

# Development and Implementation of a Simple, Engaging Acid Rain Neutralization Experiment and Corresponding Animated Instructional Video for Introductory Chemistry Students

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## S Supporting Information

**ABSTRACT:** Here we describe an acid rain neutralization laboratory experiment and its corresponding instructional video. This experiment has been developed and implemented for use in the teaching laboratory of a large introductory chemistry course at Brown University. It provides a contextually relevant example to introduce beginner-level students with little or no acid–base chemistry background to the basic theories of solution chemistry. First, students measure the conductivity of water samples with different ionic compositions, serving as an introduction to the conductivity of solutions. Second, to simulate the neutralization reaction between acid rain and limestone as it occurs in nature, students pass a sulfuric acid solution through a column containing calcium carbonate and monitor the conductivity of the resulting solution. Students are then required to graph conductivity versus volume of sulfuric acid added to the calcium carbonate column and use the resulting plot to calculate the equivalence point. Additionally, an instructional video containing animated features was created and utilized to engage students in learning new chemistry concepts by relating chemistry to their daily lives and helping them visualize experimental setups. Significantly, the experiment has been adapted to include the use of a pH probe or multimeter to make it more accessible to K–12 classrooms and teaching laboratories without access to conductivity probes.

**KEYWORDS:** *First-Year Undergraduate/General, High School/Introductory Chemistry, Hands-On Learning/Manipulatives, Collaborative/Cooperative Learning, Environmental Chemistry, Conductivity, Green Chemistry, Laboratory Equipment/Apparatus, Laboratory Instruction*

## INTRODUCTION

The objective of laboratory curriculum development, in addition to reinforcing core concepts, is to design experiments that students are actively engaged in without generating large amounts of chemical waste. In the teaching laboratories at Brown University, an emphasis is placed on exposing students to a wide variety of theories and modern experimental methods. Furthermore, as an instructor, it is also important to continuously evaluate, modify, and develop new methods to effectively present course content. Context-based learning is one of several teaching styles that has been shown to be successful in chemistry courses.<sup>1</sup> It is proposed that student interest and enjoyment increases with context-based learning, and “traditional approaches are not motivating students to study chemistry at more senior levels”.<sup>1</sup> Additionally, through context-based learning, students may more easily see and appreciate the connection between science and their lives, which can lead to a deeper understanding of difficult concepts.<sup>1</sup> However, there are some proposed limitations to context-based approaches. For example, if the connection between context-based examples, that is, environmental science, and course concepts are not apparent, students may feel as if the course is fragmented or may not be able to connect ideas between course topics.<sup>2</sup>

Because of the relevance of implementing “green” chemistry initiatives and public awareness regarding climate change caused by green house gases and other industrial sources of

air pollution, we aimed to design an environmental chemistry experiment. More specifically, an experiment explored acid rain neutralization, introduced the topics of acid–base chemistry and conductivity, and was suitable for integration into a K–12 curriculum. Importantly, we wanted to emphasize to students the connection among experimental concepts, lecture concepts/discussions, and the real world.

Experiments modeling acid rain neutralization have been previously performed, most commonly, by monitoring pH changes. For example, in 1985, Ophardt et al. proposed a simple experiment in which students would collect rainwater and measure its acidity via titration with sodium hydroxide.<sup>3</sup> Baedeker et al. described an experiment in which students would spray slabs of marble and limestone with acidic solutions, collect the runoff, and measure its pH to determine the extent of the stone erosion.<sup>4</sup> Schilling et al. passed sulfuric acid through a column containing sand mixed with calcium carbonate and titrated the acid to determine its concentration.<sup>5</sup> Powers et al. designed a laboratory experiment in which students would examine the buffering capacity of calcium carbonate.<sup>6</sup> These aforementioned experiments involve lengthy titrations and require that students have an in-depth understanding of acid–base chemistry.

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In contrast to monitoring pH changes, others have conducted acid rain experiments by alternative methods. In 1973, Gleason proposed an experiment in which students would collect rainwater and measure its nitrate concentration via reduction by cadmium, which changed the absorbance of the solution.<sup>7</sup> Experiments have also been designed to measure the sulfate concentration of rainwater by the thoron colorimetric method<sup>8</sup> or through the use of a turbidity meter following a precipitation reaction with barium chloride.<sup>9</sup> However, no prior work has been reported on using a conductivity probe to monitor the neutralization of a solution mimicking acid rain.

In this article, we report a simple, engaging acid rain neutralization experiment and corresponding animated instructional video. This experiment was developed and implemented for introductory chemistry students. Students pass a sulfuric acid solution through a column containing calcium carbonate to simulate the neutralization reaction between acid rain and limestone as it occurs in nature. Additionally, an instructional video containing animated features was created and utilized to engage students in learning new chemistry concepts, relating chemistry to their daily lives, and helping them visualize experimental setups. Significantly, the experiment has been adapted to include the use of a pH probe or multimeter to make it more accessible to K–12 classrooms and teaching laboratories without access to conductivity probes.

### Acid Rain, pH, and Electrical Conductivity

While normal rainwater has a pH of approximately 5.6, the pH of acid rain is usually 4.5–2.0 and can be even lower.<sup>5</sup> In parts of the northeastern United States, pH values of rain have been measured at 4.2–4.5, which is 15–30-times more acidic than unpolluted rain.<sup>9</sup> Fortunately, a variety of different mechanisms exist by which excess acid in rain is neutralized by sand and soil. These reactions involve the consumption of hydrogen ions by basic compounds found in natural minerals; one such mineral is limestone, which contains calcium carbonate,  $\text{CaCO}_3$ .<sup>5</sup>

Acid rain is typically caused by pollutants in the atmosphere often resulting from the combustion of fossil fuels. These pollutants react with water molecules in the atmosphere to produce acids. The two major anthropogenic acids in acid rain are sulfuric acid ( $\text{H}_2\text{SO}_4$ ) and nitric acid ( $\text{HNO}_3$ ). Sulfur dioxide ( $\text{SO}_2$ ) is released into the atmosphere during the combustion of sulfur compounds in fossil fuels. In the presence of oxygen ( $\text{O}_2$ ), sulfur dioxide ( $\text{SO}_2$ ) can be oxidized to form sulfur trioxide ( $\text{SO}_3$ ), which is then converted to sulfuric acid ( $\text{H}_2\text{SO}_4$ ) in the presence of water. Nitric oxide ( $\text{NO}$ ) and nitrogen dioxide ( $\text{NO}_2$ ) in the atmosphere (also combustion products) are the main precursors of nitric acid.<sup>9</sup> In acid rain on the west coast of the United States, sulfuric and nitric acid are found in approximately equal ratios, but in the northeastern United States, sulfuric acid dominates the composition of acid rain by a factor of 3 to 2.<sup>9</sup>

Water found in nature is never completely pure and contains a variety of electrolytes. Conductivity probes can be used to measure the number of ions that are dissolved in a solution; they are therefore appropriate instruments to use when studying electrolytes. The classical example used to explain conductivity of solutions, in both the college and K–12 setting, is to demonstrate the ability of different solutions (most commonly water, sugar, and salt) to complete an electric circuit and turn on a light bulb. However, a case study from *Research and the Quality of Science Education* showed that conductivity is

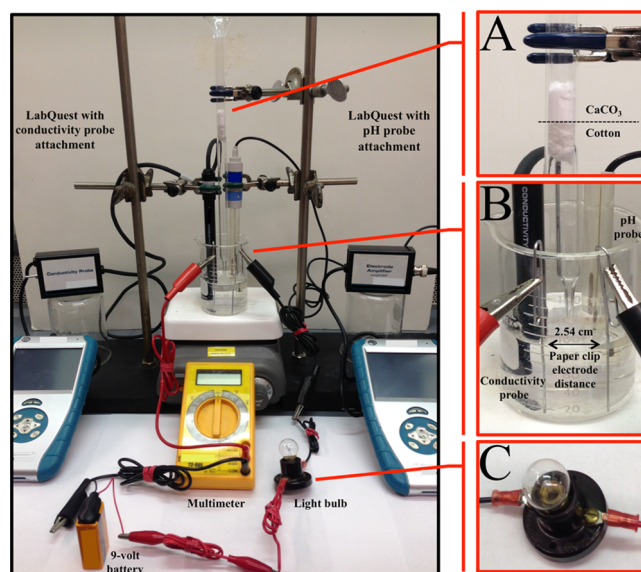
a particularly problematic concept for high school students.<sup>10</sup> Namely, the identity of the charge carriers in different materials such as metals versus electrolytes.<sup>10,11</sup> Indeed, there are also misconceptions about the ability, and magnitude, of ions to conduct electricity based on chemical identity and balanced equations.<sup>12</sup>

There is a relationship between the pH and conductivity of a solution. However, conductivity may be conceptually challenging for students because there are more factors that affect the conductivity of an electrolytic solution (i.e., concentration of all ions present and ionic mobility).<sup>13</sup> One of the goals of this experiment was to address the difficulties students have with the understanding of conductivity.

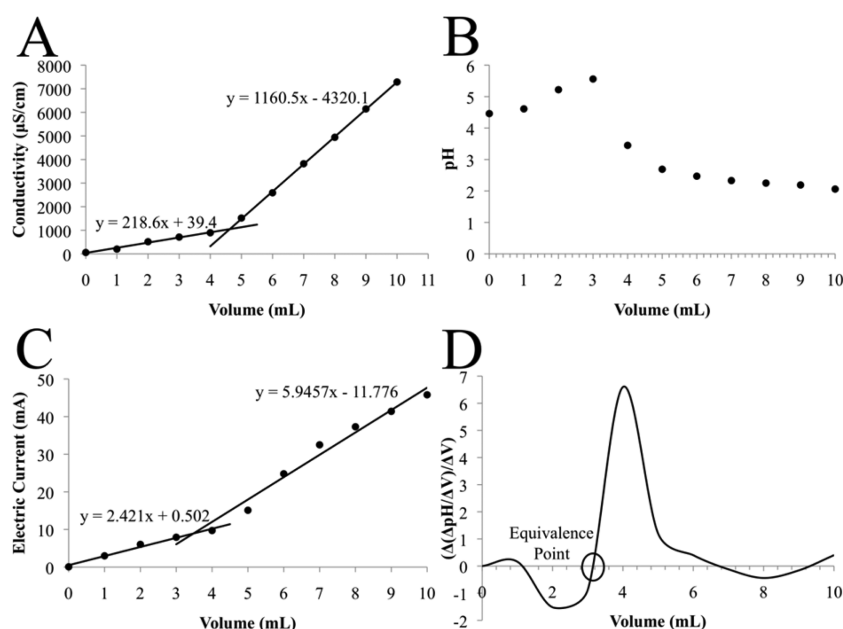
### LABORATORY DESCRIPTION

This experiment has been performed at Brown University with class sizes of up to 500 students since the spring of 2014. Our introductory chemistry teaching facilities allow for laboratory sections of 16–18 students, and students are required to work in pairs for this experiment. At Brown, enough instrumentation was necessary to perform the experiment simultaneously with approximately 50 pairs of students per afternoon. A step-by-step procedure and laboratory report for students can be found in the [Supporting Information](#). The costs of LabQuests and conductivity probes provided for this experiment may be prohibitive to some universities and, likely, many K–12 institutions. However, this experiment can be performed using a pH probe, commonly found in university teaching laboratories, or a multimeter, commonly found in K–12 science classrooms. An image of the experimental setup and a sample set of experimental data for all three methods are shown in [Figures 1 and 2](#).

This experiment contains a visualization component as well. It is known that the visualization tools enhance learning and interest in science. Many online videos are readily available for helping students understand chemistry concepts. Students are



**Figure 1.** Experimental setup required for the experiment showing the pH probe (right), multimeter (center), and conductivity probe (left). (A) The cotton and calcium carbonate plug in the glass column. (B) The position of the probes and paper clip electrodes. (C) The light bulb wired to the setup using the multimeter.



**Figure 2.** Experimental data for the neutralization of sulfuric acid by calcium carbonate monitored by (A) conductivity probe, (B) pH probe, and (C) multimeter. (D) Second derivative plot of pH versus the volume added plot given in panel B for the determination of the equivalence point.

also encouraged to create their own YouTube videos for learning specific chemical concepts taught in the classroom. For example, students were challenged to create and upload YouTube videos that could be used to help themselves and others learn the rules of solubility and organic and polymer chemistry concepts.<sup>14–16</sup> For this particular experiment, original instructional videos containing both animated features and a short film were developed and used to engage students in learning environmental science concepts, relate chemistry to real-world issues, and help them visualize experimental setups prior to entering the laboratory.

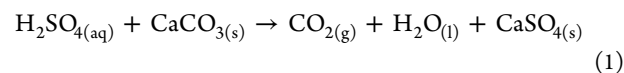
In the first part of this laboratory, the conductivities of various water samples are examined using a conductivity probe in combination with LabQuest, a Vernier program used for science education. The unit of conductivity used in this experiment is the microSiemens per centimeter, or  $\mu\text{S}/\text{cm}$ . When the experiment is performed for measuring electric current using a multimeter, the unit used is the Ampere. Water samples selected for this experiment can include deionized, tap, ocean, pond, pool, rain, or any other water samples that the instructor chooses to use. Students can classify the water samples as strong, weak, or nonelectrolytes based on the conductivity or current measured.

To complete the first part of this laboratory, students should assemble the conductivity probe and multimeter, utility clamp, and ring stand as instructed in the experimental procedure (Supporting Information). The water samples should be provided to students in capped vials and can be saved for use after the measurements are taken. The conductivity probe provided with the LabQuest hardware can be used to measure conductivity on three different levels of sensitivity; the three settings are 0–200  $\mu\text{S}/\text{cm}$ , 0–2000  $\mu\text{S}/\text{cm}$ , and 0–20000  $\mu\text{S}/\text{cm}$ . For accurate readings, students should measure the conductivity of the ocean, pool, and pond water at the 0–20000  $\mu\text{S}/\text{cm}$  setting and the tap, deionized, and rainwater at the 0–200  $\mu\text{S}/\text{cm}$  setting. The most appropriate setting for the multimeter was 20 mA, but this setting may vary based on the water sample used at other institutions. Additionally, the

applied voltage was 9 V, provided through the use of a 9-V battery (Supporting Information). It is important to emphasize to students that the measurement of current by this method is significantly dependent on the position of the paper clip electrodes. The distance between the paper clips should remain consistent throughout the experiment and must not be changed or manipulated to prevent the occurrence of additional errors. In the experiments reported here, the paper clip electrode separation distance was 2.54 cm for all water samples. Although not tested, the first part of the experiment could be also conducted using a pH probe.

It is recommended that instructors emphasize to the teaching assistants the importance of actively engaging students in the discussion of the relationship between electrical conductivity and pH. This will help students understand broader concepts and prepare them to interpret the results of the acid rain neutralization part of experiment.

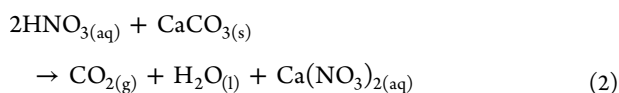
In the second part of this laboratory, a dilute solution of sulfuric acid is used to simulate the properties of acid rain. Sulfuric acid was chosen because it is the acid that dominates the composition of acid rain in the northeastern United States.<sup>9</sup> The “acid rain” solution is passed through a column containing calcium carbonate to simulate the neutralization of acid rain by limestone (Figure 1A). The reaction of sulfuric acid with calcium carbonate is shown in eq 1:



The products of this reaction as well as the equivalence point between the sulfuric acid and the calcium carbonate can be monitored using the conductivity probe, multimeter, or pH probe.

The solid calcium sulfate product will not conduct electricity well. Although it is an ionic compound, it is only marginally soluble in water, and the ions do not dissociate to an appreciable extent to conduct electricity. Sulfuric acid, however, is a strong molecular acid and therefore will be a good conductor of electricity. Although nitric acid is also a major

contributor acid rain, it was not used in this experiment because the product of its reaction with calcium carbonate (eq 2), calcium nitrate, is highly water-soluble and the conductivity reading will be complicated by all of the ions ( $\text{H}^+$ ,  $\text{Ca}^{2+}$ , and  $\text{NO}_3^-$ ) present in solution:



When excess acid is run through the column containing calcium carbonate, the conductivity of the solution passed through the column will increase due to the strong dissociation of the acid. This will lead to a change in the slope of the line when conductivity is plotted against the volume of acid added (Figure 2). The point on the  $x$ -axis at which the slope of the line changes corresponds to the equivalence point of the reaction. Students are given an excess volume of an unknown concentration of sulfuric acid solution and are required to determine the equivalence point to calculate the concentration of the acid solution.

To complete this second part of the laboratory, students deliver the sulfuric acid solution to the calcium carbonate column in 1 mL increments using a calibrated automatic pipet. To prepare the column, students can use disposable Pasteur pipettes or other similar glass pipettes. The column contains a small amount of calcium carbonate and a small piece of cotton, which holds the calcium carbonate in place (Figure 1A). Students should clamp the prepared column upright next to the probe and place a stir plate beneath the column and the conductivity probe, paper clip probe, or pH probe. A clean beaker containing a small amount of distilled water is used to catch the liquid that passes through the column. The conductivity probe, paper clip probe, or pH probe should be submerged in this water for an accurate reading (Figure 1B).

As the acid is added to the calcium carbonate, students will observe bubbles forming within the column as carbon dioxide is produced. The acid added to the column will not typically flow freely through the column, and students will need to push the liquid through the column using a pipet bulb. This must be done slowly to give the acid enough time to react with the calcium carbonate in the column. It is important to note that this process is likely a source of error since there is the chance of the acid not being fully neutralized if it "leaks" through the column or is pushed through too fast. The air from the pipet bulb will force liquid to pass through the column, but it may also push the cotton lower into the column. This is not a problem, as the cotton will become stuck at the bottom of the column where the glass pipet narrows.

The amount of calcium carbonate recommended for use is  $0.1000 \text{ g} \pm 0.0100 \text{ g}$ . The actual quantity used will likely vary between students, but it is important to instruct them to record the exact mass used. The sulfuric acid solution of 0.180 M was provided to the students. The instructor, depending on the time and materials available, may vary the experimental parameters; however, students should run multiple trials for practice and error analysis.

The second part of the laboratory experiment involves data analysis using Microsoft Excel or a similar graphing program. Students plot the values measured for conductivity, pH, or current versus the volume of acid added to their column. Next, students should find the best-fit linear line for points 0–5 mL and points 6–10 mL, separately. To find the equivalence point, students set the two best fit lines equal to one another and

solve for  $x$ . In the case of analysis using the pH probe, the equivalence point is determined from the  $x$ -intercept of the second derivative plot of pH versus volume of acid added (Figure 2D) or it can be estimated from the inflection point of the plot of the raw data. From this information, students can calculate the concentration of the acid they were provided and determine the percent error of their measurements. This data analysis can give the instructor a measure of the quality of the data collected by each student.

## HAZARDS

Sulfuric acid is corrosive and should be handled with care. If any reagents contact the skin, wash off immediately. If you spill the acid on wood cabinets or benches, please wipe off and rinse with water.

## SAMPLE RESULTS AND DISCUSSION

A sample set of conductivity and current values measured for first part of the experiment is shown in Table 1. All of the water

**Table 1. Conductivity and Current Readings for Various Water Samples**

Sample	Conductivity ( $\mu\text{S}/\text{cm}$ )	Electric Current (mA) <sup>a,b</sup>
Deionized	3	Not measured
Tap	168	Not measured
Rain	24	0.5
Pond	690	7.1
Pool	6980	41.1
Ocean	29140	69.1

<sup>a</sup>The applied voltage, for the experimental setup requiring the use of a multimeter and light bulb to quantitatively and visually monitor electric current, for all of the water samples was 9 V. This applied voltage was provided through the use of a 9-V battery and is described in further detail in the Supporting Information. <sup>b</sup>The paperclip electrode separation distance, for the experimental setup requiring the use of a multimeter and light bulb to quantitatively and visually monitor electric current, remained constant between all of the water samples at a distance of 2.54 cm.

samples were collected in Rhode Island. The conductivity probe is sensitive enough to distinguish all six types of water. The pond, ocean, and pool water samples have the highest conductivities, while deionized and rainwater have very low conductivities. Students can even observe a difference between tap and deionized water and draw conclusions on the relative ion composition of these samples from their results. When electric current of the samples was measured using the multimeter, similar trends were observed. The pool and ocean water have the highest current readings. It is important to note that the multimeter is markedly less sensitive than the conductivity probe, and current readings are prone to higher error due to differences in readings based upon the positioning of the paper clip electrodes (Figure 1B). Using the multimeter may more effectively allow younger students to appreciate the theories of conductivity and current because the solutions with the largest ion concentration will cause the light bulb (Figure 1C) to glow the brightest.

Students can classify the water samples as strong, weak, or nonelectrolytes (Table 2) based on the conductivity values measured. This laboratory will provide an experimental introduction to the concept of dissociation and conductivity, as discussed in a typical lecture course. From their data,

Table 2. Electrolyte Classification for Various Water Samples

Sample	Classification
Deionized	Nonelectrolyte
Tap	Weak or nonelectrolyte
Rain	Weak or nonelectrolyte
Pond	Weak electrolyte
Ocean	Strong electrolyte
Pool	Strong electrolyte

students can also draw conclusions about the ion content of the samples studied. For example, students should be able to infer that the rainwater has low ion content or contains ions that do not sufficiently conduct because the measured conductivity of the rainwater sample is low. At Brown University, this further translates to an understanding of acid rain in Rhode Island, which is not very acidic. Students learned from the data collected in the laboratory that air pollution in Rhode Island is not a major problem and does not lead to significant production of acid rain. However, if this experiment were implemented in other parts of the country, the conductivity of a typical rainwater sample would likely be different and should therefore lead the students to draw different conclusions. In their laboratory reports, students are asked “What would you expect the approximate pH of the rain water sample in Rhode Island (where your school is located) to be, and why?” (see [Supporting Information](#)).

In the second part of the experiment, students used conductivity measurements to monitor the reaction between sulfuric acid and calcium carbonate. In parts of the world where

acid rain is a more pressing problem, students could collect rainwater themselves and use it in place of the sulfuric acid required for the above experiment. [Figure 2](#) shows a sample data set for monitoring changes in pH, electric current, and conductivity during the reaction between sulfuric acid and calcium carbonate. A change in slope of conductivity is clearly visible at an acid volume of approximately 5 mL shown in [Figure 2A](#). The best fit lines for the first and second half of the data are also given in [Figure 2A](#). Students can set these two equations equal to one another and solve for  $x$  to give the volume of acid at the equivalence point of the reaction. This volume can then be used, in combination with the exact mass of calcium carbonate placed in the column, to calculate the concentration of sulfuric acid provided to them. Similarly, the equivalence point and acid concentration can be determined from the analysis of the electric current plot given in [Figure 2C](#). However, the equivalence point determined from pH measurements is obtained from the second derivative plot of the pH versus volume plot given in [Figure 2B](#). It is important to note that the second derivative plot shown in [Figure 2D](#) may not be very accurate because it is generated from 11 individual data points. However, it is still in agreement with the equivalence point determined visually from the inflection point of the pH curve in [Figure 2B](#). Collecting more data points may help with the accuracy of the second derivative plot for the pH measurements. The equivalence points, experimentally calculated sulfuric acid concentrations, and their errors based on the actual concentration of 0.180 M for various methods are listed in [Table S1](#) ([Supporting Information](#)). The experimental errors of sulfuric acid concentrations depend on the method used for

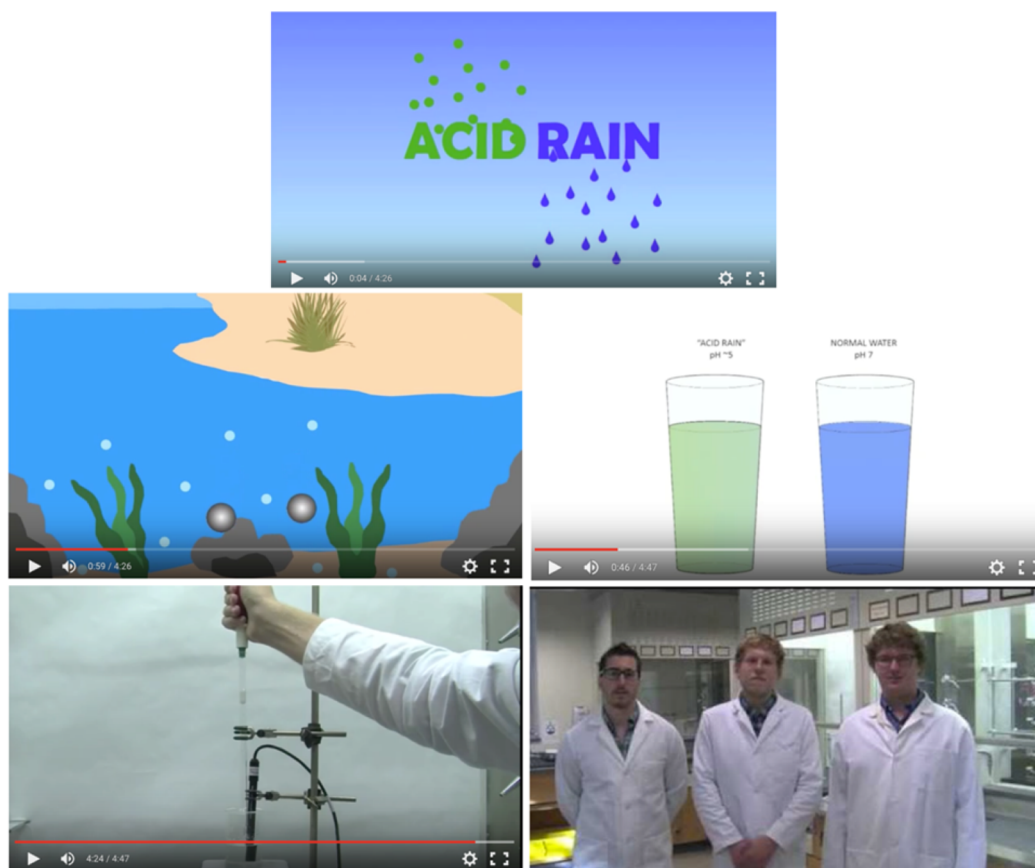


Figure 3. Selected video screen shots from the animated instructional video made for the acid rain laboratory.

monitoring the reaction. The conductivity meter, with the highest sensitivity, gives the best fitting data and a concentration closest to the actual concentration (more discussions on experimental errors and the standard deviation can be found in the [Supporting Information](#)). It is not surprising that relatively large errors are found for the calculated acid concentrations due to the limitations of simple experimental procedures. In the laboratory report ([Supporting Information](#)), students are asked to calculate experimental errors and identify possible sources of errors associated with the measurements. From this simple experiment, students not only learn about acid rain neutralization and how to determine the equivalence points, but also are introduced to the experimental errors and possible sources of errors associated with the measurements.

### ■ ANIMATED INSTRUCTIONAL VIDEO

The animated instructional video, which accompanied the experiment, was developed through a collaborative effort between the faculty and students. The video can be watched on Youtube.<sup>17</sup> [Figure 3](#) displays a few screen shots from the students' animated instructional video explaining acid rain and their video demonstration of the laboratory. The instructional video contains animated features that highlight the importance of acid rain in the real world. The short film, which captures a live demonstration of laboratory equipment setup and key procedures performed by our undergraduate students, allows students to visualize the experimental techniques used prior to entering the laboratory. Students can watch these videos as part of their laboratory preparation. The use of such media helps students understand highlighted concepts and get familiar with the laboratory equipment setup before the experiment.

Our previous studies<sup>18,19</sup> have shown that involving undergraduates in developing new pedagogical methods through collaborative teaching enabled us to create engaging material that stimulates students' interest and enhances their learning. This animated instructional video is an example of collaboration between faculty and students to develop a new pedagogical approach: using visualization tools in teaching an introductory chemistry laboratory course. The video for the acid rain laboratory was our first effort at using an animated video to engage students in their learning of general chemistry. Although this laboratory is relatively simple, many experiments in the introductory chemistry course at Brown University involve complex equipment setups and procedures; as such, it has been very challenging for many freshmen with little or no prior experience in chemistry laboratories to carry out these experiments despite our best efforts at revising the laboratory manual. Without visualization of laboratory equipment and key steps in the procedure, it is difficult for students to follow the manual. Students often get confused and frustrated, which results in loss of interest in laboratory education. Therefore, it is important to develop visualization tools to help students learn general chemistry laboratory skills and increase their interest in science. The live-action portion of the video is used for demonstrating laboratory setups and basic techniques as well as providing tips or suggestions that are key to the student's understanding and successful completion of the experiments. Alternatively, the animated portion of the video serves to introduce and explain scientific concepts relevant to the experiment in a simple and engaging way so that students will gain a better sense of the purpose of the laboratory and

ultimately a greater understanding of the topics they are learning in the course.

### ■ CONCLUSION

Our acid rain experiment utilizes the concept of conductivity to ensure that students make the connection between chemistry in the classroom and chemistry in the real world at an early stage. With the aid of illustrated animations, students are more engaged in learning new concepts since the animation video can highlight the importance of the topics being discussed in a more striking manner than classroom lecturing. Additionally, videos demonstrating the techniques that students will need to use in the laboratory ensure that students are better prepared for new experiments and should improve student performance in the laboratory.

This experiment is simpler and more engaging than the typical acid–base titration laboratories. Instead of performing a lengthy titration with burets, students used autopipettes to pass the “acid rain” onto the limestone packed in a glass column to simulate the interaction of acid rain with soil in nature. Simultaneously, students were able to observe the formation of CO<sub>2</sub> gas bubbles in the column as a result of the reaction. In addition, this laboratory involves “green” procedures that minimize the usage of harmful chemicals. The chemicals used are safe for beginner-level students, as the acid solution used is dilute. The conductivity probe, pH probe, and multimeter are easy to use and require only a basic understanding of electrolytes and solution chemistry. It is therefore more feasible to implement this laboratory at the beginning of an introductory chemistry course than it would be to prepare students for a similar laboratory involving just pH measurements. Moreover, the simple data analysis required allows students to practice skills such as plotting data in Excel or other graphing software and obtaining useful information from their measurements. This simple, affordable, and engaging laboratory can be adapted into different formal or informal learning environments including classroom demonstrations for K–12 students.

### ■ ASSOCIATED CONTENT

#### 📄 Supporting Information

The Supporting Information is available on the [ACS Publications website](#) at DOI: [10.1021/acs.jchemed.5b00635](https://doi.org/10.1021/acs.jchemed.5b00635).

Experimentally determined equivalence points, sulfuric acid concentrations, and experimental errors; detailed procedure for the experiment and use of the conductivity probe, pH probe, and multimeter; laboratory report for experiment distributed to students ([PDF](#), [DOCX](#))

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D.R. and C.J.Y. contributed equally to this project.

#### Notes

The authors declare no competing financial interest.

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