A CONTROLLED DRUG-DELIVERY EXPERIMENT USING ALGINATE BEADS

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Drug delivery is a burgeoning field that represents one of the major research and development efforts of the pharmaceutical industry today, with new drug delivery system sales exceeding $10 billion per year.[1] Chemical engineers play an important and expanding role in this exciting and inherently multidisciplinary field, which combines knowledge from medicine, pharmaceutical sciences, chemistry, and engineering.

Controlled drug delivery systems are engineered to deliver a drug to the body at a predetermined rate for an extended time. Controlled-release systems have expanded from traditional drugs to therapeutic peptides, vaccines, hormones, and viral vectors for gene therapy. These systems employ a variety of rate-controlling mechanisms, including matrix diffusion, membrane diffusion, biodegradation, and osmosis.[2].To design a drug delivery system, an engineer must fully understand the drug and material properties, the mass transfer mechanisms, and the processing variables that affect the release of the drug from the system.

While the role of the chemical engineer is vital to the development of new drug-delivery systems, undergraduate chemical engineering students are rarely exposed to drug delivery through their coursework. This paper describes an experiment that introduces students to drug delivery system design, formulation, and analysis from an engineering point of view. Students produce drug-loaded calcium alginate beads, obtain release data, and analyze the rate of release from the beads. They investigate effects of drug molecular weight, extent of polymer cross-linking, geometry and surface area, and external mass transfer resistance on the release rate of the drug. Using Excel and Polymath, students compare their results to a mathematical model in order to determine the rate-controlling mechanism of the release. Through this experiment students explore many concepts and tools that they will use throughout their engineering careers:

- *Application of chemical engineering principles (transport, materials, thermodynamics, mass balances)*
- *Instrument calibration*
- *Concentration measurement*
- *Design of experiments*
- *Use of spreadsheets for calculating and graphing*
- *Data analysis and parameter evaluation*
- *Design of drug delivery systems*

This experiment has been implemented in the Freshman

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Engineering Clinic at Rowan University, and its impact on student learning has been evaluated. While this paper describes the details of a freshman-level experiment, it may easily be adapted to more advanced courses such as mass transfer or a bioengineering/drug delivery elective course.

BACKGROUND INFORMATION

Drug Delivery

A conventional drug such as a tablet would be taken periodically, resulting in cyclical periods of ineffectiveness, effectiveness, and possibly toxicity.[3] Sustained-release delivery forms are designed to release a drug at a predetermined rate by maintaining a therapeutic drug level for a specific period of time. With targeted drug delivery, the drug is delivered to a desired type of cell or location in the body, while avoiding systemic administration that could harm other types of cells that are not the desired target. Some advantages of controlled-release delivery systems include the reproducibility of the release rate, less frequent required administration, decreased side effects, smaller quantity of drug needed, and improved patient compliance.

The most common methods of drug administration are by ingestion and injection. In recent years, several other routes of administration have been explored, including pulmonary (through the lung), transdermal (though the skin), and transmucosal (through a mucous membrane).[4]

Topics related to drug delivery are scarce in the chemical engineering educational literature. Farrell and Hesketh[5] presented a drug-delivery experiment using a dissolving matrix. Prausnitz and Bommarius[6] describe an undergraduate and graduate course on pharmaceutics that includes topics in drug delivery. Simon, et al.,[7] developed continuous stirred tank experiments to introduce topics of pharmacokinetics and drug transport to chemical engineering students. A review of chemical engineering course websites reveals that drug delivery is a topic included with increasing frequency in bioengineering elective courses at universities across the country.

Microsphere Drug Delivery Systems

Microsphere drug delivery systems are microscopic beads that comprise a polymer matrix that contains a drug. The polymer may be in the form of a solid bead throughout which the drug is dissolved or dispersed, or the drug may be encapsulated within a polymeric shell. Polymer microspheres have been used in controlled release and drug targeting to organs such as the liver, spleen, lung, and kidney.[8] Microspheres made from biocompatible natural and synthetic polymers can be used as drug-delivery systems for administration by injection, intramuscular, and through the nasal route. Microspheres can easily be modified and are compatible with many drugs, allowing them to be easily developed to contain a desirable drug. Moreover, the size of microspheres is easily controllable by modification of the preparation method.

Mass Transfer

The rate of release of a drug from a polymeric device can be controlled by Fickian diffusion through the polymer,[10] by external mass transfer resistance, or by polymer relaxation in the case of a swellable polymer.[11] In some cases, polymer degradation or erosion can also contribute to the rate control. The rate of diffusion depends on the molecular weight of the drug molecule and the cross-linking density of the microspheres.[4] A large molecule or a high degree of polymer cross-linking will result in slower diffusion. A high stirring rate is usually used in *in vitro* experiments to eliminate boundary-layer resistance and to simplify mass transfer analysis.

Ritger and Peppas present a simple model for drug release from a polymer that can be used to identify the mechanism of rate control.[10]

$$\frac{M_t}{M\infty} = F = kt^n \qquad (1)$$

Where M_t is the mass of drug released at time t, M_∞ is the mass of drug released after infinite time, F is the fraction released, k is a constant that depends on the diffusion coefficient and diffusion length, and n is an exponent which is indicative of the rate control mechanism. For Fickian diffusion in a slab, n = 0.5; for Fickian diffusion in a sphere, n = 0.43. This short-time approximation is valid for $M_t/M_\infty \leq 0.6$. A non-uniform particle size distribution results in a value of $n<0.43$; smaller beads cause an acceleration of drug release at early times, whereas larger beads cause a retardation of transport at later times.[10]

When the polymer is swellable, diffusion and/or polymer relaxation may govern the release rate.[11,12] For relaxation control, n = 1.0 for a slab and 0.85 for a sphere. When n lies between the values for Fickian diffusion and relaxation control, both diffusion and relaxation contribute to rate control.

The normalized release rate, $\frac{dF}{dt}$, can be found by differentiating Eq. (1):

$$\frac{dF}{dt} = knt^{n-1} \qquad (2)$$

Alginate

Alginate (or alginic acid) is a biopolymer derived from the cell walls of brown algae. Its sodium salt forms a viscous gum when dissolved in water. Calcium alginate, an insoluble hydrogel formed by ionic cross-linking with calcium ions in solution, is nontoxic and biocompatible, and has wide applications in cell immobilization and drug encapsulation, for drug delivery via different routes of administration. In clinical trials, an oral alginate-antacid formulation has been used in humans for the effective treatment of GERD,[13] and an alginate-based drink formulation has produced a robust

reduction in hunger to battle obesity.[14] Chitosan-treated alginate beads have been used for oral delivery of the drug Metronidazole for the treatment of H. pylori and resulted in 100% clearance of the infection in mice stomachs.[15] Oral delivery of the anti-diabetic drug gliclazide from alginate beads resulted in a significantly greater and more prolonged hypoglycemic effect over the conventional gliclazide tablet (Gliclazide®) *in vivo* in diabetic rabbits.[16] Alginate beads have been used for sustained delivery of vascular endothelial growth factor from alginate beads *in vitro* for vascular tissue engineering and wound healing applications.[17] Alginate implants have been used for delivery of the growth factor TGF-β for the improved repair of articular cartilage in rabbits.[18] Cells encapsulated in alginate have been used to deliver recombinant proteins to malignant brain tumors in rats.[19]

An important property of alginate is its ability to form gels by ionic cross-linking with divalent calcium ions. When sodium alginate solution is combined with calcium chloride in aqueous solution, ionic cross-linking of alginate chains occurs instantaneously. This cross-linking results in a matrix at the interface between the two solutions.[4] When drops of alginate solution are added to the calcium chloride, ionic cross-linking occurs at a spherical interface resulting in a polymer shell that encapsulates a solution of drug in alginate.

MICROSPHERE EXPERIMENT

Objectives

In this experiment, students produce drug-containing alginate spheres and investigate the factors that affect the rate of release of the drug from the polymeric beads. The model drug used in this experiment is tartrazine, a yellow food dye. Drug-release studies are performed by placing the drug-loaded beads in a beaker containing water and monitoring concentration as a function of time. Concentration measurements are made periodically by measuring absorbance of the surrounding solution (into which dye has been released) using a spectrophotometer. The release rate of the drug from the microspheres is analyzed using Excel. Through comparison to the mathematical model, the mechanism of rate control can be identified. Students investigate the effect of stir rate, surface area, cross-linking, and molecular weight on the release rate of the drug and the mechanism of rate control. Expected skills and measurable outcomes are summarized in Table 2 in the Evaluation section.

Microsphere Preparation

Materials

- *10 mL tartrazine (model drug, Acros Organics) solution (0.5 mg/mL), in small vial*
- *0.1 g alginic acid, sodium salt (Acros Organics)*
- *6 wt% calcium chloride solution (80 mL in 1 large weigh boat)*
- *Disposable syringe (without needle)*
- *Magnetic stir rod, small*
- *Magnetic stir plate*
- *Vacuum filtration set-up*
- *Tweezers*

Procedure

1. The alginate powder was added to the tartrazine solution in the small vial.
2. This was stirred vigorously until a smooth, uniform yellow solution was formed.
3. 3 mL of the alginate solution was loaded into the disposable syringe by immersing the tip of the syringe in the alginate solution and pulling up on the plunger.
4. The alginate was slowly dispensed into the weigh boat containing calcium chloride solution. By pushing very gently on the plunger, alginate solution was dispensed dropwise generating beads of alginate solution that solidify instantaneously on contact with calcium chloride solution. Drops falling on top of other drops should be avoided. This method produces approximately 70-100 beads in about 60s, depending on the rate at which the plunger is depressed.
5. The beads were immediately separated from the calcium chloride solution by filtration.

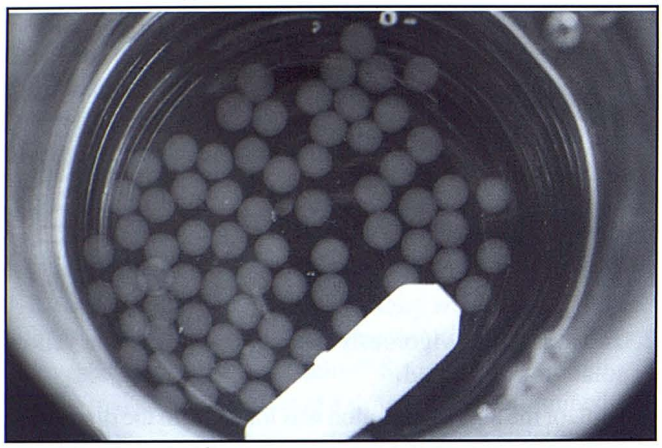
Measurement of Dye Release

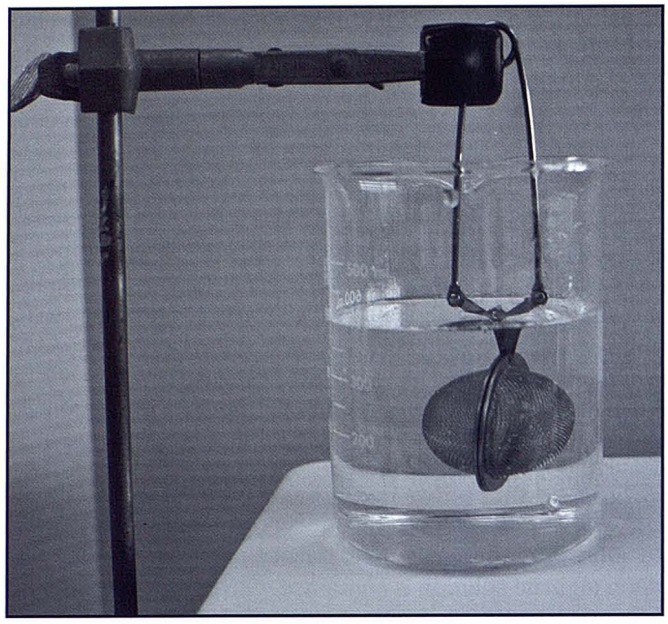
Materials

- *150 mL beaker*
- *Tweezers*
- *100 mL DI water*
- *Disposable pipette (2 mL) or disposable dropper*
- *Stir plate and magnetic stir rod*
- *Spectronic 21 spectrophotometer (Thermo Spectronic, Rochester, NY)*
- *Disposable cuvettes (Fisher Scientific)*
- *Dye-loaded alginate beads*

Procedure

1. A 150 mL beaker was filled with 100 mL of deionized water.
2. Alginate beads were transferred into the beaker filled with deionized water.
3. The beaker was stirred at 300 rpm using a magnetic stir bar.
4. Samples were removed with a pipette, and the absorbance was measured on a spectrophotometer at 427 nm every 10 minutes for 60 minutes total. Care was taken to ensure that beads were not withdrawn with the sample.
5. The measured sample was returned to the beaker to maintain constant volume.





Figures 1. *The experimental setup for beads and blob geometries. The beads (**a.**, above) are simply placed in a beaker with a stir bar and become suspended when stirring commences. The blob (**b.**, right) requires protection from the stir bar and is therefore encased in a tea infuser.*

Variations on this experiment were the following:

- Extent of cross-linking: Rather than removing the beads immediately on contact with calcium chloride, the beads were removed after 10 minutes contact. Alternately, they may be contacted with $CaCl_2$ for the duration of the release experiment.
- Large molecule release: Bovine Serum Albumin (Fisher Bioreagents, Fraction V, approximate MW 66776 Da) was used instead of tartrazine (MW 534.4 Da). BSA release was quantified with a Micro BCA Protein Assay Kit (Pierce) per the manufacturer's instructions.
- Geometry/surface area: Instead of making beads, alginate solution was quickly dispensed from the syringe to form a solid mass of undefined geometry (referred to as a "blob")
- External mass transfer resistance: studies were performed using stir rates ranging from 100 – 400 rpm.

The experimental setups for bead and blob experiments are shown Figures 1. The beads become suspended when stir rate increases, and are therefore not disturbed by a stir bar. The blob requires protection from the stir bar and was therefore suspended using a tea infuser.

Analysis of Results

After the experiment was completed, the students used an Excel spreadsheet for data analysis. The students converted the recorded absorbance measurements into concentration values using the provided equation from the calibration curve given in Figure 2. Calibration data are provided with the lab instructions. Students are guided toward using only the linear portion of the calibration data; when this range is exceeded, an increase in concentration will not result in a proportional increase in absorbance. From the absorbance measurement for the calcium chloride filtrate, the concentration of tartrazine is calculated and the mass of tartrazine in solution is determined. The amount of dye remaining in the beads at the beginning of the experiment is determined by mass balance.

Students set up an Excel spreadsheet to calculate the following quantities at each sample time: Concentration of tartrazine in solution (C), mass of tartrazine released (M_t), and fraction of tartrazine released (F). The concentration is determined from the calibration equation:

$$C = 0.0231A \qquad (3)$$

The mass of dye released is determined from the concentration and volume (V) measurements.

$$M_t = CV \qquad (4)$$

Infinite time is considered to be when the absorbance does not change for three consecutive measurements over at least 30 minutes. After "infinite time" the drug concentration in the water is less than 0.01% of the saturation concentration, and some drug will always remain in the beads at equilibrium.

After converting the measured absorbance values to fraction of dye released, the students create a plot showing the fraction of dye released over the time of the experiment. Students are asked to predict how different factors would affect the release rate: polymer properties such as cross-link density, the drug molecule size, stirring rate, bead size, temperature, etc. Many of these factors were investigated experimentally by teams using shared data.

According to Eq. (1), a plot of the log of fraction released vs. log of time will result in a straight line with a slope of n. The value of n is used to identify the rate controlling mechanism as explained above. The release rate is calculated from Eq. (2) and plotted as a function of time.

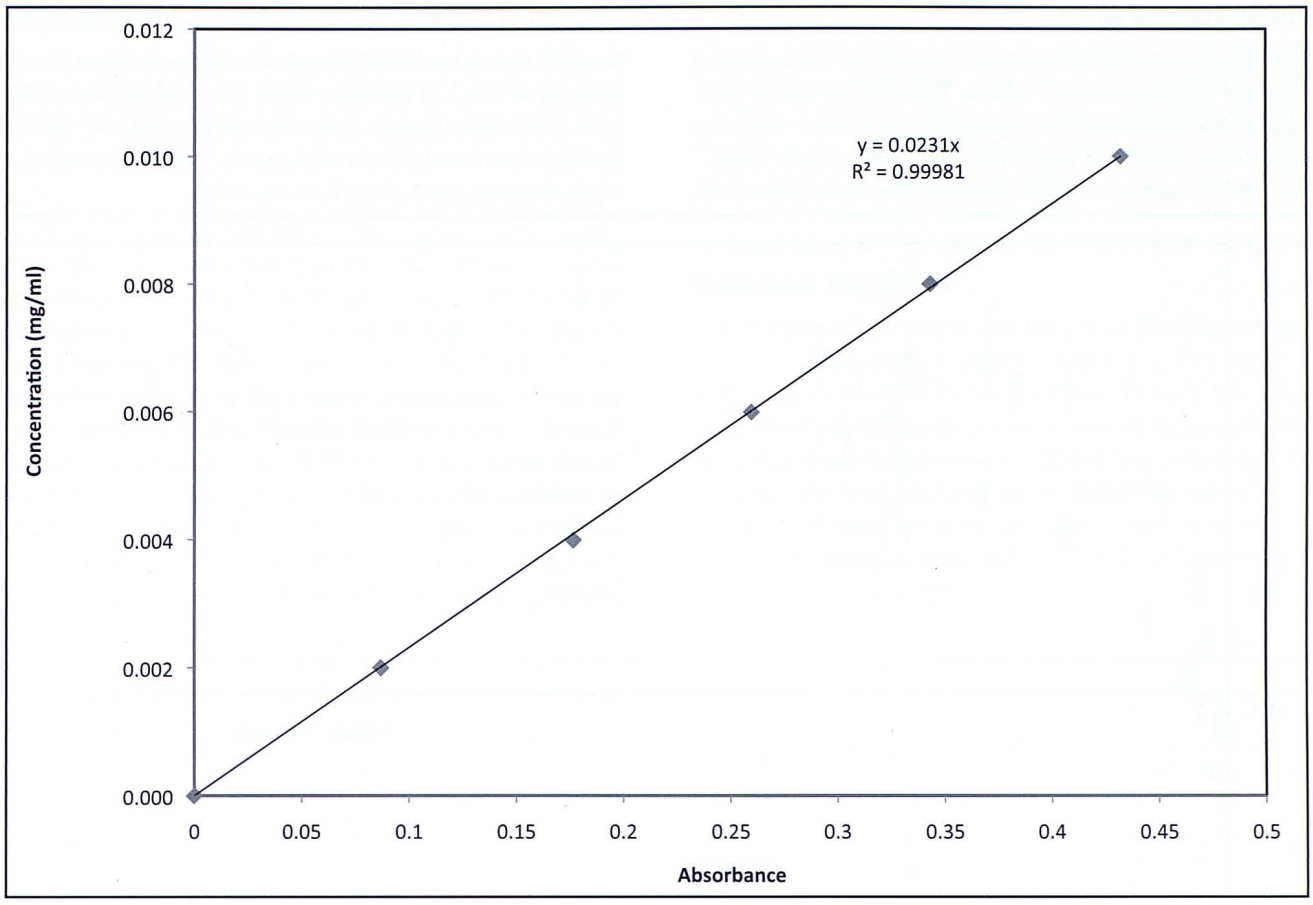


Figure 2. *Calibration curve for tartrazine at 427 nm.*

EXPERIMENTAL RESULTS

Effect of Stir Rate

If a mass transfer boundary layer exists, an increase in stir rate will result in faster drug release. Figure 3 shows the release profile for experiments conducted at 100, 300, and 400 rpm. Since an increase in stir rate from 100 to 300 rpm results in faster release, we may conclude that external mass transfer was significant at the lower stir speed. Increasing the stir speed to 400 rpm did not affect the release rate, so it was concluded that external mass transfer resistance was insignificant at 300 rpm. For subsequent experiments a stir speed of 300 rpm was used in order to study rate control within the beads.

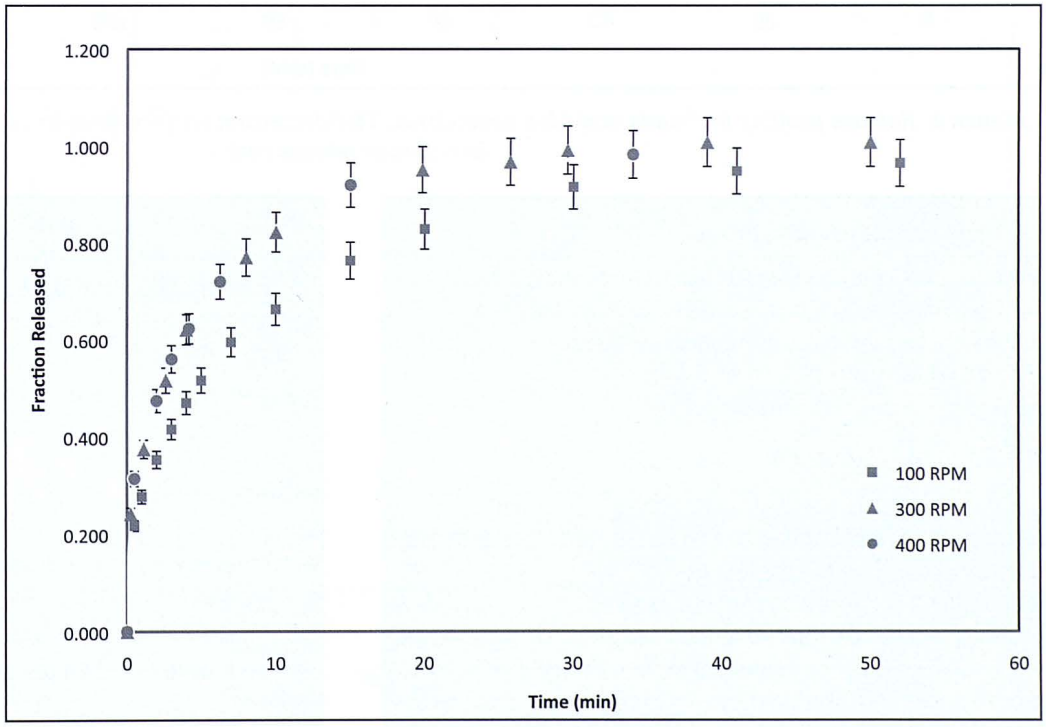


Figure 3. *Release profiles using different stir speeds. The external mass transfer resistance is significant at 100 rpm. At 300 and 400 rpm, the external mass transfer resistance is eliminated.*

Effect of Surface Area

Another parameter that affects drug release is the surface area of the hydrogel with respect to its volume. The effect of surface area-to-volume ratio can be analyzed by conducting release studies on hydrogel beads along with larger non-spherical hydrogel "blobs." Figure 4 shows sample results for bead and blob hydrogels release study at 300 rpm. The decreased surface-area-to-volume ratio of the blob results in slower release. The blob continues to release drug for about 130 minutes, while the bead releases drug for only 30 minutes. Figures 5 are photographs of a blob and beads prior to experiment. The bead diameter is approximately 4 mm, while the blob spans about 3 cm in width.

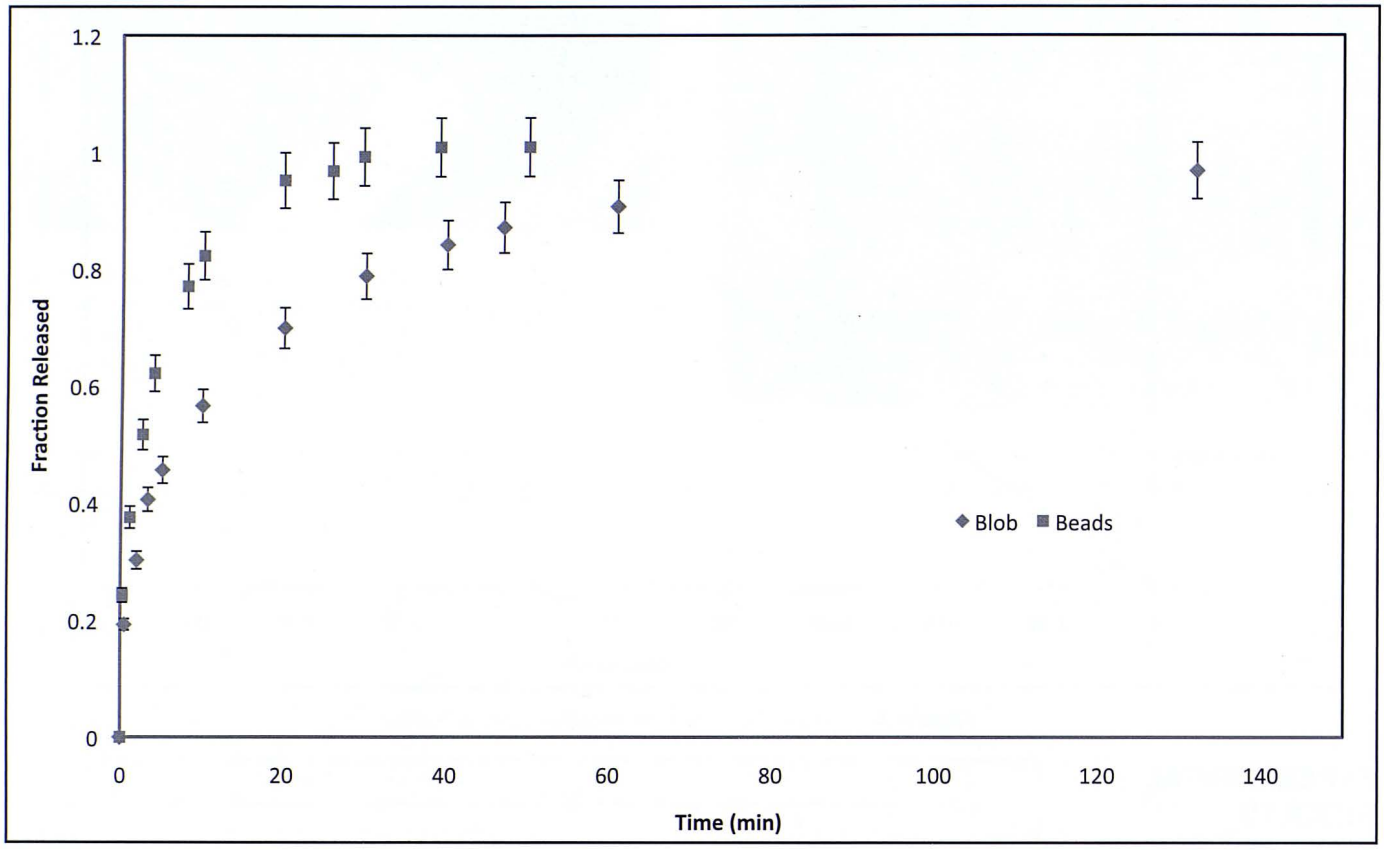
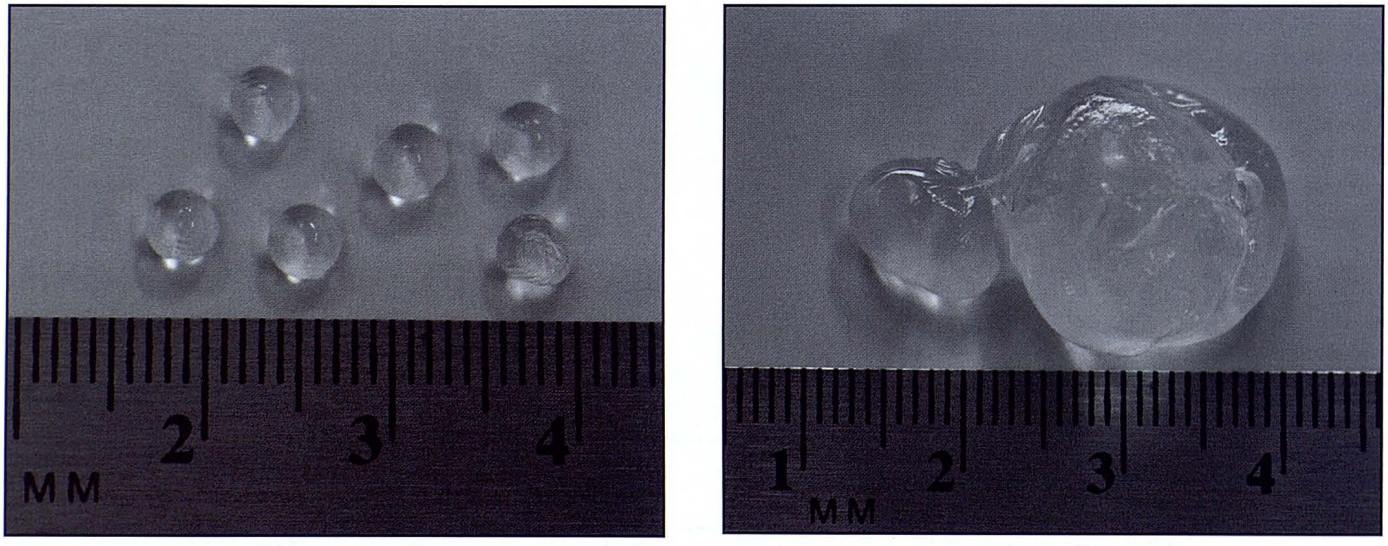


Figure 4. *Release profiles for beads and blob geometries. The decreased surface-area-to-volume ratio of the blob results in a slower release rate.*



Figures 5. *Alginate beads (**a.**, left) and an alginate blob (**b.**, right), prior to experiment. The bead diameter is approximately 4 mm, while the blob spans about 3 cm in width.*

Effect of Cross-Linking

The formation of the hydrogel beads is a direct result of the cross-linking that occurs when alginate is contacted with calcium chloride. By changing the time for which the alginate beads are contacted with the calcium chloride, the effect of cross-linking can be explored. A longer contact time results in more penetration of the calcium ions into the alginate bead and the formation of a thicker cross-linked shell surrounding drug in alginate solution. This can be investigated in an experiment in which $CaCl_2$ was the release medium for the duration of release. The results can be compared to those from the control experiment, where the beads are removed within 80s after the first bead was formed. The higher degree of cross-linking (thicker cross-linked shell) results in a slightly slower release of dye as shown in Figure 6. In another experiment, a 10 minute cross-linking time was used. There was no statistical difference between the 10 minute cross-linking time run and the $CaCl_2$ release medium run. Cross sections of beads produced by 2 minute and 10 minute contact times in calcium chloride are shown in Figures 7 (next page). The beads that were cross-linked for only 2 minutes show a distinct cross-linked shell and alginate core region, while the beads cross-linked for 10 minutes are cross-linked through the entire bead. The bead produced using a 2 minute contact time has an elongated shape because it was slightly deformed when it was cut.

Molecular Weight

The effect of the molecular weight of the drug on the release rate is shown in Figure 8 (next page). The larger BSA molecules (MW=66776 Da) diffuse through the polymer more slowly resulting in a slower rate of release of BSA in comparison to tartrazine (MW = 534.4 Da). While the release of tartrazine was near complete within 30 minutes, BSA release continued for over 24 hours. After 30 minutes, the fraction of tartrazine released was 0.992, and the fraction of BSA released was 0.389.

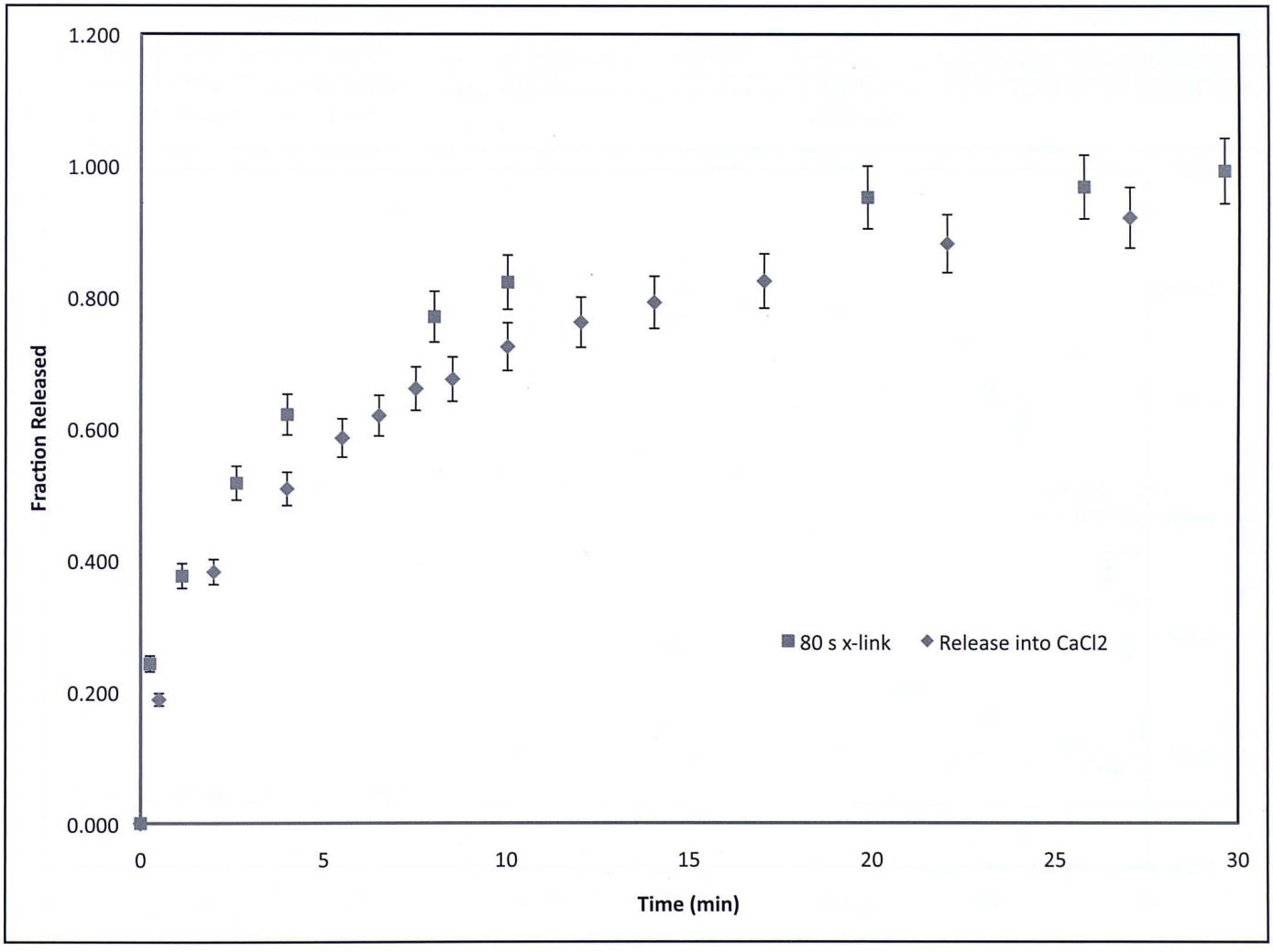
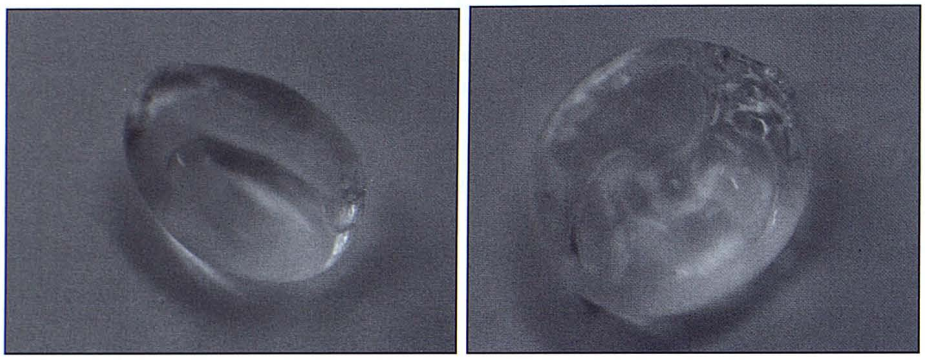


Figure 6. *Longer contact between alginate and calcium chloride results in a thicker cross-linked shell that slows the release rate of the drug. Profiles are shown for beads using 80s and 10 min contact time with* $CaCl_2$.

Mechanism of Rate Control

Figure 9 shows a plot of ln(F) (for F < 0.6) vs. ln(t) for two experiments using beads: an 80s contact time and a $CaCl_2$ contact time for the duration of the release (both with a stir speed of 300 rpm). The slope is equal to the value of n. For the case of short contact time, the value of n is equal to 0.33. Since this is less than n=0.43, the value expected for Fickian diffusion control, the data suggest that the rate control could be Fickian with an effect of non-uniform particle size distribution. For the longer contact time, the larger value of n (n=0.4749 > 0.43) indicates that the effect of swelling is present. Again, the effect of non-uniform particle size is probably significant. To confirm these conclusions, the effect of particle size distribution should be eliminated. This was done outside of class by conducting experiments using single beads. For a single bead and short contact time (80s), the value of n is equal to 0.4379, which confirms that Fickian diffusion is the rate controlling mechanism. For a single bead and a long contact time, the value of n was equal to 0.6813. Since this value is greater than n=0.43, it is concluded that swelling has an effect on the release rate. This is due to the thicker cross-linked shell in which swelling is significant. These beads were seen to double in diameter over the course of the experiment.



Figures 7. *The effect of $CaCl_2$ contact time on the thickness of the cross-linked shell of alginate beads. The bead on the left (**a.**) was cross-linked for 2 minutes in $CaCl_2$ and shows a distinct shell and core region. The bead on the right (**b.**) was cross-linked for 10 min and shows that the cross-linked region extends through the bead.*

Once the value of n has been determined, the rate of release can be found using Eq. (2). Figure 10 (page 106)

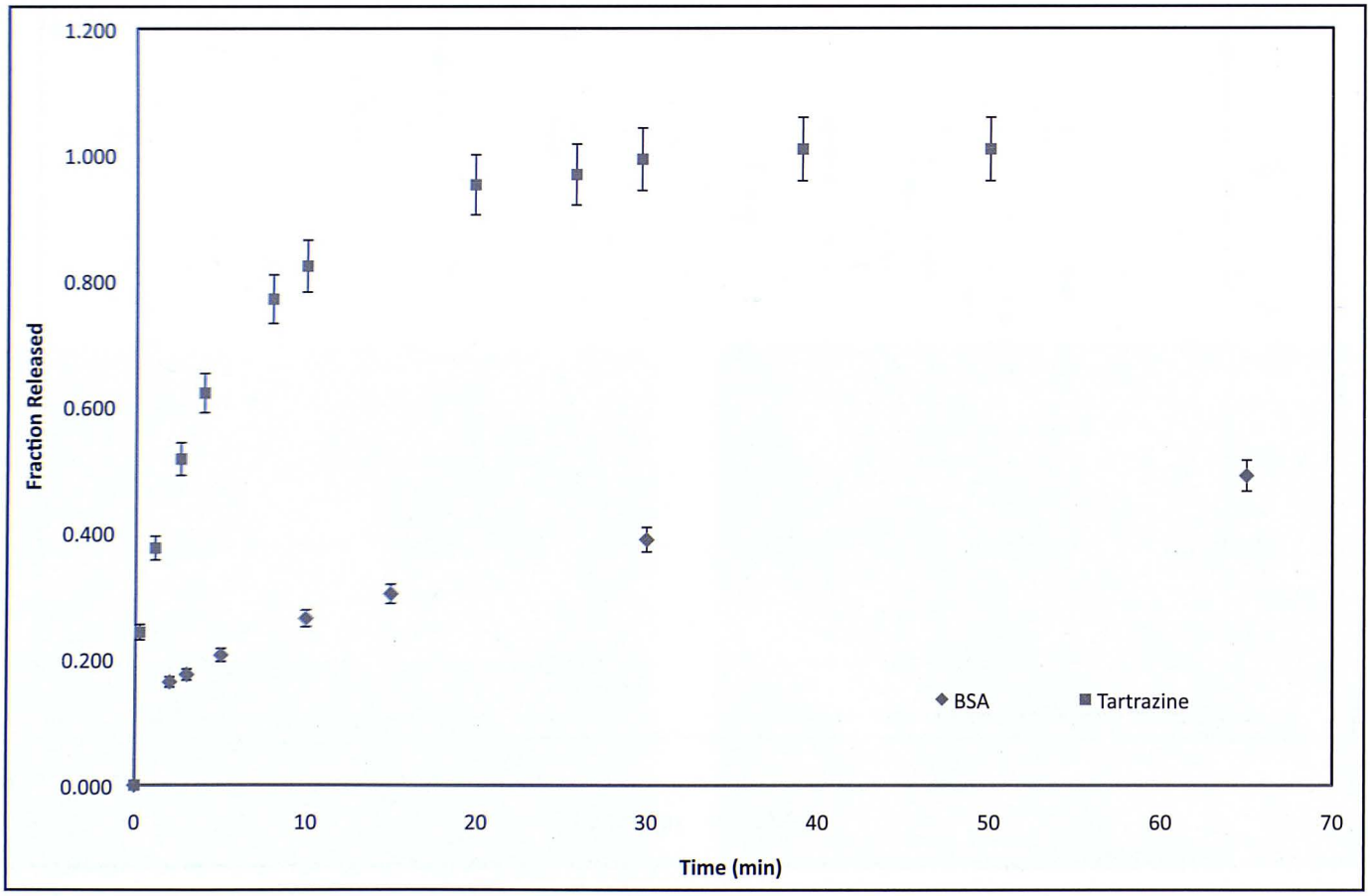


Figure 8. *The effect of molecular weight on release profile. The release of BSA is slower than the release of tartrazine. After 30 min, F = 0.389 for BSA and F=0.992 for tartrazine.*

shows a comparison of release rates for the short contact time (Fickian diffusion control) and long contact time (swelling control).

EVALUATION

To evaluate the impact of this experiment on student learning, a quiz was administered to students before and after the lab. The quiz comprised 15 questions (12 multiple-choice, two choice-between-two-options, and one explanation) that were mapped to course and lab objectives and ABET objectives. An example of a multiple-choice question is:

The diffusion rate is directly proportional to

a) Equilibrium

b) pH

c) Molecular weight

d) The magnitude of the concentration gradient

The quiz questions covered topics of diffusion, hydrogels and cross-linking, surface area, material properties, release kinetics, release mechanism, and drug-delivery design. The questions were designed to evaluate whether the experiment was effective in introducing basic principles of drug delivery; reinforcing concepts of science, math, and engineering; and teaching skills of data analysis and representation. A summary of the quiz questions is provided in Table 1 (page 107) in which multiple-choice questions are presented as correct statements for brevity.

Questions were mapped to Rowan Engineering Clinic II course objectives and ABET outcomes as shown in Table 2 (page 108). The Table also shows the measurable skills that are associated with each outcome. Figure 11 (page 108) shows the average score on the pre-test was 56%±22% for n=14 students, and the average score on the post-test was 82%±9.9% for n=15 students.

For each outcome, the percentage of correct responses increased between 13-24% between the pretest and the post-test. The highest percentage of correct responses for both the pre- and post-tests was for outcome ABET C; students showed the lowest percentage increase for this outcome most likely because the pretest scores were so high. The lowest performance was

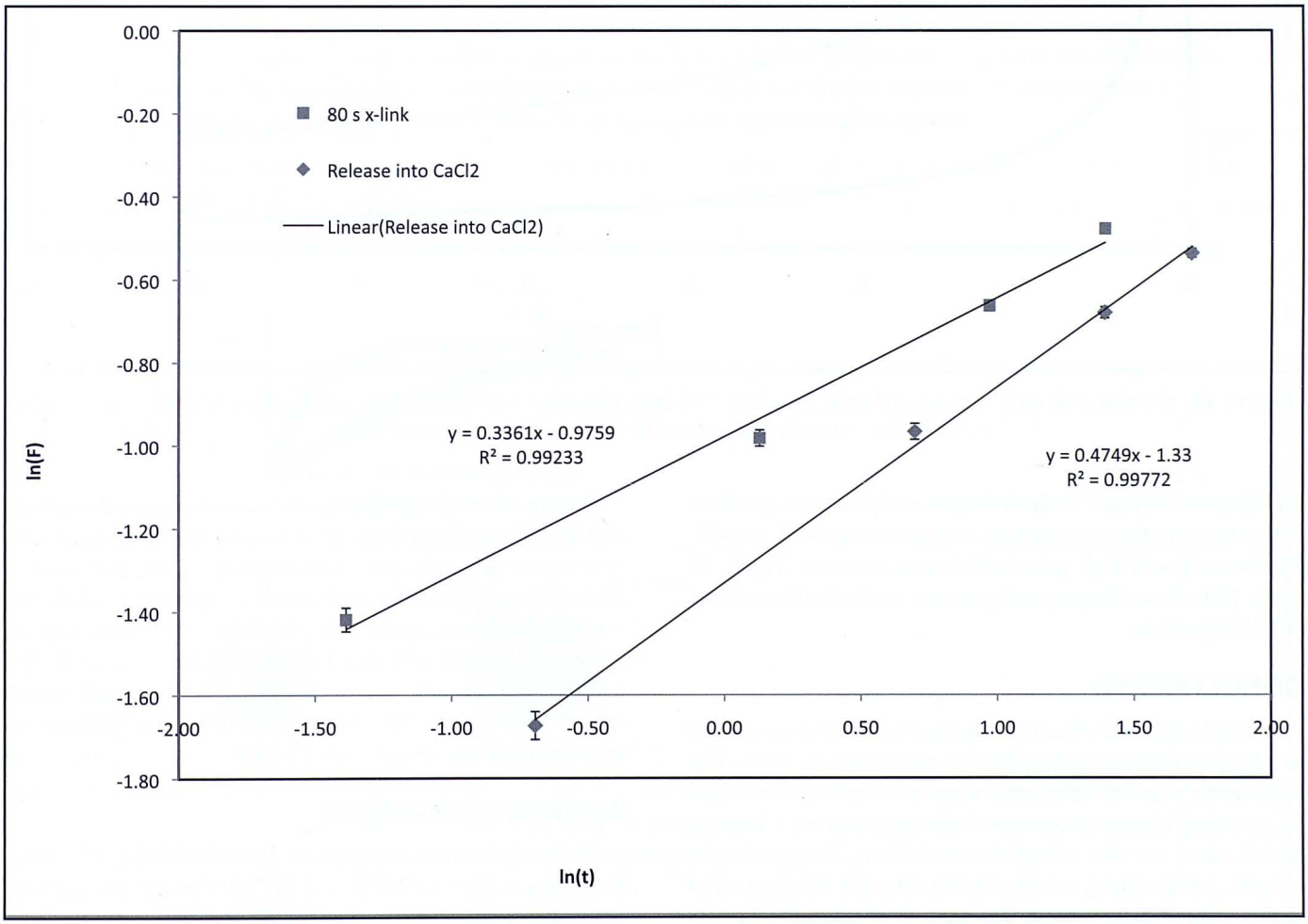


Figure 9. *Evaluation of rate controlling mechanism. The value of the slope is equal to the exponent n in Eq. (1). Longer cross-linking time results in the formation of a thicker shell in which swelling is significant over the course of the experiment. The shorter cross-linking time results in a thin shell and Fickian diffusion as the rate-controlling mechanism.*

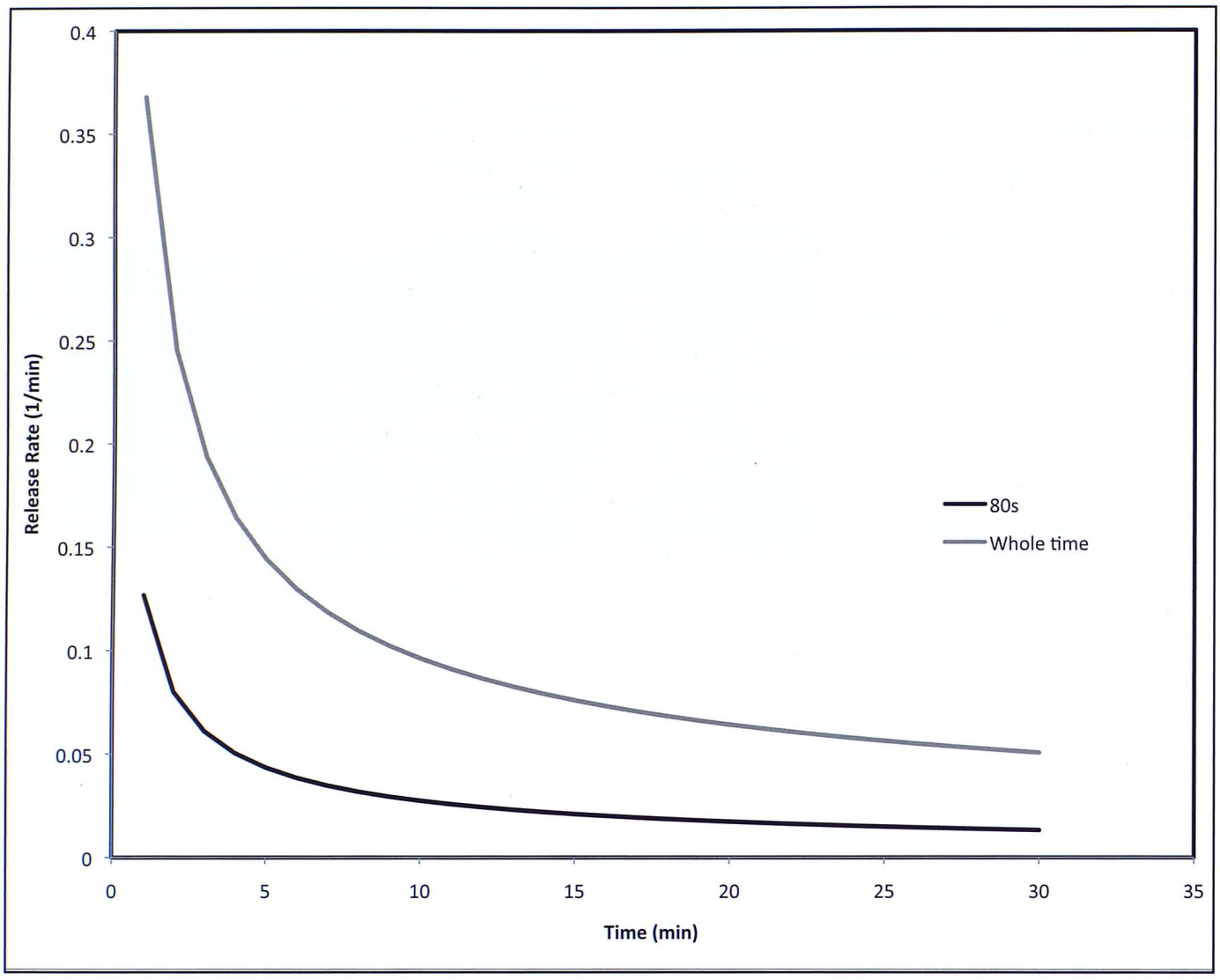


Figure 10. *Release rate as a function of time for short and long exposures to $CaCl_2$. The longer cross-linking time results in a thicker cross-linked region in the bead and slower release.*

for objective Rowan 2 for both the pre- and post-tests, in which percentage of correct responses increased from 40% to 64%. Students showed high gains in this area, however. Figure 12 (page 109) shows the pre- and post-test results for Rowan and ABET objectives.

CONCLUSIONS

A simple and cost-effective experiment has been developed to introduce students to drug delivery using alginate beads. The experiment was implemented in a multidisciplinary Freshman Engineering course at Rowan University. Students explore the effects of stir rate, extent of cross-linking, drug molecular weight, and geometry on the release rate and mechanism of drug release from the system. The analysis of experimental data introduces students to mass balances, spreadsheet calculations, data representation, and mathematical modeling.

Students showed significant gains in several areas: the science and art of design by evaluating the work of practicing engineers; new science principles such as mass balances, transport, materials and thermodynamics; application of knowledge of science, math, and engineering; the ability to design and conduct experiments and analyze and interpret data; and the ability to design a system, component, or process to meet desired needs within realistic constraints. The gains for each objective between the pre- and post-test ranged from 13-24%.

ACKNOWLEDGMENTS

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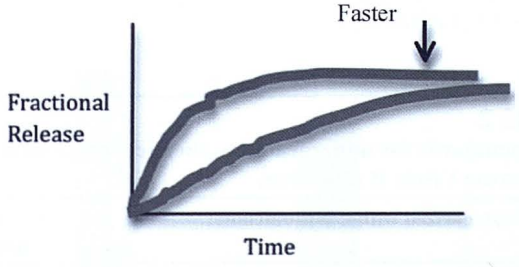
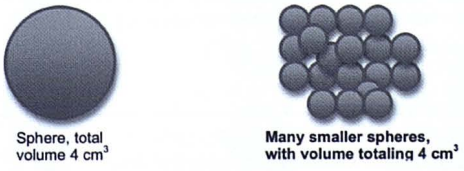
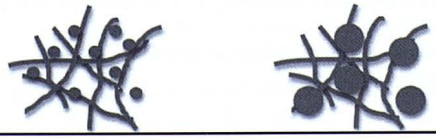
TABLE 1
Pre- and Post-module questions presented as correct statements.
The bold font indicates the choice that correctly completes each statement.

Question #	Correct Statement
1	The movement of molecules from a region of high concentration to one of low concentration is called **Diffusion**
2	The diffusion rate is directly proportional to **the magnitude of the concentration gradient**
3	Diffusion results in an increase in system **entropy**
4	Hydrogels are **three-dimensional networks of water-loving polymers**
5	In polymers, a cross-link is a **covalent, ionic, and physical connection that bonds one polymer chain to another, forming a "net" of polymer chains.**
6	Cross-links make a polymer material **insoluble in a solvent**
7	Drugs can be loaded into hydrogels, and they will be subsequently released from the polymer by a process called **diffusion.**
8	What is meant by the phrase, "The hydrogel is permeable to the flow of solute?" **A solid is dissolved inside the water that is absorbed by the hydrogel. The solute can diffuse through the hydrogel with little resistance.**
9	What is meant by surface area to volume ratio? **The area of the outer surface of an object per unit volume of the object.**
10	Someone hands you an object and asks you to describe its material properties. What is meant by material properties? **All of the above (color, electrical conductivity, hardness, surface roughness).**
11	The total US healthcare expenditures on biomaterials in 2000 totaled $1,400,000,000,000. As you can see, the need for engineers who design these materials is quite large. What is an example of a constraint that biomedical engineers have to take into account while designing materials that are to be implanted into patients? **(Correct answers include nontoxic, biocompatible, biodegradable or nonbiodegradable depending on application, functional constraints such as compatibility with drug in delivery system, desired properties in physiological conditions)**
12	Which of the following statements is true? **Diffusion rate of a drug through a hydrogel is inversely proportion to the molecular weight of the drug.**
13	Which curve represents a drug delivery system with a faster release rate? 
14	Which of the below systems have higher surface area to volume ratios? 
15	In which of the following scenarios does the hydrogel network have a higher permeability to the dissolved drug? **(The scenario on the left. Smaller molecules result in higher permeability)** 

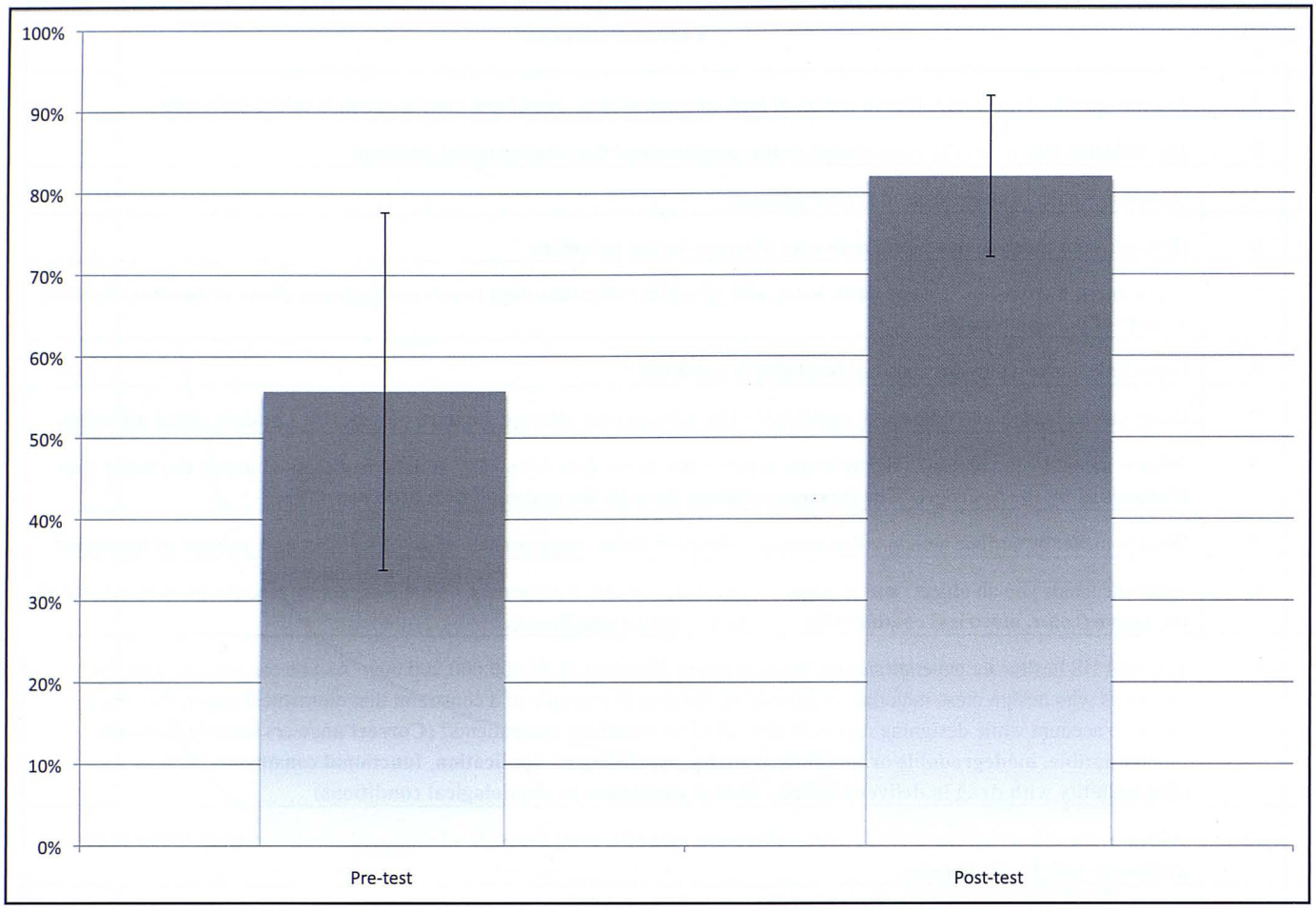


Figure 11. *Average pre- and post-test scores for the alginate drug delivery module. For the pretest, n=14 students. For the post test, n=15 students.*

TABLE 2
Pre- and post-module assessment questions alignment to: ABET standards for undergraduate chemical engineering students and Rowan University Engineering Clinic II objectives

Outcome	Measurable skills categorized within this outcome:	Pre- and post-test questions
Introduce students to the science and art of design by evaluating the work of practicing designers (Rowan 1)	To identify how hydrogel-based drug delivery systems work; how to measure drug release; connect engineering principles to the design of these systems	1,2,7,8,9,12, 13,14,15
Introduce multidisciplinary teams of engineers to science principles such as mass balances, transport, materials, thermodynamics (Rowan 2)	Identify variables that drive mass transfer; use structure-property in hydrogels to predict mass transfer behavior	2, 5, 6, 7, 8, 12, 14, 15
An ability to apply knowledge of mathematics, science, and engineering (ABET-A)	Successfully apply fundamental concepts of chemistry, material science, and transport phenomena to biomaterial science and drug delivery systems	1-8, 12-15
An ability to design and conduct experiments, as well as to analyze and interpret data (ABET-B)	Experience with the preparation and characterization of a drug delivery system will give the ability to identify key variables, analyze data, and evaluate its significance	3, 9, 12, 13, 14, 15
An ability to design a system, component, or process to meet desired needs within realistic constraints (ABET-C)	Students will identify scientific, safety, and economic constraints relevant to biomaterials, successfully apply them to the design and characterization of polymeric drug delivery system	11

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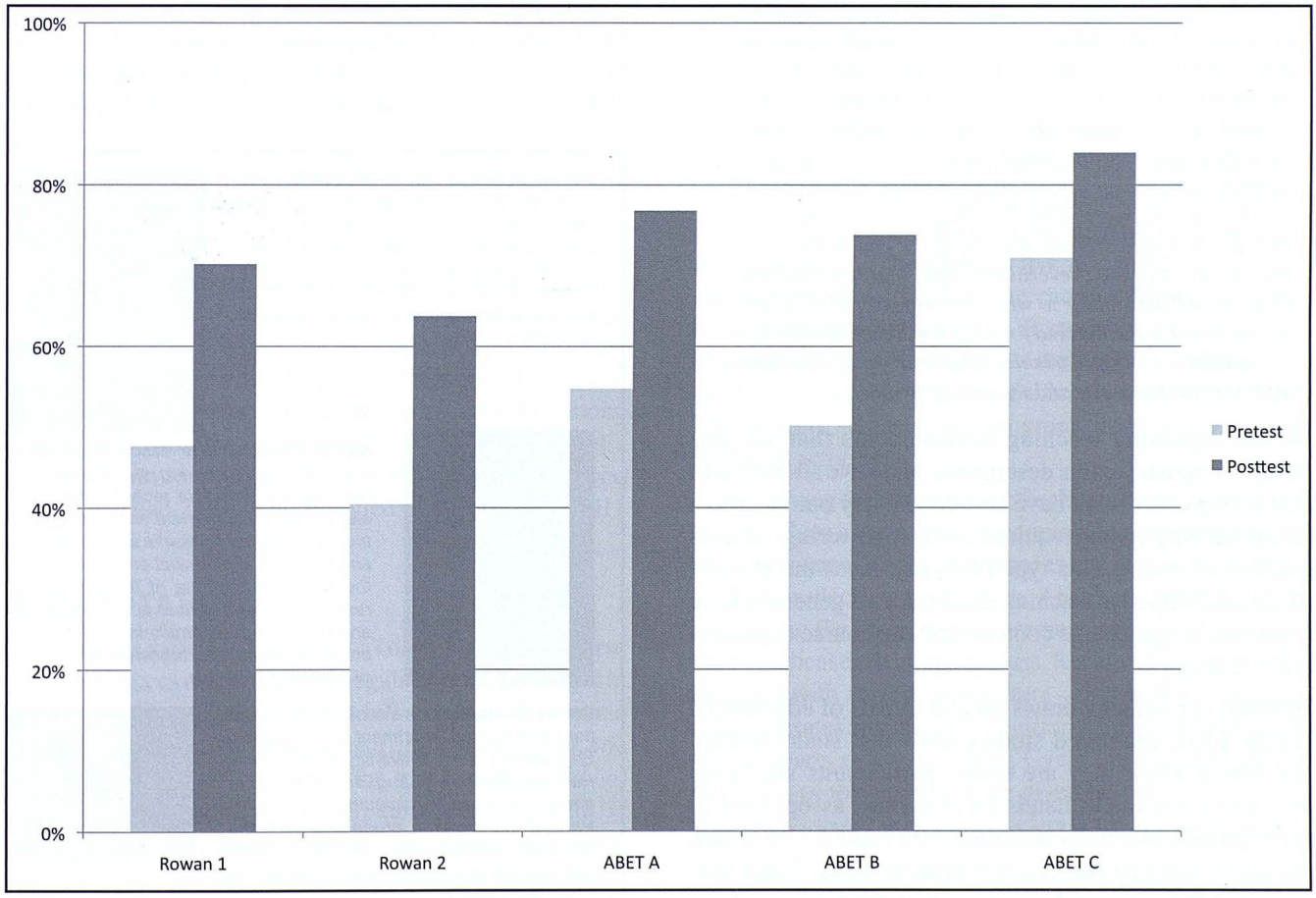

Figure 12. *Percentage of correct responses for each learning outcome as described in Table 2. The percentage includes responses for all questions mapped to a particular outcome.*