Combinatorial methods have opened exciting new prospects for screening materials for application in a growing number of technological fields ranging from drug discovery\(^1\) to materials science.\(^2\)\(^3\) More recently, these efforts have been paralleled by the use of quantum mechanical calculations to explore the properties of yet to be synthesized materials incorporating just about every stable element in the periodic table as illustrated by the pioneering work of Ceder and collaborators at MIT in the area of cathode materials for Li-ion batteries.\(^4\) Despite the growing number of applications of combinatorial techniques to the study of systems of electrochemical relevance,\(^5\)\(^6\) including electrocatalysis,\(^7\)\(^8\)\(^9\)\(^10\) energy storage,\(^11\)\(^12\)\(^13\)\(^14\)\(^15\)\(^16\) and photoelectrocatalysis,\(^17\)\(^18\) the only contribution that describes the use of an automated liquid dispensing system involving non-aqueous solvents is that of Su et al.,\(^19\) who examined the properties of 2,5-di-tert-butyl-1,4-bis(2-methoxyethoxy)benzene (DBBB), a redox active material displaying promising attributes for non-aqueous flow batteries.\(^19\)

This contribution describes a unique instrument capable of producing large numbers of non-aqueous electrolyte mixtures involving the most common organic carbonate solvents either currently in use or being considered by the Li-ion battery industry. The ability of this device to accurately dispense computer-controlled mixtures of often highly volatile solvents was validated by comparing the intended formulations against data collected by gas-chromatography-mass spectrometric analysis which yielded results within 3.5% of each other. Key to the success of this powerful combinatorial strategy was the use of temperature-controlled reservoirs to decrease the vapor pressure of the solvents involved, as well as the selection of an appropriate solvent and technique to prevent solvent mixing during the aspiration-delivery steps.

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Experimental

All organic solvent formulations were prepared with a programmable non-contact liquid handling instrument (Digilab MicroSYS) placed inside an Ar (Airgas Ar PP300)-filled high quality glovebox (MBraun UNIlab) to avoid contamination with atmospheric components and reduce safety hazards. This box was equipped with a special internal filter for the capture of organic solvent vapors placed in front of the catalyst stage involved in the removal of oxygen and water from the atmosphere within. During operation, the pressure in the glove box varied between 2.0 and 6.0 bar. Schematic diagrams of the system are shown in Fig. 1. The solvents examined in these studies were all provided by BASF (formerly Novolyte, Independence, OH), and included, propylene carbonate (PC), diethyl carbonate (DEC), dimethyl carbonate (DMC), ethyl methyl carbonate (EMC), and a solution of the room temperature solid, ethylene carbonate (EC), in EMC (50:50 by weight).

**SynQUAD aspiration/dispensing mechanism.**— The Digilab MicroSYS instrument employs proprietary technology\(^{20}\) (SynQUAD) for the non-contact, high-speed aspiration and/or dispensing of liquids. A photograph of the overall system is shown in Panel A, Fig. 1. Its operation relies on the coupling of a fixed, high-resolution 1 mL syringe pump (see Panel B, Fig. 1), with a high speed solenoid valve (Panel C, Fig. 1) mounted on a computer-controlled YZ stage (C). This assembly enables accurate computer control of the motion of a system fluid, (B), contained in a fixed glass reservoir kept at room temperature connected through a T valve (not shown) to a coiled Teflon tube ending in a ceramic tip (I.D. = 190 μm) attached to the stage. This instrument incorporates a computer-controlled single axis (i.e. X-axis) translation stage (Fig. 1A), which houses a four-quadrant aluminum reservoir (each quadrant volume = 60 mL, V&P Scientific, Inc. Part #: VP531G-AL, Fig. 1A) filled with approximately 30 mL of solvents to be mixed, labeled as a-d in Panel A. Additionally, this tray holds a sample tray with 2 mL gas chromatography glass vials (LEAP PAL Parts and Consumables LLC, Part #: XAR-1156, Fig. 1A), where the combinatorial formulations are prepared, and other stations involved in the priming and rinsing of the dispensing section of tubing, the disposal of spent liquids, and a vacuum drying station.

The temperature of the sample tray is held at −10 °C by a refrigerated circulating bath (Fisher Scientific, Model # AC200-A40, not shown) placed external to the glovebox, using a 50/50 vol% mixture of ethylene glycol and water as a coolant (see inlet and outlet in A, Fig. 1), to prevent evaporation of the combinatorial specimens during their preparation. Tygon tubing extended from the refrigerated bath through the glovebox walls to the sample tray and back thereby preventing water vapor or oxygen from entering the glovebox environment via the cooling fluid. Great care was exercised to select components incorporating materials impervious to attack by the solvents involved, which included: 316 stainless steel, alumina 203, polyether ether ketone (PEEK), poly(p-phenylene sulfide) (PPS) and ethylene propylene diene monomer (EPDM). Prior to the actual synthesis of the mixtures, the reservoir and the Teflon coil were filled with propylene carbonate, PC, the organic carbonate that displays the lowest vapor pressure among the liquid solvents selected for these studies and thus best suited to serve as system fluid. Direct contact between system fluid and the organic carbonates during aspiration and dispensing is avoided by interposing one or more Ar bubbles between the two liquids held in place by surface tension, as depicted in Panel D, in Fig. 1 (vide infra).
Figure 1. Photographs of the key components of the Digilab MicroSys instrument (Panels A through C). Panel D provides a schematic diagram of the strategy implemented in this work to prevent intermixing between the system solvent buffer and that being aspirated and delivered as part of the combinatorial mixtures.

The basic Digilab MicroSYS operations, including platform positioning and syringe displacement, are controlled by AxSYS, a software program provided by the vendor. For more complicated procedures, a LabVIEW program was written to interface with AxSYS, allowing full control over all relevant system parameters, including the solvent buffer volume, Ar bubble volume, positions and velocities of motors, and all others associated with the filling of the GC vials with the desired combinatorial mixtures. This program is capable of taking any arbitrary tabulated formulation of up to four solvents (within the dispensing precision of the Digilab machine) and directly synthesizing it.

The synthesis procedure is initiated by filling and emptying the tubing completely with PC three times. Once refilled, an Ar bubble, typically 5 \( \mu \text{L} \) in volume (larger volumes were found to be unstable and broke apart into multiple smaller volumes, while smaller volumes did not span the cylindrical tubing enough to prevent cross contamination) is introduced into the end of the Teflon tubing through the tip followed by a droplet of the first solvent selected, say A, for delivery. This strategy was found to be insufficient to prevent cross contamination, as evidenced by presence of PC in the GC-MS analysis of combinatorial mixtures not involving this species. These problems were later solved by introducing a second Ar bubble and solvent drop. At this stage, the YZ stage moves the tip to the target tray to aspirate a volume of A, ca. 0.8 mL maximum. After each aspiration, the pressure inside the syringe and the tubing is allowed to equilibrate with the atmosphere to help ensure accuracy while dispensing. The tip is then placed above the specified vial in the tray and A is dispensed. It should be stressed that the SynQUAD technology dispenses liquids at high velocities creating a jet out of the ceramic tip, and the solenoid valve acts to quickly cut the fluid flow. In this fashion, one can eject the entire volume of liquid into the vial, thereby preventing droplets from remaining adhered to the external walls of the tip which would otherwise reduce the accuracy of the process.

This protocol is then repeated until all the vials are filled with the desired amount of solvent A. At that point, the gas bubbles and solvent droplets are ejected from the tip of the tubing into the waste tray, and the ceramic tip is cleaned by the vacuum station to remove any residual A clinging to the walls. A new sequence of Ar bubbles and liquid drops is then assembled using the second solvent, B, and the entire aspiration-delivery procedure repeated. For each of the mixtures, the sum of all of the volumes delivered was set at 1 mL, which does not necessarily correspond to the actual final volume of the mixture. Once the total synthesis is fully completed, i.e. solvents C and D had been dispensed, the vials are sealed with air-tight PTFE/Silicon caps (LEAP PAL Parts and Consumables LLC, Part #: XAR-1575).

Initial testing of the robot performance was conducted outside the glovebox and aimed at verifying that the LabVIEW program correctly controls the Digilab instrument and involved the use of deionized (DI) water as the system fluid, and aqueous solutions containing in each case three food colorings, i.e. Red, Blue and Yellow. A computer program was written to prepare 360 \( \mu \text{L} \) of 35 different solutions containing these colorings in prescribed proportions into the wells of a conventional combinatorial tray. Out of this set, seven solutions were selected at random and diluted in a 1 to 5 ratio to obtain a volume large enough for measuring their UV visible spectra in a 1.5 mL quartz cuvette, and, subsequently, stored in sealed plastic containers to minimize evaporation. Separately, solutions of the same compositions as the seven selected based strictly on the Digilab program instructions were prepared by hand using an analytical micropipette (Eppendorf).
Figure 2. Ultraviolet-visible transmission spectra of four aqueous mixtures, labeled as A, B, C, D, involving three different coloring dyes. The relative compositions of the mixtures are given in Table I. The blue and black curves represent manually-, and robot-prepared samples, respectively.

and diluted as specified above. A UV visible spectrophotometer (Cary 50 Bio) was then used to record the spectrum of all the solutions allowing direct comparisons to be made between those obtained from those prepared by hand and by the use of the Digilab. These are shown in blue (thick line) and black (thin line) in Panels A through D, Fig. 2, respectively, where the actual volume ratios of the dyes in the mixture are given in each panel. The spectra of each of the pure colorings are given in the Supplementary Material. The good agreement between the two sets of data for all the specimens examined serves to validate both the program as well as the overall operation of the Digilab instrument.

**GC-MS measurements.**—The composition of all organic solvent mixtures prepared by the combinatorial robot was assayed using a Hewlett Packard GC/MS (controlled by Xcaliber) equipped with an Rtx-200MS GC column (30 m in length, 0.25 mm I.D. 1 μm, RESTEK Corporation). The temperature of the injector, as well as that of the interface and ion source, was 200°C. The injection method is split, and the split ratio is 1:100. The carrier gas employed was He at constant linear velocity mode, the velocity is 40 cm/s, the GC column temperature was set at 40°C at 3 min, and increased at a rate of 8°C/min to 220°C, and maintained at that temperature for 5 min. Ionization mode is EI for the MS, acquisition mode is scan, the m/z scan range is 35–350. Event time is 0.3 s. For all the measurements, a 1 μL aliquot of the materials to be analyzed, including the standards, were dissolved in 1 mL acetonitrile (HPLC purity, Sigma Aldrich) and injected into the GC-MS with a 5 μL syringe (Fisher Scientific). Standard plots of the integrated area and volume or weight of the solvent of interest in acetonitrile were constructed from data collected from runs involving each of the solvents at four different concentrations. Plots of the integrated area under the chromatographic peak as a function of concentration are shown in Figure S2 and the statistical linear fits for each of the solvents in Table S2 in the Supplementary Material, respectively.

A typical chromatogram of a mixture of all the solvents in acetonitrile, shown in Fig. 3, illustrates the differences in the retention times of the solvents involved in the measurements reported in this work. As specified above, the robot delivers each of the solvents as prescribed volumes which are specified in the corresponding column for each of the mixtures. The conversion to mol and then to molar fraction was performed through elementary calculations based on the density, ρi, and molecular weight, MWi, of the solvent i (see Table S1 in the

![Figure 3](https://example.com/figure3.png)

Figure 3. Typical chromatogram of a mixture of all the solvents of relevance to this study.
### Table I. Intended Delivered Volumes, $V_{int}$ (in mL) and Intended, $X_{int}$, and Found Molar Fractions, $X_{found}$ (in %), and Errors, $E$ (in %), for the Various Combinatorial Solvent, $S$, Mixtures Prepared by the Robot.

| S   | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.25      | 28        | 24.8        | 2    |
| EMC | 0.25      | 36.5      | 39          | 1.3  |
| DEC | 0.25      | 19.5      | 18.7        | 0.8  |
| EC  | 0.25      | 16.1      | 17.5        | 1.8  |
|     | 0.50      | 53.9      | 57.5        | 0.5  |
|     | 0.50      | 46.1      | 42.5        | 0.5  |
|     | 0.25      | 28.8      | 25.3        | 0.8  |

| A2  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.20      | 22.6      | 20.7        | 1.4  |
| EMC | 0.30      | 41.5      | 43.8        | 1.3  |
| DEC | 0.25      | 19.7      | 18.8        | 1.3  |
| EC  | 0.25      | 16.2      | 16.6        | 0.5  |
|     | 0.25      | 55.1      | 56.6        | 1.5  |

| A3  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.20      | 23.4      | 21.2        | 1.2  |
| EMC | 0.20      | 30.5      | 32.4        | 1.3  |
| DEC | 0.40      | 32.6      | 32.6        | 0.5  |
| EC  | 0.20      | 13.5      | 13.8        | 0.35 |
|     | 0.50      | 54.9      | 52.4        | 0.5  |

| B1  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.25      | 26.7      | 23.5        | 1.3  |
| EMC | 0.10      | 12.9      | 10.5        | 1.3  |
| DEC | 0.10      | 18.6      | 20.2        | 0.2  |
| EC  | 0.10      | 15.3      | 15.4        | 0.0  |
| PC  | 0.25      | 26.4      | 27.8        | 0.8  |

| B2  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.25      | 27.2      | 25.3        | 0.8  |
| EMC | 0.10      | 10.4      | 7.5         | 1.5  |
| DEC | 0.20      | 20.8      | 20.6        | 0.4  |
| EC  | 0.70      | 39.8      | 42.3        | 0.5  |
| PC  | 0.0      | 0.0       | 0.0         | 3.5  |

| C1  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.10      | 9.9       | 7.1         | 1.8  |
| EMC | 0.30      | 39.6      | 40.9        | 0.7  |
| DEC | 0.20      | 23.4      | 23.1        | 0.2  |
| EC  | 0.30      | 23.4      | 23.1        | 0.2  |
| PC  | 0.20      | 23.4      | 23.1        | 0.2  |

| C2  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.10      | 10.8      | 8.9         | 0.9  |
| EMC | 0.0      | 0.0       | 0.0         | 3.5  |
| DEC | 0.30      | 40.3      | 41.6        | 1    |

| C3  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.10      | 10.4      | 7.5         | 1.5  |
| EMC | 0.45      | 51.9      | 55.7        | 1.9  |
| DEC | 0.20      | 20.8      | 19.4        | 0.5  |
| EC  | 0.15      | 17.6      | 16.1        | 0.35 |
| PC  | 0.0      | 0.0       | 0.0         | 3.5  |

| C4  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.10      | 10.4      | 7.5         | 1.5  |
| EMC | 0.15      | 30.9      | 32.5        | 0.8  |
| DEC | 0.25      | 20.5      | 19.4        | 0.15 |
| EC  | 0.15      | 17.6      | 16.1        | 0.35 |
| PC  | 0.0      | 0.0       | 0.0         | 3.5  |

| D1  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.25      | 19.5      | 18.7        | 0.8  |
| EMC | 0.70      | 71.2      | 74.7        | 0.2  |
| DEC | 0.20      | 13.1      | 13.1        | 0.2  |
| EC  | 0.20      | 22.7      | 22.3        | 0.8  |
|     | 0.0      | 0.0       | 0.0         | 3.5  |

| D2  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.20      | 38.7      | 40.8        | 1.1  |
| EMC | 0.0      | 0.0       | 0.0         | 0.5  |
| DEC | 0.20      | 15.4      | 14.1        | 0.5  |
| EC  | 0.40      | 24.8      | 24.5        | 0.5  |
| PC  | 0.20      | 21.5      | 20.5        | 0.5  |

| D3  | $V_{int}$ | $X_{int}$ | $X_{found}$ | $E$  |
|-----|-----------|-----------|-------------|------|
| DMC | 0.25      | 55.1      | 56.6        | 1.5  |
| EMC | 0.50      | 54.9      | 52.4        | 0.5  |
| DEC | 0.0      | 0.0       | 0.0         | 0.0  |
| EC  | 0.75      | 67.8      | 70.1        | 0.75 |
| PC  | 0.25      | 32.2      | 29.9        | 0.75 |

Supplementary Material). For example, in the case of A1 in Table I, for which the volumes of DMC, EMC, DEC, and EC/EMC delivered were all 0.25 mL, the number of mol of DMC is $V_{DMC} \times \rho_{DMC} / MW_{DMC} = 0.25 \times 1.07 / 90.08 = 2.97$ mmol, and those for EMC and DEC can be calculated accordingly. For EC, the number of mol would be given by $V_{EC} \times \rho_{EC/EMC} 50% / MW_{EC} = 0.25 \times 1.2 \times 0.5 / 88.06 = 1.7$ mmol, where the symbol $\rho_{EC/EMC}$ represents the density of the 50:50 EC/EMC (by weight) solution measured independently. The actual composition of the EC/EMC solution was confirmed by GC-MS. The contribution to the total amount of EMC in the mixtures derived from addition of the EC/EMC was added to that of the single solvent. On this basis, the mol fraction of each component $i$ in the mixture in percent, $%n_i$, would be given by $%n_i = 100 \times n_i / \sum N_j n_j$ leading to the ratio 28.0:36.5:19.5:16.1 as shown under $X_{int}$ in Table I.

Shown in Fig. 4 are histograms showing the intended (dark bars) and found (via GC-MS analysis, adjacent light bars) solvent mol fraction for eight different solvent formulations prepared by the robot. The measured mol of each solvent was calculated from standard curves (Supplementary Material).
prepared from solutions of each of the solvents in acetonitrile (see Fig. S2). Based on the results obtained, the differences between the intended and measured formulations for all the mixtures examined were found in the range 0.5% to 3.5% providing ample support for the reliability of the robot.

In summary, a Digilab MicroSYS instrument was judiciously adapted to dispense with very high degree of accuracy prescribed formulations of mixtures of solvents commonly used in the lithium-ion battery industry. The system displays sufficient flexibility to handle a much larger array of solvents and additives to extend its use to other technological areas, such as supercapacitors, and thus contribute to the discovery of electrolyte formulations with optimized performance.

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