# Interpenetrating Networks for Delivery Systems


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**Abstract**

A suitable solution for drug delivery and healing of large surface area wounds has been created by Professor John Kao. Interpenetrating networks composed of gelatin cross linked with polyethylene glycol diacrylate (PEG-dA) provide a promising solution to this problem; however, the current reconstitution and administration methods of this product are clinically undesirable. The goal of this project is to create a novel delivery mechanism to reconstitute the components of an interpenetrating network. Two different design approaches, research and addition of a heating element, have been thoroughly considered. The most appropriate approach, research, has been selected by means of a design matrix which weighted different design constraints set forth by our client. While preliminary data has been collected, further experimentation, literature research, and testing are all necessary to ensure the successful design of a novel delivery mechanism for interpenetrating networks.

## Introduction

*Background*

Large surface area and chronic non-healing wounds significantly impair the quality of life for millions of people in the United States (Harding et al, 2002). These wounds are characterized by a loss of skin and underlying tissue which do not heal properly with conventional types of treatment (Falanga, V., 2004). Instead, intensive treatment is required that is costly and requires a lengthy recovery period. Hence, solutions have been investigated to aid and advance the wound healing process. Numerous "bioactive dressings" as well as "skin substitutes" have been created, however few are currently operational in a clinical setting (Harding et al, 2002). Our client, Professor John W. Kao, has created a biocompatible interpenetrating network that offers a drug delivery mechanism and promotes healing in large surface area wounds that is ready for clinical implementation.

Interpenetrating networks are beneficial for healing advancement of large surface area wounds due their physical and chemical properties. First, IPNs are able to cover large surface area wounds that are often irregularly shaped. The fluid nature of IPNs allow it to properly conform to these irregularly shaped wounds, promoting more rapid and uniform healing with minimal bacterial infection. Similarly, the moist environment provided by IPNs promote re-epitheliazation and improve healing time. In addition, IPNs can be created to contain therapeutics in either a solvent form or as a covalent attachment to gelatin (Kao et al, 2003). The drugs are then administered to the patient via diffusion or cleavage, respectively, further aiding in the healing process. Professor Kao's laboratory has obtained positive results in wound treatment study issuing IPNs (Kao et al, 2003). However, while IPNs offer an exceptional

solution to improved healing time and drug delivery, there are many problems associated with the current administration techniques.

*Current Methods*

Current IPN preparation and administration methods (see figure 1) are only suitable for a laboratory setting. To create an IPN, PEG-dA, gelatin, and a photoinitiator must all be mixed and then heated at 60 degrees Celsius for approximately five minutes to ensure complete dissolution. However, in a clinical setting, a hot plate would not be available to aid in the dissolution and time is limited. In terms of application of the solution, a syringe is currently being used; yet, IPNs are intended to treat large surface area wounds. Syringes provide for tedious and uneven administration of the IPN solution. In order to begin using IPNs in a clinical setting, these issues must be resolved.

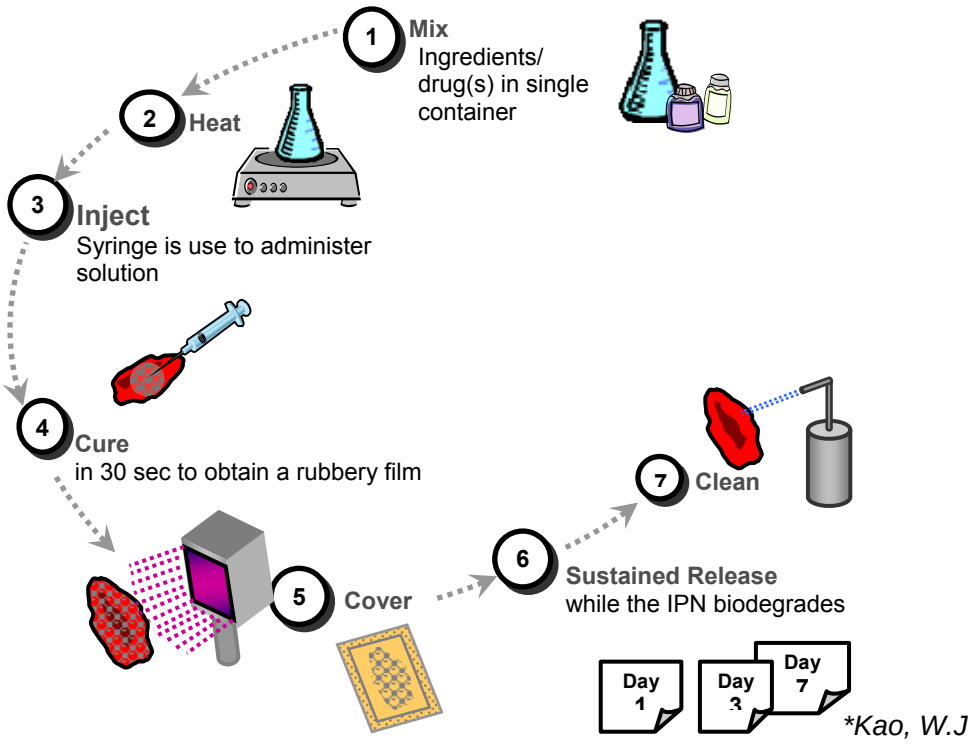



**Figure 1** Current method for administering an interpenetrating network to a wound. Main ingredients used include PEG-dA, gelatin, and a photoinitiator.

*Problem Statement*

Interpenetrating networks are a type of biomaterials that polymerize in situ and have been used in drug delivery, wound healing, and tissue engineering applications. The goal of our project is to develop a novel delivery mechanism and create a simple reconstitution method for the components of an interpenetrating network. This design must be suitable for a clinical setting, and the final product must also satisfy the design constraints presented by our client.

**Design Constraints**

Our client has instituted several restrictions to our design approaches. The most important restriction to consider will be the clinical applicability of the final result. In order for a product to be clinically applicable, it must fit seamlessly into the hospital environment. The utility of our product will center on several factors, including shelf life, the ability to reconstitute each component without the need for additional equipment, and the ease of application.

In the interest of shelf-life, our client has requested that our equipment be one-time use only. Disposable medical equipment is more practical because after application sterilization is not required. Similarly, single use products reduce risk of contamination due to minimized exposure to oxidizing agents and microbial invasion. Overall, the capacity for prolonged storage in a sterile environment could lead to increased product applicability.

In addition, reconstitution is a major barrier of this project because it must be accomplished at room temperature. PEG-dA is a compound that reconstitutes after lyophilization in nearly any water-based environment. Gelatin, however, is a thermosetting material. Thermosetting materials are ones which strengthen through the addition of heat energy. For this reason, the typical method to reconstitute gelatin is the use of 60ºC water. This proposes an interesting predicament for the clinician, since most hospitals do not have readily-accessible

60ºC water. Therefore, our design must either circumvent the problem by modifying the physical properties of gelatin, or it must introduce a heating element that can raise the solution to a temperature suitable for dissolution. Reconstitution will be the most important step of application of this product. For that reason, the components must consistently dissolve in entirety.

Another important factor of clinical applicability will be the ease with which our design can be implemented. The reconstitution method must be simple as well as efficient. Several complicated steps or a long preparation time could limit the clinical applicablility. Similarly, the final solution must be viscous enough to stay in the area onto which it has been applied, yet not too viscous for unimpeded spraying. Finally, the time it takes the PEG-dA to crosslink and form an interpenetrating network cannot exceed 60 seconds. This requirement is for the benefit of both the patient and the clinician. In essence, the quicker the IPN can be formed, the better.

The success or failure of this product will ultimately hinge on whether it is accepted by the medical community as an efficient and beneficial treatment to its intended wounds. By making the application of our product as simple as possible, we can greatly increase the probability of it becoming a successfully marketed product.

**Ethical Considerations**

Ethics are of utmost importance in our design. Safety and efficacy will be placed before the marketing advantage for our product, as we seek to design a product that minimizes patient risk. Similarly, it is suggested that consent is given for the application of the IPN and that healthcare professionals are aware of the constituents and have been trained in the methodology for reconstitution. Lastly, ethical considerations will be made during any animal experimentation or clinical trials that maybe necessary.

**Design Approach 1: Heating Element Design**

One solution to meet the previously-mentioned design requirements would be to add a heating element in the package. This design would solve the issue of gelatin dissolution by raising the temperature of the water to a point where gelatin is known to dissolve. Heating can be accomplished by one of two methods - either an exothermic reaction or by the use of a resistive heating circuit. Both designs will require enough energy to be released in order to heat water from room temperature to 60ºC. One calorie is, by definition, the amount of energy required to raise one gram of water by one degree Celsius and is equivalent to 4.184 Joules. Because room temperature is around 20ºC, and each design requires the use of around 20mL of water, at least 40 calories (167 J) must be released by each heating method in question.

The first design would be an exothermic reaction similar to one used in Hot-Hands® hand warmers. In that product, heat is produced by the oxidation of iron; although, similar products utilize somewhat different methods. This element would have to be separated from the other components of the IPN for fear of contamination. Restricting the reaction in a container within the spray bottle would accomplish this goal.

The second design would be to introduce a resistive heating circuit. *Figure 2* shows a circuit diagram of this proposed design, which features Nichrome®, a commonly-used resistive heating element made from a nickel-chromium alloy. This design implements a 9V battery in addition to approximately 1 meter of Nichrome®

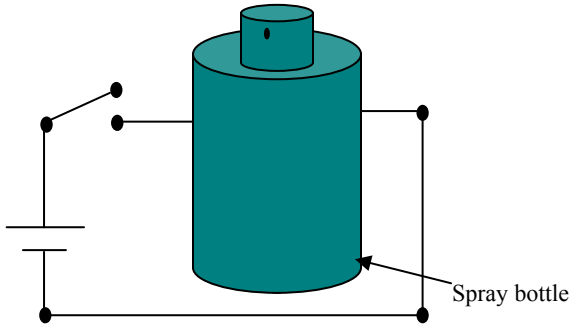



**Figure 2**. Circuit diagram of the heating element design.

wire. The derivation in *Figure 3* demonstrates that this setup could release sufficient energy. This derivation uses Joule's Law to find the time needed to release the energy required to heat the water to the desired temperature. A resistive element can effectively increase the solution to the desired temperature in nearly 2.5 minutes.

$$R = \rho(l / A) = 110 \times 10^{-8}(\Omega m) * (1m / 1.26 \times 10^{-7} m^2) = 8.73\Omega$$
$$I = V / R = 9 / 8.73 = 1.03 A$$
$$Q = (I^2 * R * t) * \varepsilon$$
$$t = Q /(I^2 * R) = (167\ J /(1.03 A^2 * 8.73\Omega)) * 8 = 2.40 \text{ min}$$

**Figure 3**. The derivation of time needed to create energy required to heat water. $\rho$ is the resistivity of Nichrome® Gauge wire. $l / A$ is the length used divided by the cross sectional area (18G wire). ε is the predicted efficiency of the system, and Q is the energy required.

*Pros*

Many qualities of exothermic reactions and resistive elements prove to be advantageous in the dissolution of IPN components. Since addition of a heating element would raise the temperature of the solution, complete dissolution would be achieved. Additionally, these designs solely require the user to activate the reaction, with minimal active procedures. Lastly, resistive elements and exothermic chemical reactions are commonplace and can be incorporated into our design to provide a reliable, consistent method to reconstitute all of the IPN components.

*Cons*

Exothermic reactions and heating element designs have several disadvantages. The extra chemicals and circuit elements required to achieve the desired temperature will add cost to the final product. Also, heat exchange will be difficult to contain safely within the spray bottle. In addition, reactions which release enough energy to heat up the water can be highly unstable and

unreliable when stored for prolonged periods. Lastly, these designs present potential risk of water contamination by chemicals and resistive wires used to create heat.

**Approach 2: Laboratory Research**

Our second design approach emphasizes the research of reagents and/or reactions which will dissolve all elements of the IPN at room temperature. Chemical reactions and modifications that can increase the probability of dissolution without disruption of the structural properties of gelatin are the main objective of our research. Currently, the laboratory research approach will investigate the following affects on gelatin dissolution: pH alterations, surfactants, and buffered solutions.

The chemical composition of gelatin is a denatured form of collagen which is not likely to be further disrupted in the presence of extreme pH ranges. In order to increase the probability of dissolution, the addition of varying pH ranges could decrease hydrogen bonding and other non-covalent interactions which affect the secondary and tertiary structure of gelatin. Modified secondary and tertiary structures due to the presence of varied available hydrogen ranges would change the hydrophilic and hydrophobic interactions allowing for easier dissolution in water.

Another technique which would increase the probability of dissolution of gelatin in water is the addition of surfactants. Surfactants are wetting agents that lower the surface tension of a molecule, allowing easier spreading and increased surface area (Zhang & Somasundaran, 2006). Due to the amphipathic composition of organic surfactants, they decrease surface tension between two liquids (Zhang & Somasundaran, 2006). A surfactant such as tween 20, could facilitate the complete dissolution of gelatin at room temperature by significantly decreasing surface tension between gelatin, water, and all other IPN compounds.

Additionally, buffered solutions could aid the dissolution of gelatin due to varied side-chain compositions. An amine side chain, found in Tris buffer, could modify the secondary and tertiary structures through non-covalent interaction which would allow for increased interaction between the solvent and gelatin. Other biocompatible buffers such as Hepes and Citric acid buffers are likely to have different interaction with gelatin creating different probabilities that gelatin will dissolve.

In order to completely dissolve the IPN in room temperature a combination of the above listed techniques may be required. Biocompatible buffered solutions at varied pHs with low concentration of surfactants could lead varied capacities for gelatin dissolution. Although extreme pH's and buffered solutions may increase the ability to dissolve all components of the IPN, consideration must be taken knowing that IPN's are applied directly to open wounds.

*Pros*

Some of the many advantages of the results of a research approach are the reconstitution time, cost, and client preference. In order to make a suitable IPN the solutes must reconstitute quickly to minimize human factor errors. A chemical reaction or reagent which can facilitate the dissolution of the IPN components will create an adequate solution upon mixing. Simple buffers, surfactants, and/or pH solutions are relatively inexpensive and can be included in the final product with little effect on the overall cost. Lastly, the client prefers a chemical research based solution that could potentially include all components needed to create the IPN in a single container. This solution would eliminate the need for a modified spray bottle.

*Cons*

Some of the limitations include in the research approach are feasibility, safety, and the active mixing procedure. While a combination of surfactants, buffers, and/or pH ranges could

present an ideal solution to the problem, there are no current findings which suggest that these solutions can efficiently dissolve gelatin at room temperature. Also, if gelatin only can be dissolved at extreme pH ranges, neither the patient nor the medical staff preparing the IPN should be in contact with these solutions before buffering to a biological pH range. Buffering the solution to a biological pH range and the addition of IPN components adds complications. The medical staff preparing the IPN is assumed to have minimal knowledge regarding the IPN thus each additional step involved in dissolution increases possibility of human error.

**Design Matrix**

In order to decide which approach will be pursued, a design matrix was compiled. Categories were created and weighted between five and fifteen points based on importance to the problem statement. The two approaches were then compared with each other in order to provide a numerical value for each category. Although many categories had comparable values, client preference, feasibility, and cost were the aspects of separation. Although the heating element provides a more feasible approach because the necessary components currently exist, the cost added and client preference outweighed the heating element approach. Overall, the design matrix favored the laboratory research which will be the approach pursued for this project.

| Criteria | Weight | Heating Element | Research |
|---|---|---|---|
| Client Preference | 15 | 4 | 15 |
| Feasibility | 15 | 12 | 8 |
| Viscosity | 15 | 10 | 7 |
| Reconstitution Time | 10 | 7 | 9 |
| Safety | 10 | 6 | 6 |
| Cure Time | 10 | 9 | 9 |
| Human Factors | 10 | 8 | 7 |
| Sterility | 5 | 5 | 5 |
| Shelf Life | 5 | 5 | 4 |
| Cost | 5 | 1 | 4 |
| **TOTAL** | 100 | 67 | **74** |

**Experimental Testing**

Since PEG-dA readily goes into aqueous solution, the effectiveness of the final design relies heavily on maximizing gelatin's rate of dissolution. Consequently, initial research has targeted only the gelatin component of the final product rather than the interactions between multiple components. The first series of tests were run to determine a means for efficiently manipulating the environmental conditions and inducing gelatin dissolution in a clinically acceptable solution.

*Part 1: Effect of Gelatin Concentration on Dissolution at 60° Celsius*

The conventional approach of dissolving gelatin utilizes an external heat source to break apart the hydrogen bonds that maintain its solid structure, so the first series of tests aimed to verify the extent of this effect at varying concentrations. Dissolution time, changes in viscosity, and solution physical characteristics were analyzed at a range of concentrations determined from previous research. This data was collected in an effort to establish a standard for evaluating solubility in future tests. For 10% concentration, 0.5g of porcine gelatin was added to 5 mL di$H_2O$ at a constant temperature of 60° Celsius. The solution was then shaken/vortexed for five minutes while assessing the extent of dissolution. Each subsequent concentration was mixed in the same manner. *Figure 4* below shows the results of this experiment.

| Weight % Gelatin (g/mL) | Dissolution Time (min) | Physical Characteristics of Final Solution |
|---|---|---|
| 10 | 3 | clear gel, dissolved completely |
| 15 | 3 | clear gel, dissolved completely |
| 20 | No dissolution | not thoroughly dissolved, gelled quickly |
| 25 | No dissolution | not thoroughly dissolved, cream-colored |

**Table 4** The figure above shows which concentrations were considered acceptably dissolved at a constant temperature of 60° Celsius. These concentrations are indicated in blue. It also shows the physical characteristics of the final solution so the data could potentially serve as a qualitative baseline for assessing optimal dissolution in future testing.

As shown in blue, gelatin at 10 and 15% were the only concentrations to go into solution after five minutes, so future experiments only tested these concentrations.

*Part II: Effect of pH on Gelatin Dissolution at Room Temperature*

The hydrogen bonds in the gelatin structure may also be broken through other stimuli, such as pH. In the next series of tests, 10% porcine gelatin was added to solutions composed of varying concentrations of 1M HCl and NaOH, since they are considered to be benchmark acids and bases in research. The pH standards were created in separate vials by adding 1M HCl and neutralizing it gradually with 1M NaOH, or vice versa. The new pH values were aliquotted into new vials at room temperature, forming a full pH range from 1-14. These solutions were added to vials containing the gelatin and vortexed/shaken. To assure comparable results with the previous test, 0.5g of gelatin and 5 mL solution were combined in each experiment. Extent of dissolution and the change in pH value between initial and final measurements are shown in the figure below:

**Figure 5:** Dissolution of 10% gelatin was tested at a full pH range. The extent of dissolution was rated as (+), (+/-), or (-), and the change in pH was also noted after 5 minutes. The trials highlighted in blue represent the most advantageous results.

| Initial pH | Final pH | Δ pH | Dissolved |
|---|---|---|---|
| 14 | 14 | 0 | + |
| 11 | 10 | 1 | + / - |
| 9.4 | 8.3 | 1.1 | + / - |
| 9.1 | 8 | 1.1 | + / - |
| 8.2 | 7.5 | 0.7 | +/- |
| 7 | 7.5 | 0.5 | - |
| 5 | 6 | 1 | + / - |
| 4 | 5 | 1 | + / - |
| 3.1 | 4.5 | 1.4 | + / - |
| 2.2 | 3 | 0.8 | + |
| 1 | 1 | 0 | + |

**Table Key:**

+ represents full dissolution

+/- represents a dispersion

- represents phase separated solution.

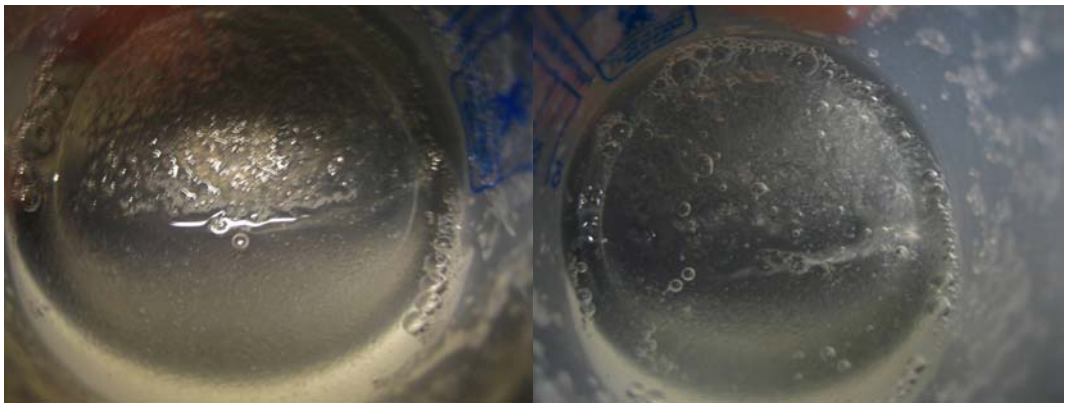
Once again, the most extreme conditions (highest and lowest pHs) produced the most positive results, similar to tests at 60° Celsius where the lowest concentrations had the best dissolution

rates. The tests also revealed that there may be a tendency for pH to buffer around 7.0 upon the addition of gelatin. Addition of gelatin usually brought the pH one degree closer to 7.0 from either extreme. To further indicate this possibility, the Δ pH was the least at the most neutral pH values. This observation may become relevant in future tests.

In coordination with the individual pH tests, an experiment was also performed to determine whether the properties of the solution changed once an extreme pH solution was neutralized to become more biocompatible and appropriate for administration. For this test, a solution was made of 20% gelatin in NaOH, since bases are generally more biocompatible than acids. Then, acid was added drop-wise with the intention of neutralizing the base and creating approximately a 10% solution. Since it was difficult to perform this objective accurately without overshooting the equivalence point of NaOH, the closest final pH that could be reached was 2.2. Although the method could be improved upon, the experiment yielded interesting results. Instead of gelling or staying completely dissolved, the final solution had a sol-gel consistency that was maintained for several days. Further research into the subtleties of this process could prove advantageous for the final design.

There were a few obstacles limiting acquisition of ideal results in each of the above experiments. First, the type of tube used to mix the gelatin solution was conical, so some of the gelatin solid became stuck at the tip in several trials, effectively lowering the weight percent. Additionally, the gelatin at the most extreme pH was speculated to be completely denatured, including denaturation of the primary structure, which would permanently alter its structural properties. In addition, the pH tests revealed how difficult it may become to ensure consistency in observation of dissolution and that the qualitative rating system may not be accurate enough to interpret the results. Several pictures were taken in an effort to make the rating system more

accurate (see *Figure 6* below, as an example); however, even these pictures are difficult to distinguish between dispersed solutions, phase-separated solutions, and those samples that are fully in solution.



pH 8.2 – final pH 7.5 pH 11 – final pH 10

**Figure 6:** This figure shows two images of gelatin mixed with different pHs. The photos were taken in an effort to standardize the rating system for gelatin dissolution; however, it is not flawless. As shown, the pH 11 solution exhibits far fewer gelatin globules than does the pH 8.2 solution. According to the rating system, this observation indicates better dissolution.

Because of the somewhat positive results of the pH tests, other modifications were predicted to have similar, if not more controlled effects. The next set of tests also addressed variations in pH, and it overcame the conical tube issue, since tests were run in flat-bottomed glass vials. The only other differences in the method were that dissolution was measured for both 10 and 15% gelatin and that the middle-range pH values were eliminated to focus on those pHs that produced the most positive results in the first set of trials. The results are shown in *Table 7* below:

**Table 7:** Dissolution of 10 and 15% gelatin was tested at pHs from 1-4 and 10-13. The extent of dissolution was rated as (+), (+/-), or (-), and the change in pH was also noted after 5 minutes. The results clearly differ from the original trials in that no dissolution was observed after 5 minutes, although some did occur initially

| Weight Percent | Buffer | initial pH | final pH | Δ pH | Dissolution |
|---|---|---|---|---|---|
| 10% | N/A | 1.1 | 6 | 4.9 | - |
| 15% | N/A | 1.1 | 6 | 4.9 | - |
| 10% | N/A | 2.1 | 5 | 2.9 | - |
| 15% | N/A | 2.1 | 5 | 2.9 | - |
| 10% | N/A | 3.1 | 5.5 | 2.4 | - |
| 15% | N/A | 3.1 | 5.5 | 2.4 | - |
| 10% | N/A | 4.1 | 5 | 0.9 | - |
| 15% | N/A | 4.1 | 5 | 0.9 | - |
| 10% | N/A | 10 | 6 | 4 | - |
| 15% | N/A | 10 | 6 | 4 | - |
| 10% | N/A | 11 | 6 | 5 | - |
| 15% | N/A | 11 | 6 | 5 | - |
| 10% | N/A | 12 | 7 | 5 | - |
| 15% | N/A | 12 | 7 | 5 | - |
| 10% | N/A | 13 | 12 | 1 | - |
| 15% | N/A | 13 | 12 | 1 | - |

**Table Key:**

+ represents full dissolution

+/- represents a dispersion

- represents phase separated solution.

Clearly, the results of these trials differ from the initial ones. Some of this could be attributed to the fact that all the gelatin was completely dissolved from the bottom of the vial, but it could also be attributed to the wider radius of the vials which allows the solution more exposure to air. Increased air exposure could reduce the time it takes for the solution to gel. This possibility will be monitored in further tests to substantiate, elaborate upon, or refute.

*Part III: Effects of Different Buffers on Dissolution*

The final set of experiments that were conducted to date involved mixing 10 and 15% gelatin with several common, biological buffers of varying pHs and chemical properties. The findings are shown in the figure below:

**Table 8:** Four different buffers were mixed with 10 and 15% gelatin at room temperature to determine the effect on its dissolution. The rows highlighted in blue are the most positive results that will continue to be explored in future tests.

| Weight Percent | Buffer | initial pH | final pH | Δ pH | Dissolution |
|---|---|---|---|---|---|
| 10% | Phosphate | 7 | 7 | 0 | + |
| 15% | Phosphate | 7 | 7 | 0 | + |
| 10% | Tris | 8 | 8 | 0 | - |
| 15% | Tris | 8 | 8 | 0 | - |
| 10% | HEPES | 8.5 | 7.5 | 1 | + |
| 15% | HEPES | 8.5 | 7.5 | 1 | + |
| 10% | MES | 5 | 6 | 1 | - |
| 15% | MES | 5 | 6 | 1 | - |
| 10% | Citrate | 6 | 6.5 | 0.5 | + |
| 15% | Citrate | 6 | 6.5 | 0.5 | + |

**Table Key:**

+ represents full dissolution

+/- represents a dispersion

- represents phase separated solution.

The results are unique, since some buffers allowed the gelatin to dissolve rather readily at near-neutral pHs. Additionally, they seem to have the same effect of changing the pH value with the addition of gelatin as in earlier tests, where the final pH approaches 7, regardless of the initial pH value.

**Future Plans and Conclusions**

Initial literature research on both the properties of gelatin and possible approaches for stimulating dissolution of gelatin has given our group a knowledge base from which to work. A thorough consideration of different approaches to develop a functional design has uncovered advantages and disadvantages in our proposed design approach. Finally, preliminary research has been conducted to substantiate the final design approach, and through these actions and decisions, our group has been able to address the design constraints that our client shared with us while beginning to develop a design solution that will further the clinical applicability of interpenetrating networks.

Future work will constitute of continued research; as we will explore and manipulate the properties of gelatin by extending our tests of pH and buffers. We will investigate the unique

results in some of our experiments to assess the buffering capacity of a gelatin-solvent solution as well as the effect of increased solution surface area on its rate of gelation. Furthermore, we will consider using spectrophotometry to develop a more quantitative rating system for gelatin dissolution, and we will begin to test gelatin of different molecular weight/Bloom number/type to assess their effect on dissolution. Based on the results of these studies, the gelatin solution(s) will be tested in complete IPNs to determine its final viscosity and curing rate. Once these steps are completed, we will assess the feasibility and effectiveness of our design, perhaps by comparing it to the predicted properties of the alternate approach. As a result, we may reconsider our design approach and suggest a mechanical/chemical alternative to heating the gelatin solution externally.

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(((WE BE HYDROGELLIN')))

## Appendix:

## PDS

**Title: Interpenetrating Networks for Delivery Systems**

**Team:**
Ashley Huth- Team Leader
Max Michalski- BWIG
Claire Flanagan- Communicator
Adam Rieves- BSAC

**Function:** Interpenetrating networks (IPNs) are a type of biomaterials that polymerize in situ and have been used in drug delivery, wound healing, and tissue engineering applications. This design project involves the development of novel delivery mechanisms that should be clinically easy to use with improved storage life. Our device should safely, efficiently, and accurately aid in the administration of IPNs to a specific region.

**Client requirements:** Our client wishes to dehydrate the components of an IPN to a powder form, so that the powder can be stored interminably/for a prolonged time frame in a spray bottle and reconstituted with water at the time of use. He hopes that this development will make the product easier to use and that it will have a much longer shelf life, although determining what the shelf life is will not be expected of us during this term. Topics to consider will be the appropriate component concentrations, the method of dehydration, as well as the viscosity of the resulting solution and its effects on both UV curing time along and the ability to spray the solution through a narrow tube.

**Design requirements**:

**1. Physical and Operational Characteristics**

a. *Performance requirements*
Powder solution must have the correct molecular weight that when reconstituted creates a desirable viscosity. Mixing procedures should also be relatively straightforward. Final solution should be cured within 60 seconds under UV light after application.

b.*Safety*
Chemical properties of the original IPN should not be compromised.

c. *Accuracy and Reliability*
Mixing procedures should be relatively straightforward to minimize human error. Molecular formula should be standardized between bottles. Final solution should have a uniform consistency and desirable viscosity range.

d. *Life in Service*
Each bottle will be single use.

e. *Shelf Life*
Multiple years are desired, however this is not a strict requirement.

f. *Operating Environment*
Product will only be used in a sterile environment.

g. *Size*
Sizes can vary.

j. *Materials*
Components of formula will include gelatin, PEG-dA, diH20, 8 oz. spritzer bottle, pharmaceutical agents, and photoinitiator. Other materials are yet to be determined.

k. *Aesthetics, Appearance, and Finish*
Possibly color-coded for varied applications and different drugs. Product must be well-labled.

**2. Production Characteristics**

a. *Quantity*
Only one unit is desired.

b. *Target Product Cost*
Unknown, although it must be kept to a minimum.

**3. Miscellaneous**

a. *Standards and Specifications*
FDA re-approval may be necessary.

b. *Customer*
Various medical institutions.

c. *Patient-related concerns*
Trapping foreign objects in solution before administration. Sterile packaging.

d.*Competition*
Current bandage technology, including those with silver nitrile/cotton gauze.