searching for new candidate molecules</td>
</tr>
<tr>
<td>(3)</td>
<td>Molecular features module</td>
<td>The molecular features and topological connectivity of atoms in the exemplary molecule are distilled and quantified</td>
</tr>
<tr>
<td>(4)</td>
<td>SMILES generator</td>
<td>Generates a SMILES (simplified molecular-input line-</td>
</tr>
</tbody>
</table>
Embodiments described herein generally pertain to an autonomous experimental design system for automated materials testing/analysis. Embodiments described herein may be capable of one or more of the following:

- High throughput testing/analysis;
- Automated decision making;
- Autonomous science;
• Automated design of initial or follow-up experiments based on information gained from external data sources or the execution of robotic material discovery;

• *in silico* experimentation; and

• Identification of molecular analogues and substitutional replacements.

[0175] In one or more of the described embodiments, the RMTS 10 and physical materials 305 may not be co-located with the AMAS 310. In some embodiments, RMTS 10 and materials 305 may be geographically isolated from the remainder of the AMAS 310. The AMAS 310 receives collated data from data store 50, which is used by the AMAS 310 to generate a series of machine instructions for RMTS 10 to execute.

[0176] Figure 26 is a block diagram of a system for material analysis 2600 according to some embodiments wherein the AMAS 310 is connected to a plurality of RMTS 10 through a network 2620. The network 2620 may comprise any suitable communication network or combination of such networks, including public and private networks or sub-networks. The plurality of RMTS 10 may each be located at a physical site different from the site where the AMAS 310 may be located. A physical site may host one or more RMTS 10.

[0177] The execution instructions generated by the AMAS 310 may be communicated to the plurality of RMTS 10 through network links 2610, over the network 2620, to perform one or more experiments at each of the plurality of RMTSs 10. In some embodiments, the execution instructions may be stored in an intermediate data store, which can serve as a repository of instructions for the plurality of RMTSs 10. If an RMTS 10 is geographically isolated or remotely located with respect to the AMAS 310, the network 2620 can be extended across a wider public network that enables communication between the AMAS 310 and the remotely located RMTS 10.
The actual execution of experiments at the plurality of RMTS 10 may be parallelised across the plurality of RMTS 10 or staggered according to a schedule generated by the AMAS 310 or the actual execution may be scheduled independently by a specific RMTS 10 depending on its own workload. After the completion of the execution of an experiment, the results obtained by an RMTS 10 may be returned to the AMAS 310 over the network 2620 using the network links 2610. Alternatively, the results may be stored at a designated data store, such as data store 50 in Figure 3. The AMAS 310 may query the data store 50 to retrieve the stored results.

This parallelisation of experimentation enables autonomous science to be effectively delivered as a distributed service, allowing co-ordinated system level control of multiple RMTS 10 working in parallel towards the same goal. Parallelised testing via a distributed service also facilitates automated double blind replicate testing to cross-check against systematic error in any given RMTS 10 system.

In some embodiments the RMTS 10 and physical materials 305 may be co-located with the automated materials analysis system 310. This co-location may reduce the complexity and cost by hosting both the automated materials analysis system 310 and the RMTS 10, and data store 50 all on the same computer platform.

In some embodiments, the electrodes used in the RMTS 10 may be disposable or single use electrodes. Disposable electrodes may improve the accuracy of experimental results for tasks, such as for battery electrolyte formulation tasks, where build-up of persistent reaction products may obfuscate the true electrochemical response of electrodes through processes such as solid electrolyte interface layer formation. While there are methods to clean counter electrodes, some generate $\frac{3}{4}$ and $O_2$, which is less preferred, particularly in an enclosed environment. In some embodiments, the sensors or probes used may also be disposable or single use sensors or probes.

Described embodiments may have one or more advantages. Described embodiments may enable removal of human bias in the process of material analysis;
may enable discoveries of chemically unintuitive molecules, compositions or formulations; may reduce the need for labour in the process of material analysis; may improve throughput by operating outside of business hours; may automate design and execution of experiments; and/or may automate recording and interpretation of results of experiments.

[0183] Described embodiments provide a system that may be operated by a non-expert workforce. Described embodiments relate to a system and method that has a scalable and distributable architecture; parallelises execution of complex experiments; simulates and pre-screens materials using computational resources; identifies potential substitutional molecules, compounds or materials using the alternative molecule searching module 340. Described embodiments may be deployed in circumstances where traditional design of experiments planning fails due to over-estimation or extrapolation or interpolation of experimental results.

[0184] Described embodiments aim to avoid execution of a large number of tests in order to arrive at an answer, instead favouring experimental design that can efficiently conduct exploratory experiments.

[0185] Described embodiments are generally not directed to automated chemical synthesis (like drug development) and generally utilise materials or chemicals that have known constituents (even if their properties are not exactly known), which can avoid the need for analysis techniques that seek to identify the constituents in a material sample (such as by gas chromatography, liquid chromatography or mass spectrometry). Described embodiments are particularly suited to automating the testing of manufactured products and automatically screen candidate formulations of such products or coatings onto these products.

[0186] Described embodiments are capable of performing in silico pre-screening of potential candidate molecules, to reduce the number of tests required to physically executed. Described embodiments may utilise a centralised results repository and can
automatically connect to dissimilar databases and data sources to extract information for automated experimental design.

[0187] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the above-described embodiments, without departing from the broad general scope of the present disclosure. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.
CLAIMS:

1. An autonomous experimental design system for automated material analysis, the system comprising:
   at least one processor;
   memory accessible to the at least one processor and storing executable program code;
   a user interface to receive input parameters for the automated material analysis; and
   a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

   wherein the program code comprises an experimental design module configured to automatically design execution of an experiment based on received input parameters as part of the automated material analysis and to transmit execution instructions to the robotic material testing system via the material testing interface.

2. The system of claim 1, further comprising the robotic material testing system.

3. The system of claim 1 or claim 2, wherein the robotic material testing system comprises an electrochemical testing system.

4. The system of any one of claims 1 to 3, wherein the experimental design module is configured to query a data store for past experimental data that is relevant to a planned experiment and to design execution of the planned experiment based at least in part on data returned by the query.

5. The system of claim 4, wherein the planned experiment comprises a material discovery experiment and the program code comprises a material discovery module configured to control execution of the material discovery experiment.

6. The system of any one of claims 1 to 5, wherein designing execution of the experiment by the experimental design module comprises determining whether to
conduct a computer simulation of at least part of the experiment or to conduct a simulated test as a pre-cursor to the experiment.

7. The system of any one of claims 1 to 6, wherein the experimental design module comprises a plurality of experiment planning sub-modules, each of which is configured to plan a specific type of experiment.

8. The system of any one of claims 1 to 7, wherein the program code further comprises a plurality of material analysis modules, each of which is configured to interface with the robotic material testing system to control execution of a specific type of experiment.

9. The system of any one of claims 1 to 8, wherein the experiment comprises one of:
   an alternative molecule searching experiment;
   a material discovery experiment;
   a material operational window determination experiment; and
   a critical concentration determination experiment.

10. The system of any one of claims 1 to 9, wherein the experiment is a first type of material analysis experiment and the experimental design module is configured to automatically design execution of a second experiment of a second type of material analysis experiment that is of a different type from the first type.

11. The system of claim 10, wherein the second experiment is designed to be conducted based on data received from conduct of the first experiment.

12. The system of any one of claims 1 to 11, wherein the experiment is a first type of material analysis experiment and the experimental design module is configured to automatically design execution of a second experiment of the first type of material analysis experiment based on data received from conduct of the first experiment.
13. The system of any one of claims 1 to 12, wherein the experimental design module is configured to receive experimental results from the robotic material testing system via the material testing interface and to store the experimental results in a data store accessible to the experimental design module.

14. An autonomous experimental design system for automated material analysis, the system comprising:
   at least one processor;
   memory accessible to the at least one processor and storing executable program code;
   a user interface to receive input parameters for the automated material analysis; and
   a material testing interface to allow the at least one processor to communicate with a robotic material testing system;
   wherein the program code comprises a material discovery module configured to cooperate with an experimental design module to automatically design a material discovery experiment based on received input parameters and to transmit execution instructions to the robotic material testing system via the material testing interface for performing the material discovery experiment.

15. The system of claim 14, further comprising an alternative molecule searching module configured to cooperate with the material discovery module for design of the material discovery experiment.

16. The system of claim 15, wherein the alternative molecule searching module is configured to receive a molecule specification from the material discovery module and to search for alternative molecules having features that at least satisfy the molecule specification.

17. The system of claim 16, wherein the alternative molecule searching module is further configured to rank molecules identified in the search based on quantitative structure-activity relationship (QSAR) descriptors identified in the search.
18. The system of any one of claims 14 to 17, wherein the experimental design module is configured to design an in silico experiment as part of designing the material discovery experiment.

19. An autonomous experimental design system for automated material analysis, the system comprising:
   - at least one processor;
   - memory accessible to the at least one processor and storing executable program code;
   - a user interface to receive input parameters for the automated material analysis; and
   - a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

   wherein the program code comprises a critical concentration determination module configured cooperate with an experimental design module to automatically design a critical concentration determination experiment based on received input parameters and to transmit execution instructions to the robotic material testing system via the material testing interface for performing the critical concentration determination experiment.

20. The system of claim 19, wherein the critical concentration determination module is further configured to process received results of the critical concentration determination experiment using a defined metric of worth to identify best test results from conduct of the critical concentration determination experiment.

21. The system of claim 20, wherein the critical concentration determination module is configured to cooperate with the experimental design module to design a new critical concentration determination experiment to probe an immediate region around one or more of the best test results to validate previous test results or determine a new best test result.
22. An autonomous experimental design system for automated material analysis, the system comprising:

- at least one processor;
- memory accessible to the at least one processor and storing executable program code;
- a user interface to receive input parameters for the automated material analysis; and
- a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

wherein the program code comprises an operational window determination module configured cooperate with an experimental design module to automatically design an operational window determination experiment based on received input parameters and to transmit execution instructions to the robotic material testing system via the material testing interface for performing the operational window determination experiment.

23. An autonomous experimental design system for automated material analysis, the system comprising:

- at least one processor;
- memory accessible to the at least one processor and storing executable program code;
- a user interface to receive input parameters for the automated material analysis; and
- a material testing interface to allow the at least one processor to communicate with a robotic material testing system;

wherein the program code is configured to:

- generate a chemical property hypothesis based on at least one data source relating to chemical properties,

- design at least one experiment to test the chemical property hypothesis using an experimental design module,
transmit execution instructions to the robotic material testing system via the material testing interface to test the chemical property hypothesis, and

based on received results of the testing, validate or invalidate the chemical property hypothesis.

24. A computer implemented method for automated material analysis, comprising:

receiving input parameters for the automated material analysis;

automatically designing execution of an experiment based on received input parameters; and

transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the experiment.

25. The method of claim 24, wherein the receiving, designing and transmitting are performed by an automated material analysis system that is separate from the robotic material testing system.

26. A computer implemented method for automated material discovery, comprising:

receiving input parameters for the automated material discovery;

automatically executing a material discovery module configured to cooperate with an experimental design module to automatically design a material discovery experiment based on received input parameters; and

transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the automated material discovery experiment.
27. A computer implemented method for critical concentration determination, comprising:

receiving input parameters for the critical concentration determination;

automatically executing a critical concentration determination module configured to cooperate with an experimental design module to automatically design a critical concentration determination experiment based on received input parameters; and

transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the critical concentration determination experiment.

28. A computer implemented method for operational window determination, comprising:

receiving input parameters for the operational window determination;

automatically executing an operational window determination module configured to cooperate with an experimental design module to automatically design an operational window determination experiment based on received input parameters; and

transmitting execution instructions via a material testing interface to a robotic material testing system configured to perform the operational window determination experiment.

29. A computer implemented method for automated material analysis, comprising:

receiving input parameters for the automated material analysis;

autonomously generating a chemical property hypothesis based on at least one data source relating to chemical properties;
autonomously designing at least one experiment to test the chemical property hypothesis using an experimental design module;

transmitting execution instructions to a robotic material testing system via a material testing interface to test the chemical property hypothesis; and

based on results of the testing received via the material testing interface, validate or invalidate the chemical property hypothesis.

30. The steps, features, systems, sub-systems, modules, sub-modules, methodologies, techniques or equipment as described herein alone or in any combination or sub-combination.
SCENARIO 1 – Locating a minimum region

![Graph showing concentration vs. current density]

1. **START**
2. Test either side of 3
3. Best candidate selected
4. Vector established
5. STOP - is the minimum

**Requires input from user/operator**

A) Convergence cut-off
B) Fineness of optimisation: low/med/high
C) Max number of wells to be tested

**Fig. 9**
SCENARIO 2 – Locating a plateau

START

Test either side of 3

Best candidate selected
Vector established

STOP - with respect to the convergence threshold i.e. search algorithm halts when difference between adjacent tests is less than a fixed amount. The lower concentration of the two is selected as the answer.
SCENARIO 3 – Already at the minimum

Icorr (µA/cm²)

Concentration (M)

Test either side of 3

Results indicate metric of worth increases either side of 3, minimum already reached

STOP – 3 is the lowest, further tests not necessary

Fig. 11
Operational Window

Fig. 14

Operational Window

Fig. 15

Known
1. Thiol (-SH group) containing molecules are highly effective
2. Small Thiols are too reactive
3. N heterocyclic compounds shown limited effectiveness

Hypothesis test

- Adding a thiol to a N heterocyclic compound may improve effectiveness

Fig. 16
Goal is to minimise the FF

Parent molecule

\[ PMF = \text{exp. results} + \text{sim. results} \]

\[ FF1 = \text{exp. results} + \text{sim. results} + \alpha\text{Descriptor } #1 \]

\[ FF2 = \text{exp. results} + \text{sim. results} + \alpha\text{Descriptor } #1 + \beta\text{Descriptor } #2 \]

\[ FF3 = \text{exp. results} + \text{sim. results} + \alpha\text{Descriptor } #1 + \beta\text{Descriptor } #2 + \gamma\text{Descriptor } #3 \]

If no simulation results available sim. results = 0

FF3 has the lowest value among FF1-FF3, therefore FF3 is the NP#0, which is fed into the NN

New parent molecule

Fig. 20
Fig. 21

Connect to computational resources

System online and communications sys. OK

Check internal database if in silico testing is available

Calculation settings

Max number of calculations

Prepare simulation files and directory structure on computational resource(s)

Submit simulations to the queuing system on the computational resource(s)

Poll job queuing system

Calculation/job complete?

Calculation successful?

Simulation failure identification module

Wall time insufficient?

Prepare job for check-pointing or resubmission

Halt particular simulation

Halt

No

Return error message to user

To be implemented as a loop which runs until all jobs have been classified as failed or complete

NB in silico testing cannot be applied to solve every task, it is only suitable for a particular workflows/methodologies.
Alternative Molecule Searching Module 340

2210 → Search Database

2220 → Design Experiments

Yes → Tests Successful?

→ Feed results to Neural Networks

No → Design Experiments for next set of descriptors

2230 →

2240 →

Examples

1. Ranking #1 descriptor = -SH functional group
2. Ranking #2 descriptor = N-heteroatoms
3. Ranking #3 descriptor = -NH3 functional group

Fig. 22
Applies a weighting to the importance of a search term/result, i.e. number of carbon atoms may not be important, while number of epoxide rings may be very important.

Weights of importance manually defined (or automatically defined e.g. neural network derived).

Apply rejection to lowest X% of ranked molecules.

Update candidate list.

Enter results refinement GUI/script.

Apply elemental filtering (max # of elements, eliminate results which contain certain elements).

Option to apply user specified search terms, i.e. only search for molecules with a particular functional group.

Set molecular weight cut-off and/or min/max limits.

Update candidate list.

Initiate comparator module GUI/script/code.

Molecules are ranked by similarity of search term features which occur in the exemplary molecule.

Results display module.

Yes

No

# of results too large?

Finish

M04

Fig. 25
Fig. 2
Fig. 3
Fig. 6
Fig. 7

Flowchart:

1. Import system parameters
2. Testing setup module
3. Max # trials
4. # of initial tests
5. Convergence cut-off
6. Initial tests executed?
   - Yes: Run initial tests
   - No: Collate results

7. RD
8. Metric of worth
9. Identification of “best” test using metric of worth
10. Probe immediate region around data point

11. Test according to low/med/high cut-off along vector
12. Run tests
13. Collate results
14. Analyse result
15. Convergence achieved?
   - No: Identify vector
   - Yes: STOP

Additional Notes:
- Low value
- Med value
- High value
- Manually defined low/med/high values (optional)
Critical Inhibitor Concentration Initial Testing

\[
\begin{align*}
\text{Concentration (M)} & \quad \text{i}_{\text{corr}} (\text{uA/cm}^2) \\
\text{1.E-06} & \quad 300 \\
\text{1.E-03} & \quad 250 \\
\text{1.E+00} & \quad 200 \\
\text{1.E+03} & \quad 150 \\
\text{1.E+06} & \quad 100 \\
\end{align*}
\]

**Fig. 8A**

Critical Inhibitor Concentration Initial Testing

\[
\begin{align*}
\text{Concentration (M)} & \quad \text{i}_{\text{corr}} (\text{uA/cm}^2) \\
\text{1.E-06} & \quad 350 \\
\text{1.E-03} & \quad 300 \\
\text{1.E+00} & \quad 250 \\
\text{1.E+03} & \quad 200 \\
\text{1.E+06} & \quad 150 \\
\end{align*}
\]

**Fig. 8B**
SCENARIO 1 – Locating a minimum region

<table>
<thead>
<tr>
<th>lcorr (uA/cm²)</th>
<th>Concentration (M)</th>
</tr>
</thead>
</table>

[Graph showing data points and arrows indicating steps]

1. START
2. Test either side of 3
3. Best candidate selected, Vector established
4. STOP - □ is the minimum

Requirements:
A) Convergence cut-off
B) Fineness of optimisation: low/med/high
C) Max number of wells to be tested

**Fig. 9**
SCENARIO 2 – Locating a plateau

STOP - with respect to the convergence threshold i.e. search algorithm halts when difference between adjacent tests is less than a fixed amount. The lower concentration of the two is selected as the answer.

Fig. 10
SCENARIO 3 – Already at the minimum

![Diagram with Concentration (M) on the x-axis and Icorr (µA/cm²) on the y-axis. The diagram shows a U-shaped curve with a minimum at point 3. Below the diagram:

- **3**: Start
- Test either side of 3
- Results indicate metric of worth increases either side of 3, minimum already reached
- STOP – 3 is the lowest, further tests not necessary

Fig. 11
Fig. 12
Fig. 13
Operational Window

Fig. 14

Operational Window

Fig. 15

**Known**
1. Thiol (-SH group) containing molecules are highly effective
2. Small Thiols are too reactive
3. N heterocyclic compounds show limited effectiveness

![Image of N heterocyclic compound with +SH replacing one of the N atoms]

50% effective

**Hypothesis**
Adding a thiol to a N heterocyclic compound may improve effectiveness

![Image of benzene ring with an H replacing one of the carbon atoms]

?% effective

Fig. 16
Fig. 20

Goal is to minimise FF

Parent molecule

FF1 = exp. results + sim. results + descriptor #1
If no simulation results available sim. results = 0

FF2 = exp. results + sim. results + descriptor #1 + descriptor #2
If no simulation results available sim. results = 0

FF3 = exp. results + sim. results + descriptor #1 + descriptor #2 + descriptor #3
If no simulation results available sim. results = 0

NP40

New parent molecule

FF3 has the lowest value among FF1-FF3, therefore FF3 is the NP40, which is fed into the NN.
Fig. 21

Connect to computational resources

System online and communications sync OK

No

Yes

No

Check internal database database testing is available

Calculation settings

Max number of calculations

Prepare simulation files and directory structure on computational resource(s)

Submit simulations to the queuing system on the computational resource(s)

Poll job queuing system

Timer

Calculation/job complete?

Calculation successful?

Simulation failure identification module

Prepare job for check pointing or resubmission

Wait time insufficient?

Restart/Wall time hard limit

FINISHED

Download and collate results

Job marked as COMPLETE

Job marked as FAILED

Halt particular simulation

Halt

Return error message to user

To be implemented as a loop which runs until all jobs have been classified as failed or complete

(Substitue Sheets
(Rule 26)
RO/AU
Alternative Molecule Searching Module 340

2210
Search Database

2220
Design Experiments

Yes
Tests Successful?

No

2230
Feed results to Neural Networks

2240
Design Experiments for next set of descriptors

Examples

1. Ranking #1
descriptor = -SH
functional group

2. Ranking #2 descriptor
= N-heteroatoms

3. Ranking #3 descriptor
= -NH3 functional group

Fig. 22
Weights of importance manually defined (or automatically defined e.g. neural network derived)
Applies a weighting to the importance of a search term/result, i.e. number of carbon atoms may not be important but the number of epoxide rings may be very important.

Apply rejection to lowest X% of ranked molecules

Update candidate list

Enter results refinement GUI/script

Apply elemental filtering (max # of elements, eliminate results which contain certain elements)

Option to apply user specified search terms, i.e. only search for molecules with a particular functional group

Set molecular weight cut-off and/or min/max limits

Update candidate list

Initiate comparator module GUI/script/code

Molecules are ranked by similarity of search term features which occur in the exemplary molecule

Results display module

Yes

No

Finish

# of results too large?

Fig. 25
Fig. 26
A. CLASSIFICATION OF SUBJECT MATTER

GOIN 35/00 (2006.01)  G05B 15/02 (2006.01)  G05B 19/00 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPODOC, WIAP, PATENW; IPC/CPC: GOIN, G05B . CPC: G01N35/0092, G01N35/0009, G05B19/0426. Keywords (experiment, design, test, discovery, autonomous, robotic, material) & like terms, Applicant/Inventor search; Google, Google Scholar, Google Patents; Keywords (Experimental design, autonomous, material, analysis, database, robot) & like terms; Applicant/Inventor name searched in internal databases provided by IP Australia

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Documents are listed in the continuation of Box C</td>
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<tr>
<td></td>
<td>X Further documents are listed in the continuation of Box C</td>
<td></td>
</tr>
<tr>
<td>*</td>
<td>Special categories of cited documents:</td>
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<tr>
<td>&quot;A&quot;</td>
<td>document defining the general state of the art which is not considered to be of particular relevance</td>
<td></td>
</tr>
<tr>
<td>&quot;E&quot;</td>
<td>earlier application or patent but published on or after the international filing date</td>
<td></td>
</tr>
<tr>
<td>&quot;L&quot;</td>
<td>document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td>
<td></td>
</tr>
<tr>
<td>&quot;O&quot;</td>
<td>document referring to an oral disclosure, use, exhibition or other means</td>
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<tr>
<td>&quot;P&quot;</td>
<td>document published prior to the international filing date but later than the priority date claimed</td>
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<tr>
<td>&quot;T&quot;</td>
<td>later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td>
<td></td>
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<tr>
<td>&quot;X&quot;</td>
<td>document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td>
<td></td>
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<tr>
<td>&quot;Y&quot;</td>
<td>document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td>
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</tr>
<tr>
<td>&quot;&amp;&quot;</td>
<td>document member of the same patent family</td>
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</table>

Date of the actual completion of the international search 31 August 2017

Date of mailing of the international search report 31 August 2017

Name and mailing address of the ISA/AU

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Form PCT/ISA/210 (fifth sheet) (July 2009)
Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:  
   because they relate to subject matter not required to be searched by this Authority, namely: 
   the subject matter listed in Rule 39 on which, under Article 17(2)(a)(i), an international search is not required to be carried out, including

2. [X] Claims Nos.: 30  
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
   See Supplemental Box

3. [X] Claims Nos:  
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [X] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:  

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  

Remark on Protest  
[X] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.  
[X] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.  
[X] No protest accompanied the payment of additional search fees.
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Continuation of Box II
The claim/s do/does not comply with Rule 6.2(a) because it/they rely on references to the description and/or drawings.
This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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