ABSTRACT

LI, CHENXIANG. Mathematical Models to Predict the In Vitro Degradation Process of PLGA-coated PGA Nonwoven Material. (Under the direction of Dr. Martin W. King.)

In the area of tissue engineering, a precisely controllable rate of biodegradation of the scaffold material is a key factor which ensures that the device will be completely resorbed at the desired and predicted time point relative to the growth of tissue. In order to provide a better understanding and a more accurate prediction of the change in strength of the textile scaffold associated with this resorption process, a mathematical model needs to be developed based on experimental observations.

So as to explore the changes in mechanical and chemical properties during hydrolysis, a series of in vitro degradation experiments were undertaken for 24 days of incubation on polyglycolic acid (PGA) fibers and needle-punched nonwoven materials with and without a 50-50 poly(lactic-co-glycolic acid) (PLGA) coating. The progression of degradation was monitored by measuring experimentally the bursting strength of the nonwoven web together with those factors that contributed to its strength, namely, the single fiber tensile strength and the extent of fiber entanglement. FTIR spectra confirmed that there was increasing evidence of hydrolysis of ester bonds due to the growth of characteristic hydroxyl and carboxyl group peaks. As degradation continued, the DSC results showed a rise in crystallinity during the initial period, followed by a fall in crystallinity after 18 days. After 24 days all the PGA material had lost so much strength that they became too weak to be handled. The bursting strength of the PGA web alone decreased by about 65% from 285 N to 99 N in the first 4 days, and the PLGA coated samples showed a similar trend. After 6 days, no statistical difference in bursting strength could be found between
the coated and uncoated nonwoven samples. In comparison, a loss in single fiber tensile strength was not observed until Day 2, which initiated a linear reduction in single fiber strength.

A new experimental technique was developed to evaluate the interactions between fibers within a nonwoven web by measuring the single fiber extraction force. The results showed that there was an approximately linear decrease in fiber extraction force from the initial value of 10.5 gf to 3.3gf after 9 days of degradation. The presence of fiber surface damage and loss in fiber entanglements was observed by scanning electron microscopy. The SEM images were also able to identify broken fiber ends within the PGA webs after 12 days of hydrolysis. These 100% PGA webs continued to lose all their strength and structural integrity within 24 days. Whereas in the degraded PLGA coated webs, SEM images showed that broken fiber fragments were still interconnected by the PLGA coating, which helped to maintain the strength and integrity of the structure beyond the experimental 24 day degradation period.

Artificial Neural Networks (ANNs) and regression analysis techniques were used to develop mathematical models to represent this degradation phenomenon. Both techniques achieved coefficients of determination higher than 99.8%, indicating that the equations that were developed from the experimental data were precise and accurate.
Mathematical Models to Predict the In Vitro Degradation Process of
PLGA-coated PGA Nonwoven Material

by
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DEDICATION

To my beloved parents and grandpa
BIOGRAPHY

Chenxiang Li was born on October 21, 1988 in Hangzhou, China. He received his bachelor's degree in Textile Engineering in July 2011 from Donghua University, China. In pursuit of further education, Chenxiang joined North Carolina State University, USA, to start his Master's program in Textile Engineering in August 2010. He expects to graduate in July 2012 under the direction of Dr. Martin W. King. Upon completion of his master degree, he plans to attend Duke University Medical School to pursue a Master’s degree in biostatistics.
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CHAPTER 1

GOALS AND OBJECTIVES

1.1 Introduction

In the past decades, organ failure and tissue injury have become an increasingly severe problem all over the world. Current available strategies include surgical reconstruction, medical device implantation and organ transplantation. This last technique needs to deal with immunological issues that lead to the risk of rejection once the transplanted organ is recognized as a foreign material. However, in addition to the high cost and risk of rejection, the demand for organ transplantation has far exceeded the donor supply of organs, as shown in Fig1.1.

![Graph of patients on the waiting list of organ transplantation between 1998 and 2009](Image)

Fig1.1 Patients on the waiting list of organ transplantation between 1998 and 2009
(From OPTN & SRTR annual data report 2010)
In order to resolve those limitations, a new technique has been developed with a potentially promising future. Tissue engineering is a technique to repair or replace damaged tissue with biological organs generated on a scaffold. In order to encourage the growth of living cells and provide mechanical support during the procedure, porous scaffolds are required to have outstanding mechanical properties, biocompatibility and to promote surface-cell interactions. Most importantly, in order to eliminate the need for removal surgery, a controllable biodegradability is necessary for the tissue engineering scaffold which enables complete resorption at a desired rate related to the growth of the new tissue.

Among all potential materials, fibrous textile structures have proven to be successful tissue engineering scaffolds and are under intensive research. However, the rate of resorption needs to be understood precisely so that fabrication, sterilization, storage and implantation procedure of textile scaffolds can be undertaken in a controlled and predictable manner. This goal can primarily be achieved by establishing a mathematical model to predict the resorption behavior.

1.2 Goals

1. To study the effect of in vitro degradation on changes in fiber entanglement and fiber strength in a PGA needle-punched nonwoven material. So as to generate sufficient data to develop mathematical models which predict changes in mechanical properties of the PGA nonwoven web during hydrolysis and the resorption process.
2. To build mathematical models using artificial neutral networks (ANN’s) and regression analysis techniques that will analyze the observed experimental data, so as to understand and quantify the resorption process.

3. An additional study will analyze the impact of a resorbable PLGA on the in vitro degradation process. This modification will enable the mathematical models to predict the mechanical performance of the PLGA-coated PGA needle-punched nonwoven material during the hydrolysis and resorption process.

1.3 Objectives:

1. In order to generate experimental data for the preliminary models that will predict the mechanical performance of needle-punched nonwoven material during in vitro degradation, it will be necessary:

   1.1 To undertake a series of in vitro resorption experiments on Biofelt PGA nonwoven webs and PGA fibers. The degradation process will be analyzed and explained by characterization techniques such as SEM, DSC, FTIR, gravimetric measurements, probe bursting strength test, a novel fiber extraction test and single fiber tensile test.

   1.2 To obtain and calculate descriptive statistics from the experimental results described in Objective 1.1 above. Individual fiber tensile strength retention (%) and fiber extraction force retention (%) will be used as input data for the mathematical models while bursting strength retention of the nonwoven web (%) will be the output.
value.

1.3 To generate preliminary models using the observed experimental data, so as to be able to predict the changes in mechanical properties over time. The changes in the two different phenomena will be analyzed, namely:

i) Interactions between fibers.

ii) Molecular weight and polymer chemistry.

An ANN model will be trained using a feed-forward back-propagation algorithm, and a regression model will be developed based on a bilinear interpolation function.

2. The mathematical models generated in Objective 1 will be modified in order to predict the mechanical performance of a PLGA-coated PGA needle-punched nonwoven material during in vitro degradation.

2.1 To accomplish this, a series of in vitro experiments will be undertaken following the procedures described in Objective 1.1 on PLGA-coated nonwoven needle-punched permanent PET webs. Gravimetric weight loss measurements and probe bursting strength tests will be performed to evaluate changes in bursting strength caused by the degradation of the PLGA coating. (It is assumed that the properties of the PET nonwoven web will not change during the in vitro experiments, thus any observed changes will be due entirely to the PLGA coating.)

2.2 An equivalent series of in vitro experiments will be undertaken on the PLGA-coated PGA material following procedures described in Objective 1.1.
2.3 The degradation data of the PLGA coating will be used as another set of input data and the relevant output data will be obtained from the observed experimental results measured above in Objective 2.2.

2.4 Modified mathematical models will then be generated which will enable the prediction of the mechanical performance of the PLGA-coated PGA nonwoven material during in vitro degradation.

1.4 Limitations of the Study

1. The novel fiber extraction test procedure has only recently been developed. It has not been validated. This is because there is limited knowledge about fiber directions and the fiber orientation distribution in the web. In addition, the manual operation of the test did not ensure a reliable result with minimum variability.

2. After 9 to 12 days of degradation, the mechanical integrity of individual fibers became too low to withstand manual operation. Meanwhile, the bursting strength test of the nonwoven webs still showed a measurable result. So the missing individual fiber properties were calculated using regression analysis. This procedure may have led to some error or bias since observed experimental data was not used.

3. The selection of the type of mathematical model was limited due to insufficient data and partial dependence between input data sets. They were both functions of time with a limited number of data points.
CHAPTER 2

LITERATURE REVIEW

2.1 Artificial Neural Networks (ANNs)

2.1.1 General introduction

The topic of artificial neural networks (ANNs) is a branch of nonlinear modeling that is inspired by our understanding of the structure of human neural networks. Similar to the human brain, the ANNs model has a web structure composed of several interconnected junctions and switches which process signals and transfer information. This structure enables ANNs to own some unique characteristics such as the ability to learn and generalize; the compatibility to handle nonlinear functions and the tolerance to accommodate error.

The ability to learn means that ANNs can be trained with real-world results in order to explore the underlying relationship between variables. Since observing experimental data is always more straight-forward than generating theoretical models, this modeling technique can serve as a very practical approach in scientific research.\textsuperscript{[1,2,3]}

Compared to traditional models, ANNs deal solely with data, which endows them with the ability to become a universal model. As a result, we can always consider them as a substitute
method of modeling, particularly when there is theoretical model already available on the subject. [1,3]

2.1.2 Application of ANNs

These unique characteristics enable ANNs to be utilized in solving various problems. As shown in Fig.2.1, the applications come generally from seven categories, namely: pattern classification, clustering, function approximation, forecasting, optimization, association and controlling.

2.1.2.1 Pattern classification

The procedure of building a pattern classification model is to train the ANNs with certain pattern signals (for example: hand written symbols or cardiograms) and their corresponding pre-specified classes. When an unknown input pattern is assigned to the model, it would be able to classify it by recognizing one or several properties of a class. The widely used handwriting recognition technique which converts hand-writing texts into electric documents is developed based on artificial neural networks. In the textile industry, researchers have developed several ANN models to identify the pattern of a fabric.
2.1.2.2 Clustering

Different to pattern classification, clustering models are trained without any specific data. Receiving input data, the model divides them into several clusters by exploring the similarities and dissimilarities between them. This procedure enables ANNs to be developed into applications such as data compression \(^2\) and subspecies discrimination in microbiology.\(^3\)

2.1.2.3 Function approximation

Function approximation is the major application of ANNs that will be utilized in this study. As mentioned at the beginning, in most scientific and engineering research, people tend to explore the underlying relationship between parameters. When traditional mathematical models can barely satisfy the accuracy requirements, ANN models could always be considered as an alternative choice since they can

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![Diagram](image)
approximate any function to a high degree of accuracy. Given pairs of input-output data, the model is able to learn step by step and approximate the relationship between them.

The model structure and training procedure will greatly influence the accuracy of the model. Insufficient training and layers will lead to poor fitting of the function while over-fitting may occur when too much information is provided on the input side (Fig.2.1(3)). The performance of a particular model is also dependent on errors and parameters such as training steps and data normalization. These factors will be discussed with detailed examples in the following section.

The application of ANNs as a universal function approximator covers almost every area of scientific research, including atmospheric science \(^4\), chemical engineering\(^5\), clinical medicine\(^6\), ecological science\(^7\), hydrology\(^8\), etc. In the textile industry, prediction of product performance (usually mechanical properties) can be achieved by inputting several manufacturing parameters. Research has been done on different forms of textile materials, fibers, yarns, woven fabric, knitted fabric and nonwoven webs, which utilized similar approaches to the ones we developed in this study. Examples will be provided to help in understanding when ANNs modeling technique are discussed.

### 2.1.2.4 Forecasting

Given a series of data in a time sequence, the ANNs will be trained with samples to discover the trend and to predict the value at a future time point. This application is particularly important in the business. It helps in dealing with issues such as changes in stock values and
product demand, which are key factors when making decisions. In the scientific area, growth curves of cells and weather conditions are typical factors that may be described in advance by applying previous observations to ANNs. [2]

### 2.1.2.5 Optimization

Subject to certain constraints, optimization procedures try to find an input value that maximizes or minimizes the target function [2,3]. Since optimization is a classic problem that scientists in every area need to solve, there are already plenty of mature techniques from which to choose. ANNs’ specialty in dealing with nonlinear functions makes it the ideal choice when a complex nonlinear function is being analyzed. The famous travelling salesman problem, which is shown in Fig.2.1.5, is a typical example in which the salesman tries to travel through every city with the lowest possible cost [2]. In the textile area, where compromise is needed to achieve a certain quality at a relatively lower cost, a balance can be reached with the use of an ANN. For example, higher yarn twist leads to lower productivity and stiffer material while lower twist results in a lower yarn tenacity.

### 2.1.2.6 Association

When the ANNs are trained with noise-free data, they have the ability to classify data even though it may contain error. Moreover, it may actually correct the error or complete the missing data. The mechanism of this technique is implied by its alternative name: content-addressable memory. Since content data is stored at a fixed address, when part of the content
is input into memory, the address will be recalled. Then the noise-free data which is already in the memory, can be used to replace input data. As shown in Fig.2.1.6, a popular application of this technique is to separate elements contained in an image. [3]

2.1.2.7 Controlling

As seen in Fig.2.1.7, in order to have a desirable output which in this case, is the idle speed of engine, an adaptable controlling function, which is based on current outputs, will be added to the input data [2,3]. ANNs enable the development of the controlling function when a reference function is given. This application is of great importance in automated textile manufacture to achieve satisfactory and consistent quality control.

2.1.3 ANNs structure and important parameters

Artificial neural networks are named this way because their structure was inspired by biological neural networks. A neuron is a nerve cell that transmits information along the web. Signal interaction between neurons is achieved by pulses of different frequency. As a matter of fact, the signal transmitted through a single neuron is small in size, usually a few bits, so the completion of complex missions can only be done through networks of individual neurons [3]. Though the structure and size of a neuron may vary among different locations in the body, the basic mechanism of signal transmission can be summarized in Fig.2.2.
2.1.3.1 ANNs structures

The simplest artificial neuron model was described in the work of Warren et al\textsuperscript{[9]}, which used a binary threshold as the transfer function. The function outputs 1 when summation of inputs is larger than the threshold, otherwise it has a valued of 0, as shown in Equ.2.1. This design is to mimic the “all-or-none” character of the nervous system.

\[
\begin{align*}
    y &= 1 & \text{if sum} & \geq b \\
    y &= 0 & \text{if sum} & < b
\end{align*}
\]

Equ.2.1 \textsuperscript{[2]}

A single connective point in this computational model is called a node, or a neuron. It receives input signals $x_1, x_2, x_3…x_n$, similar to external stimulation in biological systems, and calculates the summation $\xi$ by multiplying each of the inputs with its corresponding weight.
$w_1, w_2, w_3 \ldots w_n$, which could be either positive or negative. The output of this neuron is an activation function ($\sigma$) of $\xi$, as expressed in Equ.2.2.

$$y = \sigma(\sum_{j=1}^{n} w_j \cdot x_j)$$  \hspace{1cm} \text{Equ.2.2}

In this case, the activation function follows Equ.2.1, however, most common applications such as the model that was designed in this study, requires a continuous and differentiable function \cite{2}. The most frequently employed function in modeling research is the Sigmoid function, whose standard equation is expressed as following:

$$f(x) = \frac{1}{1+e^x}$$  \hspace{1cm} \text{Equ.2.3} \cite{3}

The sigmoid function is ideal because it increases strictly in the range ($-\infty$, $+\infty$) and exhibits asymptotic properties, which is a preferred component of the ANNs structure \cite{3}. The structure described above is the basic unit which has a very limited ability for information transmission. However, a much more complex system could be formed in many ways, as shown in Fig.2.3. The output of one neuron can either be the output of whole network or the input of another neuron. Moreover, information transmission is not necessarily in one direction.

Any two neurons in the system can be connected in any direction with different weights. Those networks which contain feed-back connections are called recurrent networks \cite{3}. As we can imagine, recurrent networks are dynamic systems, since neurons close to the input layer receive feedback from those in the upper layers, which enable them to adjust the connection weights as needed.
The most popular method which also happens to be the structure that was chosen for this paper, of forming a network, is by organizing individual neurons into a multi-layer structure. In other words, the output of a single neuron will be the input data of every neuron in the next layer. Fig. 2.4 is a typical feed-forward ANNs with one hidden layer [8].

The first layer which receives signals from external inputs is called the input layer, while the output layer is the last layer which generates output data for the whole system. Layers in the
middle are named hidden layers since they will not have direct communication with the external environment. The determination of the number of hidden layers and the number of neurons in each layer will have a tremendous impact on the performance of the network, which will be discussed later\cite{7}. The ability to learn is the basic feature of intelligence. After the architecture is determined, our network initializes all the weights to a random number, just like a newly-born child. Basically, the learning procedure is the process that the network updates weights according to the information received\cite{1}. Based on information availability, the network usually has two learning paradigms—supervised and unsupervised.

Unsupervised learning describes the situation that no correct answer (output data) is provided when training. It explores the relationships between the input data and tries to discover the similarities or trends among them, which is usually utilized when dealing with clustering problems\cite{2}. On the other hand, supervised learning employs correct answers to train the network. An expected or correct output is provided for each input data when training. Moreover, these two learning paradigms can be used simultaneously to solve more complicated problems. Since the modeling in this study aims to discover the underlying relationship between input and output data, it satisfies the definition of supervised learning.

A typical method to update the weights in supervised learning networks is error correction learning\cite{2}. In each training cycle, the output of a neuron is compared to the correct output value, obtaining the difference as the error of each neuron. According to the errors generated during training, researchers need to choose an optimization method to modify the corresponding weights.
Generally speaking, the Perceptron Learning Algorithm is the most straightforward method, whose procedure is described below \cite{3}:

1. Initialize all weights to random numbers.
2. When receiving a set of input data (x), calculate the output number (y) with those random weights described in 1.
3. Update the weights as following:
   \[ w(t + 1) = w(t) + \phi (d - y)x \]  
   Equ.2.4 \cite{3}

Where \( w(t) \) is the weight before \( t^{th} \) training cycle, \( w(t+1) \) is the weight updated after the \( t^{th} \) training cycle, \( d \) is the desired output, \( \phi \) is the step size.

Other than the Perceptron algorithm, there are numerous optimization methods available, providing plenty of choices for researchers. As a matter of fact, none of them guarantees a better performance over the others\cite{2}. However, there is one method which is more popular and works well in most modeling cases. This is called the backpropagation algorithm (BP). It operates within the frame of multilayered structure, which contains several hidden layers to help capture nonlinear relationships between inputs and outputs \cite{1,7}. The term backpropagation indicates the way in which error is calculated and corrected, namely from the output layer, through the hidden layers to the input layer.

A derivation of BP can be found in the work of Zupan et al \cite{10}. According to Jain’s work, the BP procedure of updating weights is summarized as following \cite{3}:

1. Initialize the weights to random numbers.
2. When receiving a set of input data (x), calculate the output number (y) with those random weights described in 1.
3. Calculate the error in the output layer \((\delta_i^L)\) by:

\[
\delta_i^L = \sigma' \xi_i^L (d_i^L - y_i^L)
\]

Equ.2.5 \(^{[3]}\)

Where \(\sigma'\) is the derived function of the activation function, \(\xi_i^L\) is the net input of the \(i^{th}\) neuron in the \(l^{th}\) layer (capital L refers to the output layer), \(d_i^L\) is the desired output of this neuron and \(y_i^L\) is the output calculated from the initial weights.

4. Calculate the errors of neuron \(i\) in the hidden layer \(l\) by:

\[
\delta_i^l = \sigma' \xi_i^l \sum w_{ij}^{l+1} \delta_j^{l+1}
\]

Equ.2.6 \(^{[3]}\)

Where \(j\) is a neuron in the layer higher than \(l\) \((l+1)\), \(w_{ij}^{l+1}\) is the weight applied from \(i\) to \(j\), \(\delta_j^{l+1}\) is the error of neuron \(j\) in the \(l+1\) layer. \(l=1,2,3,4\ldots L-1\).

5. Update weights using:

\[
\Delta w_{ij}^{l+1} = \phi \delta_j^{l+1} y_i^l
\]

Equ.2.7 \(^{[2]}\)

Where \(\phi\) is the learning rate, \(y_i^l\) is the output of neuron \(i\) in layer \(l\). This equation comes from the delta rule \(^{[2]}\).

### 2.1.3.2 Important parameters

Hidden layers are the functional elements that work to capture the relationship between input and output data. The number of hidden layers determines its sensitivity to various functions. Fig.2.5 is an illustration of how the number of hidden layers would influence the performance of ANNs in classification problems. Networks with one layer (input layer) have a similar function as linear statistical models. The application is limited to linear outputs,
otherwise the accuracy could be disappointing. Theoretically, an ANN with one hidden layer is able to approximate any continuous function to a desired accuracy\footnote{1}. However, it may require a large number of hidden neurons in that single hidden layer, which leads to a longer training time and increases the risk of over-fitting. So researchers have tried more than one hidden layers and compared their performance with single hidden layer models. Some of these researches achieved a better model with more hidden layers. For example, Debnath et al found ANNs with three hidden layers gave more precise modeling than those with two or one hidden layer. The errors were 1.58\%, 5.79\% and 14.85\% respectively\footnote{11}.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Description of decision regions</th>
<th>Exclusive-OR problem</th>
<th>Classes with meshed regions</th>
<th>General region shapes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single layer</td>
<td>Half plane bounded by hyperplane</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two layer</td>
<td>Arbitrary (complexity limited by number of hidden units)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three layer</td>
<td>Arbitrary (complexity limited by number of hidden units)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig.2.5 Impact of hidden layer amount on the performance of ANNs. \cite{3}

The number of neurons (nodes) in a hidden layer has a similar impact on the performance of the ANN model, as illustrated in Fig.2.6\footnote{2, 12}. Too few hidden neurons will result in poor nonlinearity of the resulting function. Usually it will work out as a best-fit linear regression.
line for the real underlying nonlinear relationship. On the other hand, too many hidden neurons will make the model too sensitive to noise and experimental errors in the data. This will mislead the model into an over-fitted curve which passes through all the experimental data points that may contain a high level of error.

As emphasized in section 2.1.3.1, the activation function plays a critical role since it determines the way all training calculations are made. Theoretically speaking, all continuous functions can be applied as an activation functions. However, only a few functions have been tested and found capable contributing to an ANN design. They include:

- Sigmoid function, which can be found in Equ.2.3

- Hyperbolic tangent function (tanh)

\[
y = \frac{e^x - e^{-x}}{e^x + e^{-x}}
\]

Equ.2.8 [1]

- Trigonometric function
\[ y = \sin x \text{ or } y = \cos x \]  
\[ \text{Equ.2.9}^{[1]} \]

- Linear function

\[ y = x \]  
\[ \text{Equ.2.10}^{[2]} \]

There is no evidence that a certain function works better than the others, but the Sigmoid function is the most popular choice for modeling applications. Since it is not clear how the type of function will influence the performance of the model \[^{[1]} \], researchers can always try different functions to reach an optimal approximation. Moreover, the effect of activation functions in different neurons can be different. For example, a Sigmoid function may be preferred for the hidden layers whereas a linear function is used for the output layer.

In addition to the parameters discussed above, researchers may also improve the performance of ANNs by modifying several other procedures.

1) By normalizing data into small ranges, usually (0, 1). It is possible to lower the risk of overriding from larger numbers as well as avoid premature termination of hidden neuron processing. This is because training will stop when a low enough percentage of error is reached\[^{[2]} \].

2) The ratio of training sample size to testing sample size also plays an important role. Before the learning process, the portion of available data that will be used to train the model must be determined, leaving the rest for testing purposes. Usually we can find 90% to 10%, 80% to 20% or 70% to 30% training to testing ratios in articles in related technical areas. To make sure that both training and testing samples are representative, a higher
portion for the testing sample may be required when total sample size is relatively small.

3) Weight initialization. As mentioned in BP and the Perceptron Learning Algorithm, the first step of training a network is the initialization of all weights. A good estimation with small numbers will significantly reduce the training time as well as the risk of terminating hidden neuron prematurely\cite{2}.

4) Learning rate $\phi$ during BP training in Equ.2.7. A larger $\phi$ will lead to a faster learning process but a lower accuracy. Since weights are updated from cycle to cycle, with large $\phi$, the output may oscillate around an estimated value and never reach an optimized approximation\cite{2}.

2.1.4 Previous modeling researches using ANNs

In the application section, several forms of problems that ANNs are able to deal with were listed. Among them, the one that interests engineers most is the function approximation/modeling approach using multilayered ANNs. In recent years, this particular form of ANNs helped researchers from numerous areas to discover underlying relationships of various different factors.

2.1.4.1 Typical ANNs modeling applications

Theoretically speaking, an ANN is able to approximate any nonlinear function with the desired accuracy. This special property attracts researchers who need an alternative tool to traditional statistical method for modeling and prediction. The following section contains several typical applications of ANNs.
For instance, according to Gardner’s review, ANN models have been utilized in atmospheric science since the early 1990s. Researchers recorded meteorological parameters such as temperature, CO₂ concentration, and wind speed and direction as input data and surface ozone concentration as output data so as to build a multilayered model using ANNs. Similar approaches have been made to predict sulphur dioxide concentration, the incidence of tornadoes and thunderstorms, monsoon rainfall and solar radiation[^4].

The most well-known application of ANNs in clinical medicine is the diagnosis of myocardial infarctious (heart attacks)[^13]. Since misdiagnosis will lead to serious consequences, the diagnosis sensitivity was usually set as high as possible. As a result, some patients who do not experience myocardial infarctions still have to receive medical treatments[^6]. In William’s work, he used ANNs to identify the likelihood of a myocardial infarction among patients with anterior chest pain. The symptoms of 331 patients were recorded and used to train the model. To evaluate the performance of ANN models, the diagnostic sensitivity and specificity were compared with conventional methods. The results showed that ANNs had an average diagnostic sensitivity of 97.2%, and average diagnostic specificity of 96.2%, both of which are significantly higher than those obtained by conventional techniques (77.7% and 84.7%, respectively)[^13].

According to Lek’s review, by the year 1999, there were already hundreds of papers published on the application of ANNs to the area of ecology. Examples of topics included freshwater and marine system, population and community ecology, global change, ecosystem sensitivity and population genetics[^7]. Most of these papers used the same structure as that used in this study; namely a multilayered network with a BP algorithm.
In hydrological research, the use of ANNs has expanded rapidly in recent years. The rainfall-runoff process is a typical application. In Hsu’s work, a three-layer feed forward ANN was used to simulate the behavior of watersheds. It achieved a better model than linear regression and conceptual computer models. According to Dawson’s review of over 50 articles, most of them used multilayered structures (89%) and a Sigmoid activation function (64%). One hidden layer was able to achieve the desired accuracy in most studies, making it the most popular design (70%).

Also, ANNs have made a great contribution to research in energy systems. For instance, researchers set up ANN models to predict the performance of solar energy heating systems. The inputs, including solar panel collection area, system volume, the heat-loss coefficient of the material, solar radiation and air temperature, were used to predict the temperature rise of the stored water. The deviation was controlled within 2.2%. A similar approach can also be used to predict the temperature of air-conditioning systems in building or even a bus.

2.1.4.2 ANNs modeling in textiles industry

Textiles as a major part of industry, is always a research-active area. One typical characteristic of textiles is its nonlinearity since every single element in the material interacts with the other by elements abrasion and/or entanglements. One advantage of ANNs is the ability to approximate nonlinear functions which frequently occur in textile research. Also, textile materials are usually composed from smaller elements in a hierarchical structure. Taking apparel as an example, smaller elements are processed step by step into the final product, following: polymer, fibers, yarns, fabrics and eventually clothes. The prediction of
material properties at each step of this procedure is always of great interest to manufacturers and researchers since a good understanding of the influencing factors will enable them to improve the performance of the material. With the help of ANNs, researchers may use the properties of materials in a previous step as well as processing parameters as input data, to predict the performance of the final product. Related studies can be found in every step of fabrication.

2.1.4.2.1 Fibers

Synthetic fibers can be made from polymers using several different spinning technologies. Properties of the resulting fibers are highly dependent on the processing techniques and conditions. The study by Dev et al is a typical example of this particular application [16].

Researchers tried to link the water retention capacity of hydrolysed electrospun polyacrylonitrile fibers with processing variables. There were three independent parameters, alkali concentration, temperature and time, selected at three different levels, as shown in Fig.2.7 [16]. The designed network had two hidden layers, each with 5 neurons. The results indicated that all three inputs had a positive influence on the water retention capacity of the resulting fibers. A comparison between the performance of the ANN model and empirical model is provided in Fig.2.8 [16].

<table>
<thead>
<tr>
<th>Actual Values of the Variables for the Coded Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coded values</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>-1</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>+1</td>
</tr>
</tbody>
</table>

Fig.2.7 Three levels of input data [16]
Unlike synthetic fibers, natural fibers are obtained without any artificial processing. Instead of predicting product properties, a typical utilization of ANNs with natural fibers is their classification. According to She’s work, a network was designed to classify two similar animal fibers: merino and mohair \cite{17}. Prior to data input, an image capture and processing procedure was applied to divide the images into 280 mini units and extract morphological features and convert them into readable data. A multilayered network using tanh (Equ.2.8) as the activation function was used to distribute the data among the neurons \cite{17}.

### 2.1.4.2 Yarns

ANNs are frequently used as an alternative technique to predict yarn performance from fiber parameters. The breaking elongation of ring spun cotton yarns is modeled in Majumdar’s work \cite{18}. Researchers built five networks with one hidden layer containing 6, 8, 10, 12, 14 neurons to find an optimized structure. Training was finished after 2500 learning cycles when the learning rate was set at 0.1. A Sigmoid function was again chosen as the activation function. According to the experimental results, the neurons containing 10 hidden neurons gave the best prediction and these data were compared with the results from both a mathematical and statistical models, as shown in Fig.2.9 \cite{18}.

---

<table>
<thead>
<tr>
<th>Trial no.</th>
<th>Variables</th>
<th>Water retention capacity (%)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$X_1$</td>
<td>$X_2$</td>
<td>$X_3$</td>
<td>Experimental</td>
<td>Empirical</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>55</td>
<td>30</td>
<td>178</td>
<td>176</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>65</td>
<td>50</td>
<td>150</td>
<td>152</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>75</td>
<td>15</td>
<td>172</td>
<td>169</td>
</tr>
</tbody>
</table>

Fig.2.8 Performance of ANNs and empirical models \cite{16}
Similar approaches were made by Ureyen et al to predict yarn hairiness and the unevenness of ring spun yarn. A multilayered network with two hidden layers was trained using a BP algorithm with a learning rate of 0.01\textsuperscript{[19]}. Another part of Ureyen’s work focused on yarn tensile properties. The same input data, such as yarn count, yarn twist and roving properties, were given to the same network, which showed a better performance than with regression models \textsuperscript{[20]}. Khan et al also paid attention to yarn hairiness of worsted yarns. In his research, both a multilayered perceptron algorithm (see Equ.2.4) and a multivariate linear regression were applied the perceptron approach achieved a higher accuracy. Input data included fiber length, fiber diameter, yarn count, ring size and yarn twist. Twist appeared to be of greater influence among all parameters \textsuperscript{[21]}. Yarn unevenness was also modeled by Demiryurek et al. The material involved in this study was a polyester/viscose blended open-end rotor spun yarn. Parameters such as blend ratio, rotor speed and yarn count were inputs into the multilayered network trained with a BP algorithm. However, in this particular study, the conventional linear regression model produced a more accurate prediction than ANNs \textsuperscript{[22]}. Other examples could be found in Pei et al’s work to predict vortex yarn tenacity from process and nozzle variables \textsuperscript{[23]}. Also, cashmere yarn’s fineness and unevenness was forecasted by Ma et al,
using a three-layer BP ANN \cite{24}. More yarn property predictions can be found in the work of Majumdar \cite{25} and Ramesh \cite{26}.

### 2.1.4.2.3 Fabrics and seams

This is usually the final product stage and different properties are needed for different end uses. For instance, in Majumdar’s work, thermal conductivity of knitted fabrics where modeled with ANNs \cite{27}. Fabrics were knotted from 20 24 and 30 tex ring-spun yarns composed of cotton fibers, bamboo fibers and 50\%:50\% cotton:bamboo blends. Three knitted patterns were used, namely plain, rib and interlock. An ANN with one hidden layer were built with the structure shown in Fig. 2.10 \cite{27}.

![ANNs model designed for thermal conductivity prediction](image)

Again, Sigmoid function was used as the activation function. Five neurons in the hidden layer helped train the model with a 0.6 learning rate. Training stopped after 200 cycles when the decreasing error started to increase \cite{27}. 

27
Modeling of knitted fabrics using ANNs can also be found in Hossein’s work which predicted the hand value of knitted t-shirts. The results revealed that an ANN is more effective than using a linear regression model \[28\]. Wang et al tried to evaluate wet comfort performance of knitted underwear. Dimensional factors and moisture transmission parameters were inputted into a multilayered network containing seven input neurons, ten hidden neurons and three outputs. The correlation coefficient reached more than 90%, confirming a good accuracy of prediction\[29\].

The pattern and structure of a woven material has a strong impact on its mechanical performance as well as its appearance and hand. Jeon et al developed an ANN model to identify the basic woven pattern, such as plain, twill and satin weave. Similar to She’s work\[17\], images of woven fabrics were processed into readable data before being entered into the network using a LVQ algorithm\[30\]. Sardy et al did a similar study for defect detection of woven fabrics\[31\]. Behera et al used constructional parameters to predict bending rigidity of plain and satin weave cotton fabrics. The resulting model had a high correlation coefficient of 0.99\[32\]. Research done by Zeydan et al aimed to predict jacquard fabric strength with fiber, yarn and fabric parameters such as yarn count, yarn density and yarn type. The results indicated that the ANN models achieved a better approximation than Taguchi models \[33\]. Fan et al developed an ANN model for a comprehensive prediction of worsted fabric properties. Based on a large amount of information gained from a databank, researchers used thirty inputs which covered almost every aspect of worsted fabrics and outputs included all aspects of mechanical performance. The large database associated with this work enabled it to work as a expert system in this area\[34\]. The goal of Ogulata’s work was to predict the
elongation and recovery properties of stretch woven fabrics. The results revealed that ANNs achieved a similar level of accuracy to regression models in this application[35].

Seam performance is a key performance factor in the apparel industry. Fifty samples were collected from commercially available outerwear as input data in Hui’s model for the prediction of seam properties. The results in Fig.2.11 show that ANNs had slightly higher accuracy than the use of logarithm regression models [36].

<table>
<thead>
<tr>
<th></th>
<th>ANN</th>
<th>Logarithm Regression</th>
<th>ANN vs. Logarithm Regression (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For training data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Seam Puckering</td>
<td>0.932</td>
<td>0.897</td>
<td>3.90</td>
</tr>
<tr>
<td>• Seam Floatation</td>
<td>0.937</td>
<td>0.912</td>
<td>2.74</td>
</tr>
<tr>
<td>• Seam Efficiency</td>
<td>0.985</td>
<td>0.936</td>
<td>5.24</td>
</tr>
<tr>
<td>For testing data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Seam Puckering</td>
<td>0.790</td>
<td>0.766</td>
<td>3.13</td>
</tr>
<tr>
<td>• Seam Floatation</td>
<td>0.849</td>
<td>0.850</td>
<td>0</td>
</tr>
<tr>
<td>• Seam Efficiency</td>
<td>0.881</td>
<td>0.851</td>
<td>3.53</td>
</tr>
</tbody>
</table>

Fig.2.11 comparison of modeling accuracy [36].

2.1.4.2.4 Nonwovens

Nonwoven materials are textile structures with a high level of disorder since during production there is relatively poor control of fiber organization compared to other fabrics. Melt blowing is a technique that directly converts polymer into a nonwoven web by blowing the molten polymer into a random web using hot air. In Chen’s work, process variables like polymer flow rate (G), air velocity (Ua) and spinning distance (L) were used as input data; fiber diameter was identified as output data so as to train a network whose structure is shown in Fig.2.12[37]. A typical feed-forward network with one hidden layer was designed for prediction. During training, the error of the output value was decreasing (Fig.2.13)[37].
Chen also utilized the same network design to simulate the drawing factors during melt blowing \[38\]. In this series, Chen was able to predict the filtration properties of melt-blown nonwoven webs obtained from experiments were predicted by means of an ANN using input values such as air pressure, spinning distance and the number of layers \[37,38,39\]. Bo et al also worked to predict the fiber diameter of spunbonded nonwoven webs from the processing parameters \[40\].

The air permeability of needle-punched nonwoven webs were studied by Debnath et al. Jute fibers were blended with polypropylene fibers, which were then needle-punched in order to form a bonded web. A BP network was trained with fifteen sets of data for 40000 cycles with a learning rate of 0.01. Three different structures involving hidden neurons were compared. First: one hidden layer containing two neurons was compared to two hidden layers containing three and two neurons in the first and second layer respectively. The third
structure contained three hidden layers each containing three neurons. The ANN with three hidden layers behaved the best among all designs. The error was only 1.58%, significantly lower than 5.79% and 14.85% for the networks with two and one hidden layer respectively\textsuperscript{[11]}. Chen et al tried to solve a similar problem to the aim of this study, namely; modeling the properties of a nonwoven web using fiber and web structural parameters. Seven structural parameters were used, namely: fiber length, fiber count, pore volume, weight uniformity, thickness, weight per unit area and fiber density; so as to predict the mechanical properties and air permeability of the nonwoven web. A feed-forward network was designed with one hidden layer containing two neurons. A BP algorithm was modified with a Bayesian framework to prevent over-fitting. The results indicated a good simulation with an error of around 0.8% for all three parameters\textsuperscript{[41]}

2.2 Degradation behavior of PGA material

Over the past decades, the application of polymers in the biomedical area has increased explosively, enabling the invention of numerous products. Typical ones include sutures, blood vessel stents, hernia repair meshes and tissue engineering (TE) scaffolds. Among them, tissue engineering scaffolds is under intensive study because of the attraction brought by its promising future. Tissue engineering is a technique to repair or replace a damaged tissue with biological organs generated on a scaffold. According to related reviews about TE scaffolds, the general requirements for the material and structure are listed as the following \textsuperscript{[42-45]}:

1. Sufficient mechanical properties are required to maintain the required performance
after fabrication, packaging, handling, sterilization and implantation. The stress-stain curve should be similar to the target tissue.

2. Good biocompatibility is necessary for synthetic materials so as to prevent provoking severe inflammatory response.

3. Good processability and ease of sterilization.

4. Positive scaffold-cell interactions so as to induce cell activities such as adhesion, growth, proliferation and differentiation.

5. Adequate total porosity, pore volume and pore size distribution to favor cell transplantation and growth.

6. Controllable biodegradability enables the material to be completely resorbed at a desired rate related to the growth of new tissue.

Because of the multiple requirements listed above, current research have mainly focused on the following potential areas: nerve regeneration [46], blood vessels [47], bone [48], cartilages [49], heart valves [50], ligaments [51], skins [52], tendons [53], abdominal walls [54] and platelets [55].

Among the six requirements, the one that is the most challenging for polymer selection is biodegradability. During the intense research on developing degradable polymers, many new structures have been synthesized. However, very few of them have been approved by the FDA. Among them, polyglycolic acid (PGA) has the simplest chemical structure, good biocompatibility and relatively high mechanical properties. The earliest application, and also
the most well-known, is its use as a biodegradable suture. These sutures close wounds and dissolve \textit{in vivo}, without the need of an additional removal surgery. The success of PGA in the suture industry has inspired more applications such as TE scaffolds and drug delivery systems. Textile structures play a key role in the design of the scaffolds in terms of achieving adequate mechanical properties and porosity. A number of different textile technologies and process parameters have been used by researchers, for example: braiding \cite{56}, embroidering \cite{57}, flocking \cite{58}, knitting \cite{59} and weaving \cite{60}, etc. The selection of which technology to use is highly dependent on the location where the product is applied.

2.2.1 Properties and degradation mechanism

Manufacture of PGA can be done through the following methods:\cite{61}

1. Polycondensation of glycolic acid;

2. Ring-opening polymerization of glycolide;

3. Solid-state polycondensation of halogen acetates

Among the three techniques, polycondensation of glycolic acid is relatively more straightforward, but the resulting product usually has a low molecular weight.\cite{61}

Fig.2.15 shows the most common method to obtain PGA with a relatively high molecular weight: it involves a ring-opening polymerization of the diester. This reaction can be catalyzed by antimony trioxide and initiated by stannous octoate.
2.2.1.1 Chemical and mechanical properties of PGA material

Previous structural studies on PGA (as shown in Fig.2.16) indicate that it has “two planar zigzag molecules passing through an orthorhombic unit cell with dimensions $a = 5.22$ Å, $b = 6.19$ Å, and $c = 7.02$ Å (fibre axis). The chain axis has a twofold screw symmetry along the c-axis and the first chain lies on the ac plane at $b/4$, whereas the second chain, which is the mirror image of the first chain rotated 180° about c/2 lies on the ac plane at $3b/4$.”

The glass transition temperature of PGA is reported as 40 °C and the melting point being 225-230 °C. This temperature would ensure stable performance in vivo. With a degree of crystallinity of 45-55%, high molecular weight PGA cannot dissolve in water and common organic solvent.
As a result, the filaments are usually made by melt spinning. However, this characteristic makes the measurement of molecular weight difficult since only highly fluorinated solutions such as hexafluoroisopropanol (HFIP) can be used \cite{61,63}.

According to the Polymer Data Handbook, PGA has a relative high tenacity as well as elongation at break (Fig. 2.17). While these data may vary with different molecular weights and processing techniques, PGA is overall a strong material which can withstand high stresses, enabling its application to a wide range of biodegradable products. \cite{64}

<table>
<thead>
<tr>
<th>Elongation at break</th>
<th>%</th>
<th>Melt-spun fiber (diameter = 15–25 μm)</th>
<th>15–25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenacity</td>
<td>MPa</td>
<td>Melt-spun fiber (diameter = 15–25 μm)</td>
<td>690–1,380</td>
</tr>
</tbody>
</table>

Fig. 2.17. Tenacity and elongation at break of PGA fibers. \cite{64}

2.2.1.2 Hydrolysis process

According to the papers reviewed, there are some common observations about PGA degradation that were made by various research groups. Firstly, hydrolysis of the ester bond is the primary reaction that leads to biodegradation. Secondly, the mechanical properties of the PGA material, usually in suture form, gradually decrease and become too low to measure after 21 days. Thirdly, while the molecular weight continues to decrease, the material mass remains unchanged, despite the uptake of water, until a critical value, when the PGA starts to dissolve in water and aqueous solvents. Finally, the degree of crystallinity increases during the initial period of degradation before declining \cite{65-75}.

In the early 1980s, C C Chu published a series of articles \cite{65,66} explaining the degradation
mechanism of PGA, and generating a model of the PGA fiber structure which was meaningful in explaining these phenomena. He used a Dexon 2-0 suture as the raw material, which has a braided multifilament structure. In the first paper, the immersion liquid used was distilled water (pH = 6.8) in order to avoid the complex environment involved with in vivo exposure (Fig 2.18).

**In vitro Degradation Data of Dexon 2–0 Suture**

<table>
<thead>
<tr>
<th>Property</th>
<th>Duration of Immersion, days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Retention of tensile strength, %</td>
<td>100</td>
</tr>
<tr>
<td>Retention of elongation, %</td>
<td>100</td>
</tr>
<tr>
<td>Level of crystallinity, %</td>
<td>40</td>
</tr>
<tr>
<td>Degradation, %</td>
<td>—</td>
</tr>
</tbody>
</table>

Fig 2.18. Water degradation data of PGA suture

The samples were immersed in water for 7, 14, 21, 28, 49, 60, or 90 days at 37 ± 1°C in a constant-temperature oven. The parameters evaluated for each sample included the level of crystallinity and the tensile strength. Detailed experimental results can be found in Fig 2.19.

In Fig 2.19, the curves show a similar shape before day 21, each having a yield point at around 3% of strain. However, after 21 days of degradation, no significant yield point was observed in the curves. No significant fall in breaking stress was seen after the first week. However, during the second week, the tensile properties of PGA suture fell to less than half its original breaking tenacity. The initial moduli of the stress-strain curves decreased with increasing duration of degradation, and after 4 weeks, retention in stress and strain properties was less than 10%. 
From the data in the Fig.2.18, it can be seen that the change in the degree of crystallinity did not follow the same trend as mechanical properties. It increased from 40% to 52% in three weeks before slowly declining to 23% after 3 months. [65]

Fig. 2.19 Stress-strain curve of PGA water degradation after 0, 7, 14, 21, 28 days (right to left) [65]

To explain this reversing change in crystallinity, a model was designed illustrate in Fig 2.20. The degradation takes place in two steps. The first step happens in the amorphous regions, since water is only able to diffuse into amorphous regions. Those tie-molecules which
connect adjacent crystalline regions start to degrade with the presence of water, reducing the level of entanglements in the amorphous regions. As a result, more mobility is given to the remaining molecules in the amorphous regions, enabling them to form new crystalline regions. As a result, the breakage of amorphous regions and the formation of new crystalline regions results in an overall increase of crystallinity.\textsuperscript{[65]}

Fig.2.20 Degradation process of PGA fibers\textsuperscript{[66]}

Then after all the amorphous regions have been removed, the crystalline regions in the path of resorption will be attacked, leading to the second step in which degradation takes place in the crystalline regions (Fig.2.20). The rate of the second step is much slower than the first step since it is much more difficult for water to diffuse into crystalline regions.\textsuperscript{[65]}

This hypothesis was further proven by SEM images in which the shapes of the erosion cracks appeared to be the same as expected in the model (Fig.2.21)\textsuperscript{[66]}. 
Another more comprehensive study was undertaken by Antia et al on the morphological and mechanical properties of PGA nonwoven scaffolds after in vitro degradation. Fig.2.22 shows the change in thickness of the nonwoven felt. The initial increase may have been caused by the uptake of solution from the liquid environment. It then decreased due to hydrolytic breakage of ester bonds and macroscopic failure of the nonwoven structure. DSC and XRD results suggested a decrease of melting temperature from 229.4°C to 225.6°C. The change in crystallinity, which agreed with Chu’s conclusion, increased from 38.2% to 51.1% in the first 14 days, and then later decreased. FTIR study showed that a decrease in amplitude of the C-O ester bond peak as well as the carbonyl peak was observed, confirming the occurrence of ester hydrolysis [67].
Shear and compression tests were also performed to evaluate the change in mechanical properties of the PGA scaffold samples. As illustrated in Fig.2.23, both compression and shear strength of the material decreased rapidly during the first three days, and then decreased at a significantly slower rate, suggesting a different behavior from tensile properties\textsuperscript{[67]}. 

Fig.2.22 Changes in nonwoven diameter during degradation\textsuperscript{[67]}
Fig. 2.23 Stress-strain curves of PGA scaffolds in compression (upper) and shear (lower), before (a) and after 3 days(b), 7 days(c) and 14 days(d) of in vitro degradation. \(^{[67]}\)

2.2.1.3 In vitro degradation design

From the 1980’s, numerous articles have been published exploring the degradation behavior of PGA materials in various forms. Even though each of them focused on a different aspect of this degradation phenomenon, their experimental designs have some similarities. Table 2.1 is a summation of the in vitro degradation conditions described in some of these studies. Some characterization techniques to evaluate the process are also included in the table.
Table 2.1. Experimental designs for *in vitro* degradation studies

<table>
<thead>
<tr>
<th>Material</th>
<th>Solution</th>
<th>Environment</th>
<th>Measurement frequency</th>
<th>SEM</th>
<th>DSC</th>
<th>Mechanical test</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA nonwoven scaffold 60.4 mg/cc; 6mm diameter; 2mm thickness(^{(67)})</td>
<td>40 ml of PBS; changed daily for 1st week, once at day 10 and 14, then weekly</td>
<td>37°C in shaker table set at 60 rpm</td>
<td>Taken on day 0,3,7,14,28,56 after rinsed with distilled water then vacuum dried for 24H</td>
<td>Gold coated at 25mA for 10 seconds</td>
<td>5–10 mg of material temperature increased from 50–300°C at rate of 10°C/min in argon gas. 139J/g as reference of 100% crystalline material</td>
<td>Compressive test using 5N load cell at 1mm/min; Shear test using 100N load cell at 1mm/min</td>
<td>FTIR: material desolved in 1,1,1,3,3,3-hexafluorosopropano l clean crystal window as reference</td>
</tr>
<tr>
<td>2-0 PGA suture prestrained by 25% and 50% of breaking strain(^{(73)})</td>
<td>PBS, pH=7.2</td>
<td>37°C in sealed vessels</td>
<td>Taken on day 1,4,7,14,21,28 after vacuum desiccated overnight</td>
<td>/</td>
<td>/</td>
<td>2.54cm gauge 3.0cm/min speed</td>
<td>/</td>
</tr>
<tr>
<td>9 inch of 1-0/2-0 PGA suture(^{(69)})</td>
<td>PBS, pH=7.4, 0.2 molar and unbuffered PS solution, pH=5.0</td>
<td>37 ±1°C in oven material in glass tubes</td>
<td>Taken on day 7,14,21,28,42,70 or 90</td>
<td>No description</td>
<td>/</td>
<td>3 inch gauge 1 inch/min speed on wet material</td>
<td>/</td>
</tr>
<tr>
<td>PGA sheets of 0.13,0.3,0.6,0.9mm thickness(^{(74)})</td>
<td>PBS following ISO 15814</td>
<td>37°C in air-circulating oven material in 75mm*25mm glass tubes</td>
<td>Taken on day 0,3,6,9,…24 after vacuum dried at 30°C for 48 hours; vacuum level: 517 mmHg</td>
<td>Gold coated palladium alloy</td>
<td>5–10 mg of material temperature increased from 50–250°C at rate of 20°C/min 139J/g as reference of 100% crystalline material</td>
<td>/</td>
<td>GPC parameters: solution: HFIP; Prefiltration: 0.45μm PTFE filters; Calibration: PMMA; column: PL HFIP-gel 300mm*7.8mm; Rate: 1cc/min at 40°C</td>
</tr>
</tbody>
</table>

\(^{(67)}\) Reference 67
\(^{(73)}\) Reference 73
\(^{(69)}\) Reference 69
\(^{(74)}\) Reference 74
Table 2.1. Continued

<table>
<thead>
<tr>
<th>Sample Description</th>
<th>Details</th>
<th>Conditions</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 inch 2-0 PGA suture</td>
<td>30 ml Distilled water, pH=6.8 sterilized by autoclave</td>
<td>37 ±1°C in oven</td>
<td>Taken on day 7, 14, 21, 28, 49, 60, 90</td>
</tr>
<tr>
<td>100 μm PGA film; Mw&gt;300000 cleaned with n-hexane</td>
<td>24ml of three buffered solutions, pH=7.4, 10.0, 4.0</td>
<td>37°C in water bath material in 25 ml vial</td>
<td>Taken every hour after vacuum dried at ambient temperature for 24H</td>
</tr>
<tr>
<td>2-0 PGA suture</td>
<td>Broth with/without bacteria</td>
<td>37°C</td>
<td>After two weeks</td>
</tr>
<tr>
<td>12 counts of 0.2g PGA pellets, Mw=6000 and 25~35 cm of 0/4-0 fiber</td>
<td>15cc of three buffered solutions, pH=4.7, 7.0, 10.6 0.25 molar</td>
<td>/</td>
<td>Taken on week 1, 2, 3, 4, 6 after 3 times wash with distilled water then vacuum dried in desiccator</td>
</tr>
</tbody>
</table>

Vacuum-coated with graphite; 20kv electron beam

Temperature increased from 50~240 °C at rate of 10°C/min in nitrogen. 191.25J/g as reference of 100% crystalline material

20μm layer of gold coating; 5KV electron beam

3~10 mg of material temperature increased from 150~240 °C at rate of 10°C/min 49.34cal/g as reference of 100% crystalline material

Weight loss measured

Vacuum-coated with graphite; 20kv electron beam

Temperature increased from 50~240 °C at rate of 10°C/min in nitrogen. 191.25J/g as reference of 100% crystalline material

20μm layer of gold coating; 5KV electron beam

3~10 mg of material temperature increased from 150~240 °C at rate of 10°C/min 49.34cal/g as reference of 100% crystalline material

Weight loss measured

25mm gauge 30mm/min speed

Weight loss measured

2.5~5 cm fiber tested 1com/min seppd

Weight loss measured

43
2.2.2 Factors influencing the degradation rate

From Table 2.1, a various treatment conditions that the PGA material received to induce in vitro degradation can be found. In addition to an aqueous environment, which is reported as the only required factor to initialize PGA degradation\[^{65}\], researchers have used additional specific factors to explore their influence on the rate of degradation.

2.2.2.1 pH

Phosphate buffer saline (PBS) appears frequently in the experimental designs for PGA resorption studies\[^{67,69,70,73,74,75}\]. As hydrolysis continues, the product of this reaction:, glycolic acid, tends to acidify the solution, which in turn changes the pH of the environment. Buffering is the ability to control the pH of a solution within a narrow limited range. Additionally, it provides researchers with the possibility of studying the impact of pH on the degradation process of PGA materials.

In Vieira et al’s research, they recorded the strength loss of PGA filaments in different solutions, as shown in Fig.2.24. High logarithmic values indicate a faster degradation rate in vitro. The table shows that PGA degraded faster in acidic solution, and even the differences in residual strength appeared to be much smaller than those of PDO and PLAPCL\[^{68}\].

![Table](image)

Fig.2.24 Degradation rate of strength in 37\degree C\[^{68}\]
Another of Chu’s studies compared the degradation rates of PGA sutures in buffered (PBS) and unbuffered (physiological saline) solutions. The stress-strain curves (Fig.2.25) had a similar shape to the previous study \cite{65}, namely, a well-defined sigmoidal curve from Day 0 to Day 14 and Day 21 gave a lower curve. The stress-strain curves of samples degraded in unbuffered solution showed a slower rate of hydrolysis of PGA sutures, and their shapes were inconsistent through the initial periods. The change in pH of the unbuffered solution appeared to be proportional to the drop in tensile strength \cite{69}.

![Stress-strain curves of PGA sutures immersed in PBS (upper) and unbuffered solution (lower)](image_url)

Fig.2.25 Stress-strain curves of PGA sutures immersed in PBS (upper) and unbuffered solution (lower) \cite{69}
The findings of Rajiv’s research suggested that the PGA pellets degraded faster than fibers, and the degradation rates in alkaline media were much higher than those in acidic or neutral pH. Fig.2.26 indicated that the mass loss accelerated as the pH increased, while an acidic environment had a much smaller impact on the resorption rate\textsuperscript{[70]}.

Another study of Chu’s also agreed with this finding, as shown in Fig.2.27\textsuperscript{[71]}. The strength decreased faster in media with pH of 10.09 (square dots) compared to those in neutral (triangular dots) and acidic solutions (round dots) \textsuperscript{[71]}. 

![Fig.2.26 Mass loss of PGA pellets in medias with pH: 4.7, 7.0, 9.2 and 10.6 (from higher to lower)](image-url)

\textsuperscript{[70]}
2.2.2.2 Presence of bacteria

David Williams studied the influence of bacteria on the degradation rate of PGA sutures. According to Fig.2.28, the breaking strength of PGA sutures in bacteria culture decreased more slowly than those in the same broth without bacteria, suggesting that the presence of bacteria slowed down the degradation process of the PGA material \[72\].

Fig.2.27 Tensile strength retention of PGA suture immersed in solutions with pH: 5.25, 7.44 and 10.09 \[71\]
2.2.2.3 External energy

Miller et al\textsuperscript{[73]} have claimed that the absorption of external energy helps to initialize and accelerate the degradation rate of PGA material. The sutures in this study were pre-strained with 25\% and 50\% of the breaking strain before receiving treatments, as shown in Fig 2.29.

![Graph showing in vitro degradation of PGA suture as a function of applied strain](image)

Fig. 2.29 In vitro degradation of PGA suture as a function of applied strain: round dots for 0\%, square dots for 25\% and triangular dots for 50\% breaking strain \textsuperscript{[73]}
The external energy can also be in the form of radiation. Chu’s research has also suggested that γ-radiation will induce the breakage of ester backbone bonds, reducing the mechanical properties of the PGA materials. So when considering the selection of an appropriate sterilization technique, radiation related methods should be excluded\(^{66}\).

### 2.2.2.4 Morphology

In Simon Shawe et al’s article, the degradation rates of PGA films were tested with different surface-to-volume ratios. As shown in Fig.2.30, the rate of mass loss was much higher for thinner samples. That is to say that because of the longer path of water diffusion, materials degraded more slowly for thicker samples. But the rates of change in crystallinity and molecular weight seemed to be independent of thickness \(^{74}\).

Fig.2.30 Properties change of PGA films with different thickness during degradation in PBS\(^{74}\)
CHAPTER 3

EXPERIMENTAL

Guidance from ASTM F 1635–04a, states that “when comparisons have been made between in vitro and in vivo degradation rates of equivalent samples of hydrolytically degradable polymers under unloaded conditions, the results have consistently shown that in vivo acceleration of degradation is either not present or is within the error of measurement.” This guidance implies that tensile testing of materials in vitro can be conducted without cells.

3.1 Materials

Biofelt® needle-punched Poly(glycolic acid) (PGA) nonwoven web was received from Concordia Medical, co. in a vacuum sealed plastic bag. According to the company statement, the 30 cm x 20 cm sample had a thickness of 3.0 mm and a bulk density of 90 mg/cc. The fibers were tested to have a length of 6.0 cm and linear density of 2.67 denier. Biofelt was chosen because it was an extensively used material in various areas ranging from dental and urological surgery to cardiovascular and orthopedic tissue regeneration.

Poly(lactic-co-glycolic acid) (PLGA) coated Biofelt needle-punched PGA nonwoven web
was received from Tengion co. in a plastic bag with desiccant. The felt before coating was exactly the same as the material described above and the coating process can be summarized as following: two coating was applied to achieve a 50% mass increase using 50:50 PLGA solution (42.5 mg PLGA per ml methylene chloride). Samples were cut into 6 cm x 20 cm sheets in order to fit into a frame. Flat sheet which was attached to the frame by sutures was then placed into a trough with half of the first coating solution calculated. After 5 seconds, the sheet was turned over by the frame and the other half of the solution was applied for another 5 seconds. The sheet was then removed from the trough and attached to a rotator set at 20 rpm in an air stream for 5 minutes to evaporate the solvent. The mesh was removed from the rotator, and the process was repeated to apply the second coat.

![Fig.3.1 SEM image of Biofelt needle-punched web](image1.jpg) ![Fig.3.2 SEM image of PLGA coated Biofelt sample](image2.jpg)

A bobbin of 100 grams 128 denier/48 filament PGA yarn was received from Biomedical
Structures co. in a plastic bag filled with dry nitrogen. This material was selected since it was the same material utilized to manufacture the Biofelt nonwoven webs.

A nonwoven polyester web was kindly supplied by the nonwoven lab in College of Textile, NCSU. The felt containing 6 denier fibers had a basis weight of 200 gsm and was bonded with needle-punching. It went through the same coating process as described above.

All samples were kept in their original packages which were placed in a desiccator filled with dry nitrogen.

99.8% A.C.S. chloroform received from Sigma-Aldrich was used to dissolve PLGA coating from nonwoven webs, so as to explore the influence of PLGA coating on the hydrolysis behavior of PGA materials.

Phosphate buffer saline (PBS) was purchased from SIGMA-ALDRICH CO. One packet of PBS was dissolved in one liter of DI water, yielded to a 0.01 M PBS (NaCl-0.138M; KCl-0.0027M and pH 7.4 at 25 °C).

3.2 In vitro degradation

All nonwoven samples went through a treatment process before characterization tests:

All samples were cut into 6 cm x 3 cm specimens→ dried for 48 hours → weighted → immersed in standard PBS solution in a shaker bath → and pH tested during degradation. If $\leq 7.0$ pH occurred, changed all solutions → dry nitrogen was refilled every 12 hours and desiccant changed when needed → end of degradation → washed in DI water twice → dried on paper wipers till no water uptake observed → dried for 4 days → weighed → tested.
3.2.1 Specimen making

Printing paper of the same size was utilized as a template to help in making each specimen, then the 6 cm side was cut into half and 20 cm side into three segments. The needling line (cross-machine direction) was perpendicular to the 6 cm side and parallel to the 3 cm side.

![Fig.3.3 Sample cutting using paper template](image1)
![Fig.3.4 Ten groups of PGA nonwoven webs](image2)

All samples were randomized and three samples were combined as a group, which will be immersed into the same glass container. In order to distinguish samples in the same group, a corner was cut off from one sample while a square was cut off from another, the remaining one was complete.

Filaments were likely to entangle with each other since there were no twists added to those multi-filament yarns. According to ASTM D3822, sample length of greater than 10 mm is considered acceptable. So the 128 denier/48 multi-filament yarns were cut into 10 cm specimens and knotted at both ends to avoid entanglements. 30 cm and 60 cm lengths were tried and abandoned for entanglement and static electricity reasons.
Filaments were put into the glass vials before PBS was filled since samples did not have a solid body (fluffy) and tended to float on the solution, making it difficult to get into the vials filled with PBS. In case of entanglements and adhesion, three extra groups of samples were prepared. If the filaments are found entangled, the backup sample was washed immediately and dried following the same procedure.

### 3.2.2 Container cleaning

Twenty 8oz glass bottles and twelve 12 dram glass vials were purchased. Each container and cap was washed once by DI water; in order to remove dust deposited during storage. Containers and caps were then washed once with ethanol, in order to remove possible organic impurities and adhesive tape, and then three times with DI water in order to remove ethanol and possible remaining impurities.
All cleaned containers were dried and sterilized in an oven for 24 hours at 100°C.

A glass desiccator was washed following the same procedure, dried with paper towels to remove most liquid water. Then it was filled with desiccants and dry nitrogen overnight, in order to remove water vapors. A porous plate in the desiccators was washed and dried following exactly the same process as glass containers.

3.2.3 In vitro degradation experiment in standard PBS

Samples were incubated in standard PBS for 0, 2, 4, 6, 7.5, 9, 12, 15, 18 and 24 days in order to obtain data from different points of the degradation process.

PBS was purchased from SIGMA-ALDRICH CO. One packet of PBS was dissolved in one liter of DI water, yielded to a 0.01 M PBS (NaCl-0.138M; KCl-0.0027M and pH 7.4 at 25 °C). The solution was prepared in a 1 liter beaker with magnetic stirrer for 3 minutes till no particles could be observed. Each glass bottle was filled with 230 ml of PBS. The bottles were then put into a Boekel Grant ORS 200 shaker bath at 37 °C prior to experiments in order to remove potential bubbles in the solution caused by temperature increases.
Shaker bath was filled with DI water; the water level was 1 cm lower than the bottle cap. All bottles were shaking at 60 rpm, for the following considerations:

i. To mimic the heart beats in a living body

ii. To provide sufficient solution exchange between sample and the outside the sample, so as to avoid self-catalysis of PGA material.

iii. To remove bubbles generated.

iv. To remove broken fiber ends from the nonwoven web.
Because of the hydrophobicity of PLGA material, coated samples were difficult to wet and additional procedure need to be done to help the solution get access to all parts of the samples. So all coated samples were immersed into standard PBS prepared in small beakers. The beakers were then put into a vacuum desiccators, which was connected to the vacuum line in the chemical hood, and vacuumed for 1 hour. This procedure aimed to force out air contained in the samples and replace it with PBS. The vacuum-and–release cycle was repeated every five minutes, rising bubbles could be observed.

### 3.2.4 pH test and solution change

pH was tested three times every day using 6.0–7.7 range pH testing strips. The colors of pH strip were calibrated by comparing the results of 10 solutions with the value read from a pH meter. A bottle of buffered solution whose pH was 7.00 was used as reference. Once the pH of any bottle tested lower than 7.0, PBS in all bottles needed to be changed. All samples were
removed from the glass bottle and immersed into 100 ml fresh-prepared PBS in beakers for 20 minutes, in order to remove the residual acidified PBS. A sample of the used solution in the 8oz glass bottle were kept in glass tubes for pH test using pH meter, when necessary, and the remaining was discarded. After 20 minutes, samples were moved back to the glass bottles which were filled with 230 ml of fresh-prepared PBS. After 15 days, the samples were extremely weak and damage occurred when they were handled with tweezers. So the washing procedure was skipped. The frequency of solution change was recorded for reference.

Filament samples were not removed from the vials to avoid breakage.

3.2.5 Dry nitrogen refill and desiccant change

Dry nitrogen was refilled once a day to the vacuum desiccator. Two steps were involved in this process. Firstly, when releasing the vacuum, air tends to flow into the desiccator to balance the pressure. Instead of letting air flow, the nitrogen tube was connected to the vacuum hole on the desiccator, in order to fill it with nitrogen and protect the samples. Then the nitrogen tube was connected to the bottom of the desiccator, through the center hole of the porous plate, and was removed after letting nitrogen run for 20 seconds. Then the chamber was vacuumed using a vacuum line in the chemical hood continuously for vacuum strength and leakage considerations.
Drierite was used as desiccant. A little portion of indicator which will turn its color from blue to pink was mixed into 1 lb Drierite. Once desiccant was expired, another lb of Drierite would be used to replace it while the expired desiccant was heated in an oven at 220°C for 4 hours for drying. The dried desiccant was stored in the glass container before cooled down to avoid absorption of humidity from air.

### 3.2.6 Sample removal from solution

Samples which had finished their degradation treatments were removed from the glass container and rinsed in DI water twice. 1<sup>st</sup> time samples were immersed in a 1 liter beaker statically for 10 minutes. 2<sup>nd</sup> time samples were put in a 8oz glass bottle filled with DI water which was placed in a shaker bath shaking at 60 rpm, in order to remove the remaining PBS in the samples. After glass container removal, about 300 ml of DI water would be added into the shaker bath to maintain the water level.
3.2.7 Removal of liquid water

Samples were dried on paper wipers until no water uptake was found on the wiper. This procedure usually took 30 minutes. The samples between paper wipers were covered with a PYREX cover and filled with dry nitrogen to prevent chemical reaction. The water in coated samples tended to diffuse out from the side which had no coatings (ex. the side that was cut off from the larger samples). So drying took place with the uncoated side facing down, in order to accelerate the procedure with the help of gravity.

3.2.8 Decoating of coated samples

In order to explore the influence of PLGA coatings on the degradation behavior of PGA nonwoven material, PLGA coated samples after 4, 9 and 15 days of degradation were decoated to go through chemical analysis. Due to the fact that PLGA materials were soluble in common organic solvents such as acetone and chloroform at room temperature while PGA was not, about 50 ml 99.8% A.C.S. chloroform received form Sigma-Aldrich was utilized to treat 3 samples with size of about 10mm x 5mm. Each dissolving procedure lasted for 5 minutes with the help of a magnetic stirrer. Then the three samples were air-dried in a chemical hood for 24 hours before being weighed. Dissolving process was repeated until no significant change could be observed between three continuous weight measurements.
3.3 Analysis

3.3.1 Fiber extraction test

The Biofelt PGA needle-punched nonwoven samples were tested for fiber extraction force after 0, 2, 4, 6, 7.5 and 9 days of in vitro degradation so as to explore any changes in fiber interactions. Each sample contained three specimens and no more than 6 tests were performed on any one specimen to avoid major damage to the entangled structure. Samples after 12 days of resorption were too weak to be tested.

A 6cm x 3cm PGA nonwoven specimen was folded carefully in half gently, and the two 3 cm sides were joined together using two layers of adhesive tape. One fiber end measuring about 10mm in length was carefully pulled out with tweezers from the middle region along the outside of the fold. This procedure was based on the fact that fibers close to the edges were more likely to have been cut. Then the free fiber end was joined to a piece of adhesive tape, as shown in Fig.3.13. Since the operation of manually pulling out one fiber end would invariably cause some damage to the structure of the nonwoven web, a second fiber end was not pulled out until the first test had been completed, so as to minimize the error between successive tests. As a result, adhesive tape was preferred over epoxy glue which is more time consuming. The prepared specimen was mounted on a MTS Q-test Universal Test Frame. The fiber extraction test was carried out following the ASTM D3822\textsuperscript{[89]} (Standard Test Method for Tensile Properties of Single Textile Fibers), with the following parameter:

Fiber end length: 10 mm  
Crosshead speed: 10 mm/min  
Gauge length: 40 mm  
Load cell: 50 gf
As shown in Fig.3.14 the free single fiber end was attached to the piece of tape which was mounted in the plastic jaws connected to a 50g load cell. To avoid the situation where the fiber under test entangled or the fiber it was entangled would have been clamped in the bottom jaw, the tape joining the two layers of the web was clamped in the bottom jaw, instead of clamping the nonwoven sample itself. At the end of the fiber extraction test, the length of the extracted fiber was measured. Since the fiber length in the Biofelt nonwoven web was 6cm, fibers shorter than 4cm were considered too short to be representative of typical entanglement interactions in the web. Therefore, only the data obtained from fibers longer than 4cm were recorded for further analysis.
3.3.2 Probe bursting test

Due to limited amount of material available as well as the directionality of needle punched webs (they are significantly stronger in the machine direction than in the cross-machine direction), bursting strength tests were performed to evaluate the changes in mechanical properties of the nonwoven materials throughout the degradation process. A bursting cell (Fig.3.16) with a specimen platform and a metal probe with a hemispherical head was built according to the ISO7198 standard method [90] (Cardiovascular Implants - Tubular Vascular Prostheses). A 3cm x 3cm nonwoven specimen was mounted on the platform stressed to failure as the 9.5mm diameter probe with a ball-shaped end moved perpendicular to the specimen at a controlled rate of 305 mm/min.
The bursting cell was mounted on an Instron Model 5544 universal mechanical tester equipped with a 2kN load cell as shown in Fig.3.15. The test started when the probe touched the specimen’s surface and ended when the load decreased to 50% of the peak load. A peak load and its corresponding displacement were recorded for each specimen tested.

The bursting strength of the Biofelt PGA nonwoven material after 0, 2, 4, 6, 7.5, 9, 12, 15, 18 and 21 days, while the bursting strength of the PLGA coated PGA and PET nonwoven webs were measured after 0, 2, 4, 6, 7.5, 9, 12, 15, 18, 21 and 24 days. Each group had six repeated tests to calculate the average value and the standard deviation.

### 3.3.3 Fiber tensile test

Single fiber tensile tests were carried out following ASTM D3822[^89] (Standard Test Method for Tensile Properties of Single Textile Fibers). In order to control the gauge length, prevent fiber slippage in the jaws and avoid fiber breakage in the grips, “C” shaped paper card frames were made with an open window gauge length of 1 inch. A single fiber was mounted onto the card and fixed in position by double face tape and adhesive tape. The specimen was then mounted on the MTS Q-test Universal Test Frame equipped with a 50 gram load cell, as shown in Fig.3.17 and Fig.3.18. After the specimen was clamped between the top and bottom plastic grips, the vertical side was cut off (Fig.3.18). A crosshead speed of 15 mm/min was used to determine and record the breaking strength of each specimen. The PGA fibers with 2.67 denier were tested after 0, 2, 4, 6, 7.5, 9 and 12 days of degradation so as to generate input data for the mathematical models. The average value and a standard deviation for the tensile strength for each group of fibers was calculated from 8 repeated tests.
3.3.4 Fourier transform infrared spectroscopy (FTIR)

FTIR is a technique that utilizes infrared light to analyze the chemical composition of a translucent material. A Fourier transform is used to collect the signals and create the spectrum. In this research, an attenuated total reflectance (ATR) device (Fig.3.19) was used so as to characterize the chemical structure near the surface of the nonwoven fibrous web.
As illustrated in the Fig.3.20, an IR source emits a light beam which passes through an interferometer containing a beam splitter, fixed mirrors and a moveable mirror. The beam splitter divides the beam in half and the first half is reflected by the fixed mirror while the other half is reflected by the movable mirror which moves in the direction of the light. The two reflected beams are then recombined and due to the difference in optical path length, they generate an interference beam which contains waves with different frequencies. This enables the spectrophotometer to scan the sample with a whole range of different frequencies simultaneously. Then the interference beam passes through several filters to eliminate noise.[77] The specimen under test was mounted under pressure on top of the germanium crystal to produce a tight contact. The interference beam passed a few microns into the specimen before it was reflected by the set of mirrors (Fig.3.20). Because of the high refractive index of the germanium crystal, a multi-internal reflection took place between the crystal surface and specimen surface to ensure sufficient specimen reflection of light energy. Covalent bonds in the polymer material absorbed light in a narrow frequency range as induced and maintained by the vibrational state of that particular chemical bond. Irrespective of the structure of the molecule, each covalent bond has its fingerprint region corresponding to the different vibrational states. So the transmitted beam after specimen-IR interaction was analyzed and decoded so as to generate a continuous spectrum. [78,79]

In this research, the germanium crystal was cleaned with DI water and methanol before each test. In addition to the cleaning, 32 background scans were done without a specimen before each measurement, so as to eliminate the influence of impurities and air. A 10mm x 10mm square of PGA nonwoven material was mounted on top of the crystal and the FTIR analysis
was carried out using the following parameters:

Final format: Absorbance; Resolution: 4 cm\(^{-1}\)
Number of scans: 32; Range: 4000 – 400 cm\(^{-1}\)

The same procedure was repeated on PGA samples after 0, 2, 4, 6, 7.5, 9, 12, 15, 18 and 24 days of \textit{in vitro} degradation in PBS. In addition, the coated PLGA coated samples were measured after 4, 9, 15 days of degradation and after removal of the coating. A comparison between the spectra obtained from different materials at different times helped to explore the changes occurring to the chemical group during resorption.

3.3.5 \textbf{Surface morphology (scanning electron microscopy study)}

Scanning electron Microscopy (SEM) is different from traditional microscopy which utilizes an electron beams instead of visible light to generate three dimensional images of a material’s surface. It provides detailed information about the structure, morphology and even the chemical composition of sample surfaces (Fig.3.21).

Fig.3.21 SEM facility and operation computer
In this study, the nonwoven samples after 0, 6, 12, 18 and 24 days of \emph{in vitro} degradation were cut into 5mm x 5mm specimens and mounted onto standard SEM stubs. A gold-palladium coating was sputter coated onto the fiber’s surface so as to make it conductive before making observations in the JEOL 6400F Field Emission SEM machine. The magnifications ranged from x370 (which was used to observe the fiber distributions and entanglements) to x1800 (which helped to monitor any surface erosion and changes in the coating morphology of the fibers). The instruments used to make these observations of the material surface morphology are shown in Fig.3.21.

The focused electron beam was scanned across the specimen in a raster fashion causing reflection and scattering at the surface. Backscattered electrons (generated by elastic scattering), secondary electrons (generated by inelastic scattering) and X-ray signals were generated by these interactions and they were collected and recorded by the corresponding detectors. The information obtained from the detectors was then processed by the computer software to generate the SEM image.\[82\]

\textbf{3.3.6 Crystallinity measurement (differential scanning calorimetry)}

Differential scanning calorimetry is a technique used to study the amount of heat energy transition processes of polymers by recording the heat needed to increase and decrease the temperature of a sample material at a certain rate.

As shown in the Fig.3.22, a typical DSC instrument contains two aluminium pans. One of them is called the sample pan in which the specimen material is placed to be tested. The other one is the reference pan which can be left empty or holds a reference material\[65\] whose
thermal behavior is well-defined\textsuperscript{[67]}. When the test starts, the two pans will be heated and/or cooled at a certain rate such as 10, 20 or 30 °C per minute. Because the sample and reference materials require different amounts of energy to maintain the constant rate of temperature increase or decrease, the difference in heat energy required gives a measurement of the thermal properties of the sample material. The heating and cooling is controlled by a computer which plots the difference of heat flow against time or against temperature.

A typical DSC curve usually exhibits three types of thermal behaviors, namely glass transitions, crystalization and melting phenomena (Fig.3.24).

A glass transition temperature is the point above which molecular chains in the amorphous regions move more freely and thus require more heat energy. So an increase of heat flow will be observed in the DSC curve in order to maintain the constant rise in temperature. Usually during a cooling cycle the molecular chains in the amorphous regions have sufficient mobility to cause the crystallization process to take place. This procedure releases heat energy, resulting in a dip on the curve. When the temperature approaches the melting point of the polymer, the molecular chains in the crystalline regions absorb so much energy and have
so much mobility that the ordered crystalline structure is lost. As a result, a peak is observed in the DSC curve and the temperature associated with the highest heat flow is recorded as the melting point. The area under the melting peak refers to the total amount of energy absorbed given off during the melting process of crystalline regions. The degree of crystallinity can then be calculated by taking the ratio of this value compared to 100% crystalline material.

In this research, a series of DSC tests were performed with a Diamond differential scanning calorimeter in order to measure the changes in melting temperature as well as in crystallinity during the *in vitro* degradation of the PGA material. Specimens weighting 5 to 10 mg were placed in the sample pan, which was heated from ambient temperature (about 25 °C) to 300 °C at a rate of 10 °C per minute. The determination of melting points and degree of crystallinity followed the method described above. The value of 139 J/g was used as the reference heat of fusion for 100% crystalline PGA material[^67,74].
CHAPTER 4

RESULTS AND DISCUSSION

4.1 FTIR Analysis

The change in the chemical structure of the PGA needle-punched nonwoven materials before and after different degradation periods were analyzed by ATR-FTIR.

No significant change was observed until Day 9, as illustrated in Fig.4.1. The two spectra showed minor differences which could be caused by experimental error or background noise. For example, a pair of weak peaks at about 2350 cm$^{-1}$ was due to the presence of carbon dioxide. Several peaks appeared in the finger-print region of PGA. For example, the peak at...
1430 cm\(^{-1}\) referred to \(-\text{CH}_2\)- scissors vibration and the peak at 2950 cm\(^{-1}\) referred to \(-\text{CH}_2\)- stretching. The strong peak at about 1750 cm\(^{-1}\) indicated the presence of \(\text{C}=\text{O}\) bonds stretching in the ester groups. The peaks at 1150 cm\(^{-1}\) and 1080 cm\(^{-1}\) are believed to represent \(\text{C-O-C}\) anti-symmetric and symmetric stretching, and the peaks at 974 cm\(^{-1}\), 904 cm\(^{-1}\), 810 cm\(^{-1}\) and 711 cm\(^{-1}\) have all been identified previously with PGA material \([85-87]\).

A comparison of the spectra before and after 12 days of hydrolysis is shown in Fig.4.2. The occurrence of a broad peak at 1700-1560 cm\(^{-1}\) is worth noting since it refers to the \(\text{C}=\text{O}\) stretching in carboxylic acid end groups. The strong peak at 1430 cm\(^{-1}\) (\(-\text{CH}_2\)- scissors vibration) increased after 12 days of degradation, which may be due to the addition of an overlapping \(-\text{OH}\) in-plane bending peak in carboxylic acid. These two changes both point to the presence of carboxylic acid groups which are the major product of PGA hydrolysis.

Another broad peak occurred between 3600 cm\(^{-1}\) and 3100 cm\(^{-1}\), indicating \(-\text{OH}\) stretching in an alcohol group. It was not obvious in the Day12 spectrum since the absorbance was weak.
and the peak was broad. But after Day 12 it started to increase as the degradation continued.

Fig.4.3 FTIR spectra obtained from PGA material before (blue) and after (red) 24 days of degradation

In the Day 24 spectrum, large differences can be observed when compared to the spectrum of the controlled group. The broad overlapping peak of –OH stretching within the carboxylic acid end group (3600cm⁻¹-3000cm⁻¹) contributed to adding a peak in this region. Also the decreasing amount of ester bonds due to hydrolysis can be seen from the reduction of -C-O-stretching peaks in the ester bonds (1150cm⁻¹-1090cm⁻¹).

The results discussed above confirm the assumption that the in vitro degradation of PGA material takes place primarily in terms of hydrolysis. The first 9 days was the initial “incubation” period, during which no clear sign of hydrolysis was observed. This may be due to the fact that water was not able to penetrate the crystalline regions during the early days of PBS exposure. The density of the molecule arrangement in the amorphous regions is much lower than in the crystalline regions. Even though chain scission began immediately on
immersion in PBS, the amount of ester bond breakage was not significant compared to the whole structure.

As the exposure time continued, water started to diffuse into the crystalline regions at about Day 9, and multiple FTIR evidence was observed to confirm the increase in hydroxyl and carboxyl groups and a decrease of ester bonding. As a result, Day 9 was considered as a critical transitional time point to which special attention needs to be paid in the following analysis.

Fig. 4.4 FTIR spectra obtained from PGA material (red) and decoated nonwoven material after 9 days (above) and 15 days (below) of degradation
In order to explore the impact of the PLGA coating on the degradation behavior of the PGA nonwoven material, FTIR tests were performed on the decoated PLGA coated nonwoven materials after 4, 9 and 15 days of degradation, as shown in Fig.4.4. A similar conclusion was drawn for these coated samples. Before Day 9, no significant difference could be observed between the PGA and PLGA coated materials, suggesting that neither the PLGA coating nor the coating process accelerated the hydrolysis reaction.

The spectra of samples from Day15 began to show a slight difference. The peaks representing C=O stretching in carboxylic acid (1700cm\(^{-1}\)-1560cm\(^{-1}\)) and –OH stretching in the alcohol groups (3600cm\(^{-1}\)-3100cm\(^{-1}\)) appeared to be higher in the PGA material, while the C-O-C ester bond stretching peak (1150cm\(^{-1}\)) appeared to increase in the decoated sample. This observation suggests that the presence of the PLGA coating slowed down the degradation rate of the PGA material. In this research, the PLGA coating appeared to impede the solution exchange between the medium and the PGA material to a certain degree. Therefore acidic products of the hydrolysis reaction (e.g. carboxylic acid) were not easily buffered by the PBS solution, resulting in a lower pH environment inside the material. As discussed in the literature review section, previous research has been undertaken to study the influence of pH on the hydrolysis rate of PGA \(^{69,70,71}\). These articles report that the degradation rate in acidic medium was slower than that in neutral solutions, which agrees with the results shown in Fig.4.4.

### 4.2 DSC analysis

As mentioned above, the hydrolysis process for PGA material initially takes place in the
amorphous regions. This breakage of ester bonds in the amorphous regions increases the degree of crystallinity of the polymer. Meanwhile, chain scission in the amorphous regions provides more room for molecules to move and form new crystalline regions. These two processes lead to an increase of crystallinity during the initial period. Then later, after the water has penetrated the crystalline regions, the more ordered molecular chains starts to hydrolyze, reducing the degree of crystallinity of the material. Whether the crystallinity decreases or increases depends on which of these two processes is dominant at any particular time.

The DSC tests in this research showed a similar result. The DSC curve of the original PGA material before degradation is shown in Fig.4.5. Since the curves generated by each material appeared to be similar in shape and position, only one of them is included here.

Fig.4.5 DSC curve of PGA nonwoven material before degradation
The endotherm melt peak can be clearly observed between 200 °C and 240 °C. The temperature corresponding to the peak heat flow was taken as the melting point, in this case 220.9 °C. The degree of crystallinity has been calculated from the area under the peak using delta H.

The changes in the melting temperature and in the degree of crystallinity during degradation were calculated and are summarized in Fig. 4.6.

![Graph showing changes in crystallinity and melting temperature during degradation](image)

Fig. 4.6 Changes in the degree of crystallinity (left) and T_m (right) of PGA materials during degradation

Fig. 4.6 shows that the degree of crystallinity kept increasing during the first 18 days of in vitro PBS exposure. The values followed an approximately linear trend from 61% initially to 91% after 18 days of hydrolysis. This observation agrees with the first step in the degradation theory. The erosion of crystalline regions only became dominant after 18 days when it decreased rapidly to 76% within the next 6 days.

The decoated samples showed a similar trend, but with a more gradual slope. Considering the possibility of experimental error and incomplete removal of the coating, the crystallinity of
the decoated materials after 4 and 9 days of PBS exposure were close to those for the uncoated PGA samples. However, on Day 15 the decoated sample had a 5% lower value, suggesting a slower rate of degradation compared to the uncoated PGA webs. This result confirms the findings by FTIR analysis.

Fig.4.6 suggests a decreasing trend in melting temperature as degradation proceeds. The $T_m$ remained in the narrow range of 220°C-221°C during the first 12 days of PBS exposure, except for the result at Day 9, which is considered as an outlier caused by experimental error. After 12 days of hydrolysis, the reduction of molecule weight caused by chain scission became significant and a reduction in melting temperature was observed following a linear trend with longer hydrolysis times.

For the decoated sample, the $T_m$ was lower than for the PGA materials, while the falling trend was similar for both samples as illustrated in Fig.4.6. In the coated samples, a certain amount of adhesion was established between the PLGA coatings and the PGA fibers. As a result, interactive forces decreased upon the removal of the PLGA coating which resulted in a reduction in melting temperature.

4.3 Surface morphology

The SEM images obtained at lower magnification from the PGA nonwoven materials before and after different hydrolysis periods are shown in Fig.4.7. The particles on the surface were believed to be PBS residual particles which remained on the surface after washing twice with DI water. The fibers in the nonwoven web before PBS exposure had a relatively uniform and dense distribution. Also, fiber entanglements could be clearly observed. After 6 days, some
minor surface changes in fiber structure were observed while the fiber density became lower, which agreed with the statement “initial swelling upon medium absorption”[67]. As hydrolysis continued to Day 12, more fiber ends were observed, suggesting more degradation. During fabrication of the nonwoven web (i.e. fiber spinning and needle-punching), residual stresses are built up within the structure. As degradation proceeds and the fiber strength decreases, eventually it is overcome by the residual stresses within the web and fiber failure occurs. These failures change the appearance of the nonwoven structure and generated fiber ends, which can be seen in the SEM images. After 18 days of hydrolysis, the majority of the fibers within the image showed evidence of breakage. The fibers tended to congregate together through shrinkage which led to an increase in fiber density. However, the uniformity of the web decreased due to the loss of support from the fibrous structure.

The fiber diameter was measured using the image analysis software, ImageJ Version1.44. Three fibers were randomly picked from each image and 5 repeated diameter measurements were taken at different points along the same fiber. The results in Fig.4.8 show a decreasing trend whose slope increased after 12 days of hydrolysis. This is consistent with the findings of the gravimetric measurements presented in Fig.4.16. As degradation proceeded, the molecular weight decreased until a critical point, below which the fiber became soluble in water. So the fiber diameter was gradually reduced with the loss of small molecules.
Fig. 4.7 SEM images of PGA nonwoven webs before (a) and after 6(b), 12(c) and 18(d) days of PBS exposure at lower magnification.
Fig. 4.8 Change in PGA fiber diameter (including 95% confidence intervals) during PBS exposure

Fig. 4.9 (a) illustrates the morphology and distribution of the PLGA coating within and on the needle-punched PGA material. Instead of a 3-dimensionally uniform distribution, the PLGA coating tended to occupy one plane. (Further work needs to be done on cross-sectional analysis and confocal microscopy to analyze the 3 dimensional pattern of the coating distribution). The porous and dense coating connected adjacent fibers together like an adhesive, which contributed to the bursting strength of nonwoven material since it reinforced the fiber-fiber interactions. This finding was further proven by the bursting test results. As the degradation continued, the pores became larger and the coating failed to maintain the in-plane structure as fibers lost their strength and moved in response to the residual stress caused during manufacture (b and c). Figure 4.9(d) was obtained after 24 days of PBS exposure, when the uncoated PGA samples failed to maintain their textile structure because of the broken fiber fragments in the image. At that point, every PGA fiber had fallen apart.
into several segments which were only connected by the remaining coating.

Fig. 4.9 SEM images of PLGA-coated PGA nonwoven webs at low magnification before (a) and after 6 (b), 12 (c) and 24 (d) days of PBS exposure
Fig. 4.10 shows observations of the PLGA coating at higher magnification. Before PBS exposure, the dense PLGA film can be found attached to individual fiber surfaces as well as joining them together.

Fig. 4.10 SEM images of PLGA-coated PGA nonwoven webs at higher magnification before (a) and after 12 (b), 18 (c) days of PBS exposure
The density of the coating became lower and clear signs of erosion occurred after 12 days of hydrolysis. After 24 days, the PGA fibers broke into fragments and became discontinuous. Obvious gaps can be seen between broken fiber segments which previously were fixed in their original position by the coating.

### 4.4 Single fiber tensile strength

As the PGA nonwoven material studied in this research is fabricated out of individual fibers, changes in the single fiber tensile strength were of particular interest, not only because they were the input parameter for the mathematical model, but also a critical parameter to understand and explain the changes in properties of the nonwoven web.

Fig. 4.11 Single fiber tensile strength during PBS exposure (mean and 90% confidence interval)
The mean values for the single fiber tensile strength of the 2.67 denier PGA filaments during different in vitro exposure times are illustrated in Fig. 4.11, together with the 90% confidence interval for each data point. The first 2 days of exposure did not cause any change in the tensile strength of PGA fibers, as the mean values before and at 2 days fit within each other’s confidence interval. Then after 2 days the single fiber tensile strength decreased until the end of the experiment. In fact after 15 days of incubation the fibers were too weak to be handled and tested. Therefore the PGA fibers in this study lost strength following a linear trend of approximately 1.5 gf per day. Half the fiber strength was lost after only 8 days.

In order to illustrate the changes in mechanical properties of the fibrous material during the hydrolysis experiment in a more detailed way, a comparison of load-extension curves was made at 4 different time points.

![Load (gf)—Extension (mm) curves](image)

Fig.4.12 Tensile load – displacement curves for PGA fibers before and after 4, 9, 12 days of hydrolysis
The tensile load-extension curve for the initial control sample and the Day 4 sample showed a similar shape except for the break point. Both curves had a clear yield point at about 0.4 mm (1.6% strain) and almost the same initial Young’s modulus. After 9 days of *in vitro* hydrolysis, the yield point occurred earlier, suggesting a smaller Hookean region of elastic deformation. This may be due to the initial loss of amorphous regions, which was associated with an increase in the level of crystallinity. This agrees with the findings from FTIR analysis. However, a decline in the Young’s modulus was not observed until Day 12. The slope after the yield point appeared to be significantly more gradual compared to the other three curves.

### 4.5 Fiber extraction from nonwoven material

The interaction between fibers was another critical factor that contributed to the strength of the nonwoven web. The failure of the nonwoven web was due both to the failure of individual fibers, as described in the previous section, as well as the disentanglement between fibers in the web. Therefore measurement of the single fiber extraction force was an essential method to evaluate both the degree of entanglements and the level of friction between fibers that contributed to the bursting strength of the nonwoven web.

A typical fiber extraction curve is shown in Fig.4.13. It consists of four major regions representing different forces, conditions and movements of the fiber. A number of years ago a similar pattern was obtained in the study performed by Briscoe et al of pulling yarns from a fabric. [83]
Fig. 4.13 Typical curve of fiber extraction from nonwoven material

The first region of the curve, between AB, has a relatively gradual slope since only fiber straightening occurred. The fiber started to decrimp and slide by overcoming static friction in response to external forces.

The section of the curve B to C approximately followed a fiber tensile stress-strain curve in the Hookean region before the yield point. After the extracting fiber was decrimped, entanglements became the major factor that limited fiber movement. Since the load had not approached the force needed to disentangle this interaction, the fiber being extracted started to extend elastically. Simultaneously, other fibers entangled with the extracting fiber would also elongate and apply shear forces to limit the movement of the extracting fiber. As a result, the composite effect of extracting fiber extension, and other entangled fiber extensions and shearing contributed to the second region of the curve. Meanwhile, several minor instances of slippage and/or disentanglement were observed, as marked with a “1” in Fig.4.13.
The third region, identified as CD in the figure, was the part of the curve that characterized the interactions between fibers in the nonwoven material. Repeated entanglement/slippage cycles took place as the entanglements along the extracting fiber kept failing in sequence one after another. A peak occurred every time there was slippage, and the corresponding load at those peaks provided information about the fiber entanglement force, which would serve as an input value for the mathematical models. The calculation method related to these models will be discussed in detail later.

The final stage of the curve beyond D, showed a uniform low load with a certain level of noise. This region began after the loss of any remaining entanglements of the extracting fiber or failure of the extracting fiber itself. It contained only friction and noise. The frequency between successive peaks in this region would help to determine whether a peak was caused by noise and friction or by disentanglement. This will be discussed in the following section.

Since only one value is needed as an input for the mathematical model, a systematic method was required to analyze the peaks and generate a meaningful, reliable and representative value. A similar situation can be found in the standard dealing with measuring the tearing strength of fabrics (ASTM D5587, Standard Test Method for Tearing Strength of Fabrics by Trapezoid Procedure) whose solution can be utilized as an important reference here:

“After the first 6 mm of tear, determine the five highest peak forces and calculate the average of these five highest peak forces.”

This same technique was applied in this research. However, certain restrictions, similar to the “6mm rule” in the tearing strength standard, needed to be applied in order to achieve a
reasonable, reliable and representative calculation, as listed and explained below:

1. The peaks determined as the five highest peaks should not be in an increasing trend, as marked by the “1” in Fig.4.13. This rule was based on a similar concern to the “6mm rule” in the tearing strength standard which assumes that movements are not stable during the initial period.

2. If the extension difference between adjacent peaks is comparable to the frequency of the noise (or pure friction), only one of the peaks can be counted, as marked by the “2” in the Fig.4.13. The frequency of pure noise is shown only after total extraction or breakage of the fiber, i.e. after 13.7 mm in Fig.4.13. If the difference in extension between two adjacent peaks is comparable to that between two noise or pure friction peaks, they might be the product of a single peak caused by noise or pure friction and so should be omitted.

3. The difference in height of the two sides of the peak should not be larger than 50%, as marked by the “3” in the Fig.4.13. A peak is a turning point of the curve, with an increase in the left side and a decrease in the right side. If the height or load difference between the increase side and decrease side is larger than 50%, then the smaller side might be caused by noise or a minor entanglement which will not contribute to the whole structure.

4. The extension corresponding to the peak should not be greater than the breaking displacement of the extracted fiber as marked with a “4” in Fig.4.13. The curve in Fig.4.13 was obtained from samples after 6 days of hydrolysis. According to the
bursting test, the maximum strength of the nonwoven web was reached after 6.43mm of displacement. As a result, fiber extraction peaks after 6.43mm of displacement will not make any contribution to the maximum bursting strength of the nonwoven material since the web had already failed. Even though several high peaks occurred after 6.43mm, none of them will be determined as valuable in this experiment.

The fiber extraction forces after different PBS exposure periods were calculated following the method and restrictions described above. The fiber pull-out forces together with their confidence intervals during hydrolysis are shown in Fig.4.14. Because of the 3D disorder of the nonwoven structure, the random directionality of fibers in the web, making the angle between fiber direction and the applied force direction unknown, the variation was relatively high compared to the fiber tensile test results. Similar to the changes in fiber tensile strength, the decline in fiber extraction force followed an approximately linear relationship from an initial value of 10.5 gf to 3.3 gf after 9 days. This decrease may have been caused by the swelling of nonwoven structure after water uptake, which can be seen in the SEM images. As the fiber swelled, the space between the fibers became larger, providing more room for fibers to move, both the extracting fiber and the fibers entangled with it, hence facilitating the extraction process.\[67\]
Even though the fiber tensile strength remained higher than the fiber extraction force during the degradation process, their roles in determining the bursting strength of nonwoven web changed. If the fiber extraction test, which resulted in either fiber breakage or complete pull-out, occurred after the bursting failure of the nonwoven material, it was the fiber entanglements that limited the strength of the nonwoven web, since the breaking point of the fiber had not yet been reached. This is the usual situation during the first 6 days of PBS exposure, occurring in more than 75% of the cases.

However, the fibers in a nonwoven material are highly bent and entangled. So failure might occur before the break point of the single fiber tensile strength tests is reached. After 7.5 days of PBS exposure, the majority, 53%, of the fiber extraction tests ended as fiber breakage before the bursting strength displacement of the nonwoven web was reached, suggesting that
under these conditions the role of fiber tensile strength is more important than fiber extraction force.

This finding was proven using statistical correlation test done by SPSS v.19. The Pearson Correlation between the bursting strength of the PGA nonwoven web, fiber extraction force and fiber tensile strength was given in the figure below:

<table>
<thead>
<tr>
<th></th>
<th>Bursting Strength</th>
<th>Extraction Force</th>
<th>Fiber Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bursting Strength</td>
<td>1.000</td>
<td>.936</td>
<td>.871</td>
</tr>
<tr>
<td>Extraction Force</td>
<td>.936</td>
<td>1.000</td>
<td>.636</td>
</tr>
<tr>
<td>Fiber Strength</td>
<td>.871</td>
<td>.636</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Before Day 6, the bursting strength of the nonwoven material was highly correlated to the extraction force (0.998). On the other hand, the single fiber tensile strength showed a lower correlation (0.871, which failed to be included in the 10% significance interval). This statistical result suggests that fiber entanglements were more influential during the initial period, i.e. the first 6 days of PBS exposure. However, the role of individual fiber strength became more and more important at longer exposure times. From the statistical analysis performed on the data obtained after 6 days of PBS exposure, the correlation of individual fiber strength achieved a higher value (0.981) than fiber extraction force. This indicates that the mechanism of web failure and the relative importance of individual fiber tensile strength and fiber extraction force changed at about Day 6, which is in agreement with the result from the fiber extraction curve analysis.
4.6 pH measurements and gravimetric measurements

Glycolic acid, the hydrolysis product of the PGA degradation process, contains acarboxylic acid group that lowered the pH of the immersion solution during the hydrolysis experiments. Even though a buffered solution was utilized in this study to prevent acidification, once the amount of acid produced exceeded the buffering ability of a standard PBS solution, the pH decreased and influenced the degradation rate of polymer. In order to maintain the medium at a neutral pH, the pH was tested and recorded every 12 hours. And the PBS solution in every container was changed once any one of them was found to be below pH 7.0. Note that the pH of the coated PET material and PGA filaments did not decrease to 7.0 throughout the whole experiment, so no solution change was necessary for these samples.

![pH change During Degradation (Days)](image)

Fig.4.16Changes in pH of the PBS solution during the initial period of hydrolysis

As shown in Fig.4.16, the pH of the solution containing PLGA coated samples dropped faster
than for the PGA samples. This was because the PLGA coating was also degrading and producing acidic species, namely lactic acid and glycolic acid. After 7 days of hydrolysis, some of the PLGA coated samples reached the point when their PBS solution needed changing. The second solution change took place at Day 10, after which a solution change was required on a daily base. This indicated a faster degradation rate from Day 10 onwards, which agrees with the results from the FTIR test that Day 9 was a critical transition point.

![Mass Loss (%) During Degradation (Days)](image)

Fig. 4.17 Percentage of mass loss of samples after different periods of PBS exposure

![PGA nonwoven web after 24 days of hydrolysis](image)  
![Uneven PLGA coating](image)

Fig. 4.18 PGA nonwoven web after 24 days of hydrolysis  
Fig. 4.19 Uneven PLGA coating
It was acknowledged that there may have been PBS residual salt particles attached to the degraded nonwoven samples even after two washes in DI water (SEM images in Fig4.7 d). Nevertheless all weights shown in Fig.4.17 were calibrated using the change in weight of the control group before and after PBS immersion.

For the PGA and the PLGA coated PGA webs, no significant weight loss was observed until Day 9, which was in good agreement with the FTIR results. At longer exposure times a rapid loss of material was observed, which might have been caused by the following two reasons:

1. The molecular weight of the PGA had decreased to a critical point where such small molecules started to be soluble in the aqueous PBS solution.

2. Small fragments of broken fiber, which were too short to have any interaction with the nonwoven substrate, caused by hydrolysis were removed from the nonwoven substrate by the shaker bath, as shown in Fig.4.18.

Since the PLGA coating degraded at a slower rate than the PGA fibers, it would function as an adhesive to hold the small broken fiber fragments together, as shown in the SEM images obtained from the PLGA coated samples after 24 days of PBS exposure. This was the major reason why the coated samples lost less weight than the uncoated ones. However, the difference could also be caused by insufficient solution exchange with the medium, as explained earlier in the FTIR section.
4.7 Bursting test of nonwoven materials

A series of bursting tests was performed on the PGA nonwoven webs and the PLGA coated PGA webs in order to generate output data for the mathematical model. In addition, the PLGA coated PET materials went through bursting tests to provide information about the degradation pattern of PLGA coatings.

4.7.1 Bursting strength of PGA and PLGA-coated webs

Unlike the linear decreasing trend of the fiber extraction force and the fiber tensile strength results, the bursting strength data decreased following a polynomial function. When the power rose to biquadrate, a coefficient of determination ($R^2$) of 99.8% was achieved, indicating that the regression became highly accurate and predictive. The mean changes in bursting strength of the PGA nonwoven webs with and without PLGA coating during in vitro PBS exposure are shown in Fig.4.20, together with a 90% confidence interval. In addition, a regression function for uncoated samples was marked using a black line.

The mean bursting strength decreased rapidly from the very beginning of PBS exposure. This was a very different behavior from that of the individual fibers that made up the nonwoven web. The PGA nonwoven web had an initial average strength of 285 N which dropped to 99 N by Day4, a decrease of 65%. Similarly, over the same time period the strength of the PLGA coated sample dropped from 336 N to 120 N, a decrease of 64%. However, during the initial period of PBS exposure the fiber tensile strength showed no sign
of decreasing. So the decrease of bursting strength was mainly due to the loss of fiber-fiber interactions, which worked as the limiting factor during the initial period of hydrolysis. This is in good agreement with the earlier discussion to be found in the fiber extraction force section.

![Bursting Strength(N) During Degradation (Days)](image)

Fig.4.20 Bursting peak force of nonwoven material during PBS exposure (mean & 90% confidence interval)

During the initial 4 day period of PBS exposure, the strength of the PLGA coated samples was significantly higher than those without coating, but the amount of variability was relatively large (one tail p-value < 0.01 in F-tests). The strength increase was due to the adhesive function provided by the PLGA coating which reinforced the fiber-fiber interactions (Fig.4.10) and the difference in variation was caused by the uneven thickness of the coating on the nonwoven material (Fig.4.19).

The difference in breaking force between the coated and uncoated samples decreased in
terms of the average value as the PBS exposure continued. After 6 days, ANOVA tests undertaken by Excel showed there were no significant differences between the samples with and without coating (one tail p-value >0.01).

As discussed in Section 4.3, the PLGA coating served as an adhesive, which led to fiber bonding and reinforced the fiber-fiber interactions. This reinforcement role of the PLGA coating can also be observed in the load-displacement curves obtained from the bursting tests. For the initial samples before degradation (Fig.4.21), the coated materials showed a higher initial modulus and higher breaking strength than those PGA webs that had no coating. The material also became more brittle after coating, which was indicated by a lower displacement at break, since the relative movement of individual fibers in the web became limited with the applied coating. After 15 days, the coated sample still had a steeper initial slope suggesting a higher modulus, and the breaking loads were comparable.

Two different factors may have contributed to this trend, namely:

1. The strength loss of the coating itself. PLGA coating would also have been hydrolyzed in the presence of water, which would have led to a reduction in the extra strength provided. This trend will be discussed in detail in the following section.

2. The role of fiber-fiber interactions in determining the nonwoven bursting strength changed around Day 6 to a second factor, as discussed earlier. Even though the web was reinforced by a coating, the fiber-fiber interactions were no longer the major controlling factor, so no significant changes in bursting strength were observed.
Comparison of Load-Displacement Curves of PGA Nonwoven Webs With and Without PLGA Coating

Fig. 4.21 Typical load (N) / displacement (mm) curves of PGA nonwoven webs with (blue) and without (red) coating before (above) and after (below) 15 days of in vitro PBS exposure.
4.7.2 Bursting strength of PLGA coated PET nonwoven webs

The last essential element required for establishing a mathematical model that will predict the strength of the coated PGA web during hydrolysis is to understand the contribution by the addition of the PLGA coating. In order to evaluate this factor, the changes in the strength of the PLGA-coated PET nonwoven webs and the PET webs without coating after various times of PBS exposure were measured and plotted in Fig.4.22.

![Additional Strength (N) Due to Coating During Degradation (Days)](image)

Due to the unevenness of structure and the relatively small value for the strength contributed by the coating, large coefficients of variation were obtained. From the initial 57 N before hydrolysis, this parameter decreased to 25 N (43%) within 6 days. By Day15 the 90% confidence interval included 0, suggesting no significant contribution for the coating by Day 15 and at longer times. This is in good agreement with the discussion in the previous section.
4.8 MODELING

The missing data for fiber extraction force after 9 days and fiber tensile strength after 12 days were estimated by assuming both functions reached zero at Day 18. Quadratic functions were used to interpolate the data. After the required data had been generated, mathematical models were designed and modified in order to predict the strength change of the PGA nonwoven webs with and without a PLGA coating during in vitro exposure to the PBS solution. In order to achieve an optimal modeling technique, both ANN models and traditional regression analysis models were applied to explore the underlying relationship between the performance of the nonwoven web and its constituent fibers. For the PLGA-coated samples, the input data for the models contained either data obtained directly from the strength of the uncoated nonwoven webs and/or data obtained from individual fiber tensile and fiber extraction tests. All the modeling processes were operated using Matlab R2010b. An extra ANN toolbox was utilized when designing ANN models.

4.8.1 Mathematical model design for PGA nonwoven materials

In this section, mathematical models were designed using fiber extraction force retention (%) and fiber tensile strength retention (%) as the input data, and PGA nonwoven web bursting strength retention (%) as the output data. As stated in the previous section, samples were incubated in standard PBS solution for 0, 2, 4, 6, 7.5, 9, 12, 15 and 18 days and then went through mechanical tests to generate data for model development. This means that altogether 9 sets of data were obtained from experimental measurements to provide the input and output data for the models.
4.8.1.1 Regression model designed for PGA nonwoven materials

As mentioned above, altogether 9 sets of data were available for model design. This means that the number of unknown parameters that could be included in the regression function would be less than 9 in order to calculate a reliable result. In essence, the regression model was predicting the missing data between 9 known points of the real function, which made it a typical problem that could be solved by a conventional multi-linear interpolation method\[^84\].

So the structure of a typical bilinear interpolation function (which was the product of two linear functions) was selected for function approximation, as shown in Equ.4.1:

\[
axy + bx + cy + d = z \quad \text{Equ.4.1}
\]

Where \(x\) was the fiber tensile strength retention (\%), \(y\) was the fiber extraction force retention (\%) and \(z\) was the bursting strength retention (\%) of the PGA nonwoven webs. This function contained altogether 4 unknown parameters (\(a, b, c\) and \(d\)) while 9 independent equations could be drawn using the experimental data. In order to make the calculation easier for the software, the information above was expressed in a matrix form:

\[
A= \begin{bmatrix}
x_1y_1 & x_2y_2 & \ldots & x_9y_9 \\
x_1 & x_2 & \ldots & x_9 \\
y_1 & y_2 & \ldots & y_9 \\
1 & 1 & \ldots & 1
\end{bmatrix}; \quad B= [a \ b \ c \ d]
\]

\[
C= [Z_1 \ Z_2 \ Z_3 \ Z_4 \ Z_5 \ Z_6 \ Z_7 \ Z_8 \ Z_9]
\]

Matrices \(A\), \(B\) and \(C\) were defined above. \(A\) was a \(4 \times 9\) matrix containing all input data and their combinations in Equ.4.1. \(B\) was a \(1 \times 6\) matrix consisting of all unknown parameters, and \(C\) was a \(1 \times 9\) matrix containing all output data.
According to Eq.4.1, \( B \times A = C \). Since \( A \) and \( C \) contained only known experimental results, \( B \) could be calculated through computer software.

This procedure was accomplished using Matlab Ver.R2010b. A regression () function was selected and the lines beginning with “%” were explanatory notes.

```matlab
function regression()

% 9 output values;
output = [Z1 Z2 Z3Z4Z5Z6 Z7Z8Z9];
% 9 input values;
input = [X1 X2 X3 X4 X5 X6 X7X8 X9
        Y1Y2 Y3 Y4 Y5 Y6 Y7 Y8 Y9]

% assign initial matrix \( A \) containing only 1s for the input matrix
a = ones(4, 9);
% assign xy for the second line
a(1, :) = input(1, :) .* input(2, :);
% assign x and y for the 4\textsuperscript{th} and 5\textsuperscript{th} line and leave 6\textsuperscript{th} line unchanged
a(2, :) = input(1, :);
a(3, :) = input(2, :);

% compute transfer matrix \( B \) via pseudo inverse method
b = output * transpose(a) * (a * transpose(a)) \(^{-1}\);
% display the transfer matrix \( B \) and the predicted values
disp (b*a);
disp (b)
end
```

The resulting equation and its performance were shown below:

\[
0.0136xy + 0.2529x - 0.7137y + 6.3992 = z \hspace{1cm} \text{Equ.4.2}
\]
Table 4.1 Prediction performance of bilinear interpolation function

<table>
<thead>
<tr>
<th>Duration</th>
<th>Experimental data</th>
<th>Predicted data</th>
<th>Error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100.00</td>
<td>96.32</td>
<td>-3.82</td>
</tr>
<tr>
<td>2</td>
<td>54.95</td>
<td>54.86</td>
<td>-0.16</td>
</tr>
<tr>
<td>4</td>
<td>34.88</td>
<td>38.05</td>
<td>8.33</td>
</tr>
<tr>
<td>6</td>
<td>18.43</td>
<td>26.93</td>
<td>31.58</td>
</tr>
<tr>
<td>7.5</td>
<td>12.43</td>
<td>9.69</td>
<td>-28.32</td>
</tr>
<tr>
<td>9</td>
<td>7.95</td>
<td>2.44</td>
<td>-226.31</td>
</tr>
<tr>
<td>12</td>
<td>4.66</td>
<td>-0.42</td>
<td>1204.75</td>
</tr>
<tr>
<td>15</td>
<td>3.39</td>
<td>3.43</td>
<td>1.24</td>
</tr>
<tr>
<td>18</td>
<td>1.30</td>
<td>6.40</td>
<td>79.72</td>
</tr>
</tbody>
</table>

R² = 0.989060885

Fig. 4.23 Performance of bilinear interpolation function

Even though the bilinear interpolation model achieved a relatively precise prediction for the first three sets of data, the performance afterwards suggested the occurrence of large modeling error. A negative value was given for Day 12 with an error of over 1200% and the approximation curve did not follow a decreasing trend. Even though a high coefficient of determination of 98.9% indicated an accurate overall prediction, clearly modification of this
function was needed.

The preliminary results showed that the trend for the loss in bursting strength approximately followed a multinomial function. Based on this finding, two quadratic factors were selected in addition to the bilinear interpolation function, as shown below:

\[ \text{ax}^2 + \text{bxy} + \text{cy}^2 + \text{dx} + \text{ey} + \text{f} = \text{z} \quad \text{Equ.4.3} \]

Where x is the fiber tensile strength retention (%) and y is the fiber extraction force retention (%) and z is the bursting strength retention (%) of the PGA nonwoven webs. Similarly, a set of matrices were built and calculated through Matlab Ver.R2010b.

\[
A = \begin{bmatrix}
    x_1^2 & x_2^2 & \cdots & \cdots & \cdots & x_9^2 \\
    x_1 y_1 & x_2 y_2 & \cdots & \cdots & \cdots & x_9 y_9 \\
    y_1^2 & y_2^2 & \cdots & \cdots & \cdots & y_9^2 \\
    x_1 & x_2 & \cdots & \cdots & \cdots & x_9 \\
    y_1 & y_2 & \cdots & \cdots & \cdots & y_9 \\
    1 & 1 & \cdots & \cdots & \cdots & 1
\end{bmatrix}
\]

\[
B = [a \ b \ c \ d \ e \ f]
\]

\[
C = [z_1 \ z_2 \ z_3 \ z_4 \ z_5 \ z_6 \ z_7 \ z_8 \ z_9]
\]

\[
\text{function} \ \text{regression}() \\
\%
\text{9 output values;}
\text{output} = [z_1 \ z_2 \ z_3 \ z_4 \ z_5 \ z_6 \ z_7 \ z_8 \ z_9];
\%
\text{9 input values;}
\text{input} = [x_1 \ x_2 \ x_3 \ x_4 \ x_5 \ x_6 \ x_7 \ x_8 \ x_9 \ y_1 \ y_2 \ y_3 \ y_4 \ y_5 \ y_6 \ y_7 \ y_8 \ y_9];
\%
\text{assign initial matrix A containing only 1s for the input matrix}
\text{a} = \text{ones}(6, 9);
\%
\text{assign x}^2 \text{ for the first line}
\text{a}(1, :) = \text{input}(1, :) .* \text{input}(1, :);
\%
\text{assign xy for the second line}
\text{a}(2, :) = \text{input}(1, :) .* \text{input}(2, :);
\]

105
% assign y^2 for the third line
a(3, :) = input(2, :).*input(2, :);
% assign x and y for the 4th and 5th line and leave 6th line unchanged
a(4, :) = input(1, :);
a(5, :) = input(2, :);

% compute transfer matrix B via pseudo inverse method
b = output*transpose(a)*(a*transpose(a))^(-1);
% display the transfer matrix B and the predicted values
disp (b*a);
disp (b);

end

The regression model calculation is given by the function below:

\[
0.0627x^2 - 0.0607xy + 0.0174y^2 - 3.181x + 2.2245y + 1.2773 = z \quad \text{Equ.4.4}
\]

The predicted value for the PGA nonwoven bursting strength retention (%) was listed in the table below. The prediction errors for each data point were calculated and the average of their absolute value is shown as a reference. The coefficients of determination (R^2) of each model are also included. Since no obvious difference can be observed in the figure, a comparison of the experimental curve and the predicted curve will not be included in this section.

Table 4.2 Evaluation of modified regression modeling for the bursting strength of PGA nonwoven material

<table>
<thead>
<tr>
<th>Duration (days)</th>
<th>Bursting strength retention (%)</th>
<th>Regression</th>
<th>Error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100.00</td>
<td>99.93</td>
<td>-0.07</td>
</tr>
<tr>
<td>2</td>
<td>54.95</td>
<td>54.49</td>
<td>-0.82</td>
</tr>
<tr>
<td>4</td>
<td>34.88</td>
<td>34.51</td>
<td>-1.06</td>
</tr>
<tr>
<td>6</td>
<td>18.43</td>
<td>19.22</td>
<td>4.31</td>
</tr>
<tr>
<td>7.5</td>
<td>12.43</td>
<td>15.17</td>
<td>22.06</td>
</tr>
<tr>
<td>9</td>
<td>7.95</td>
<td>5.10</td>
<td>-35.79</td>
</tr>
<tr>
<td>12</td>
<td>4.66</td>
<td>3.59</td>
<td>-22.99</td>
</tr>
<tr>
<td>15</td>
<td>3.39</td>
<td>4.68</td>
<td>38.15</td>
</tr>
<tr>
<td>18</td>
<td>1.30</td>
<td>1.28</td>
<td>-1.55</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>14.09</td>
<td></td>
</tr>
<tr>
<td>R^2</td>
<td></td>
<td>0.99886</td>
<td></td>
</tr>
</tbody>
</table>
Generally speaking, this modified model had a $R^2$ larger than 99.86%, which suggested an accurate overall prediction. Even though a relatively high error rate could still be observed after 7.5 days, due to the low absolute values of <13%, the quadratic multinomial function achieved a much more stable precision. In terms of both overall performance and individual data points, the modification of the regression model presented in Table 4.2 had achieved a significant improvement.

### 4.8.1.2 ANN model designed for PGA nonwoven materials

An artificial neural network (ANN) is a network structure model that processes data between neurons through weight multiplications, bias additions and activation functions. Given a known set of input values and their corresponding output values, weights and bias will be repeatedly modified and updated until either a desired accuracy is achieved or a set number of training cycles has been completed, whichever comes first.

![Fig.4.24A feed-forward BP ANN model design with 1 hidden layer and 2 hidden neurons](image-url)
In Fig.4.24, Input1 is the fiber tensile strength retention (%), Input2 is the fiber extraction force retention(%) and the output is the bursting strength retention of the PGA needle-punched nonwoven material(%).

In this study, a feed-forward network containing one hidden layer with 2 hidden neurons was developed (Fig.4.24). The activation function between the input and the hidden neurons was a transig function, and between the hidden and output neuron, a linear function (Equ.2.10) was utilized. Transig and linear functions have been the two most commonly used functions in ANN modeling and are widely believed to achieve satisfactory predictive results in engineering based problems, especially on nonwoven material, as discussed earlier in the literature review (Section 2.1.4.2). Based on this fact, a mixture of functions was selected in order to reach a more complex yet accurate and predictive function approximation. The addition of hidden layers brought more degrees of freedom into the network, also aiming to improve the complexity of the function that the model is able to approximate. Feed-forward means that the data was only processed and passed in one direction (from input data to output data, from left to right), which was the most commonly used structure in modeling applications. Back-propagation (BP) algorithms indicate that each time the weights and bias were updated; the errors were calculated backwards from output to input.

The summation of the bias and the product of each input data multiplied by the corresponding weight advanced through an activation function in order to obtain the value for the hidden neurons. The two hidden neurons went through the same procedure to calculate the output value. Then the calculated value was compared with the known output
value and the resulting error passed backwards to update all the weights and biases. For instance:

\[ f (Input1 \times W11 + Input2 \times W21 + Bias1) = \text{input of } H1 \]

Where \( f () \) is the activation function. Since the ANN model updated every parameter during each training cycle, the more cycles that are run for training, the higher the accuracy achieved. In this case, 30,000 epoches were completed, which can be seen from the code below:

```matlab
function neur() % 9 output values;
o = [Z1 Z2 Z3 Z4 Z5 Z6 Z7 Z8 Z9]; % 9 input values;
i = [X1 X2 X3 X4 X5 X6 X7 X8 X9
     Y1 Y2 Y3 Y4 Y5 Y6 Y7 Y8 Y9]

% normalize the output values to between 1 and -1
output = (O - 50)/50;
% normalize the input values to between 1 and -1
input = (I - 50)/50;

% define the neural net structure, 2 neurals in the hidden layer, transig Function for the hidden layer and purelin for the output layer; training with Gradient descent backpropagation
net = newff(minmax(input),[2,1],{'tansig','purelin'},'traingd');

% Learning Rate
net.trainParam.lr = .1;
% Max Epochs
net.trainParam.epochs = 30000;
% Training Goal in Mean Squared Error
net.trainParam.goal = 1e-5;
% number of epoches in display
net.trainParam.show = 50;

% train the network
net = train(net, input, output);
% use the input to test the network
```
The model was accomplished using Matlab Ver.R2010b with an Artificial Neural Network Toolbox. The input and output values were normalized into a [-1,+1] range using a linear transform, since the transig function required a definitional domain between -1 and +1. The training was stopped either after 30,000 training cycles or once a mean square error lower than 1x10^{-5} had been achieved.

The weights and biases for the ANN model were modified and updated 30,000 times during training, so each result would vary greatly between different runs. The following are the parameters obtained from one run. The position of each parameter can be found in Fig.4.24:

Bias: Bias1= -1.5145, Bias2= -1.5285, Bias= 0.0074

Weights: W11= 1.2194, W12= 1.2452, W21= -1.6935, W22= 0.6016, W1= -0.5740, W2= 1.4248

The predicted value for the PGA nonwoven bursting strength retention (%) is listed in Table 4.3. The prediction errors for each data point were calculated and the average of their absolute values is shown as a reference. The coefficients of determination (R^2) of each model are also included.
The ANN models performed a precise overall approximation with an $R^2$ value larger than 99.9%. Moreover, a significant reduction in the average error of 14.09% with a regression model to 7.49% with an ANN suggests that the performance became more stable during data processing. In terms of both overall performance and individual data points, the ANN model had the best performance among the three models discussed above.

Table 4.3 Evaluation of ANN modeling results for the bursting strength of PGA nonwoven material

<table>
<thead>
<tr>
<th>Duration (days)</th>
<th>Bursting strength retention (%)</th>
<th>ANN</th>
<th>Error (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100.00</td>
<td>100.04</td>
<td>0.04</td>
</tr>
<tr>
<td>2</td>
<td>54.95</td>
<td>54.32</td>
<td>-1.14</td>
</tr>
<tr>
<td>4</td>
<td>34.88</td>
<td>36.92</td>
<td>5.84</td>
</tr>
<tr>
<td>6</td>
<td>18.43</td>
<td>16.28</td>
<td>-11.67</td>
</tr>
<tr>
<td>7.5</td>
<td>12.43</td>
<td>12.93</td>
<td>4.00</td>
</tr>
<tr>
<td>9</td>
<td>7.95</td>
<td>8.08</td>
<td>1.69</td>
</tr>
<tr>
<td>12</td>
<td>4.66</td>
<td>4.54</td>
<td>-2.66</td>
</tr>
<tr>
<td>15</td>
<td>3.39</td>
<td>3.90</td>
<td>14.97</td>
</tr>
<tr>
<td>18</td>
<td>1.30</td>
<td>0.97</td>
<td>-25.40</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>7.49</td>
<td></td>
</tr>
<tr>
<td>$R^2$</td>
<td></td>
<td>0.99943</td>
<td></td>
</tr>
</tbody>
</table>

Traditionally, a subset of the testing data, usually between 10%~20% of the total experimental database, which is not involved in the training process, is needed to test and validate the model. However, in this case, due to the limitation of the data base size, all 9 of the experimental data sets were used to train the models. As a result, it became relatively easy to find a function which offered a close approximation to the predicted data because all the data points were known to the models. Also, the problem of overfitting might have occurred in the regression model since the error between 7.5 and 15 days varied from $+38.15\%$.
to -35.79%. However, increasing the number of data points during the experimental design was not a reasonable solution. This was because the Biofelt nonwoven material lost its strength within 18 days, and 9 data points was already a high sampling frequency. If the material had been tested every day during incubation experiment, the variation within the groups could have been considerably higher compared to the real differences between the groups, thus making the data sets less reliable. So the only way to improve the performance of the mathematical models would have been to include more PGA needle-punched webs with various fabrication parameters, such as different fiber lengths, fiber thicknesses, needling densities, needle punching depths, fiber orientations and web thicknesses, etc.

4.8.2 Mathematical model design for PLGA-coated PGA nonwoven materials

The experimental results obtained from the PLGA-coated PET webs enabled the predication of the performance of the PLGA-coated PGA materials. Two different strategies of data selection were available, namely:

1. Using the PGA nonwoven material bursting strength retention(%) and the PLGA coating strength retention (%) as input data, and the bursting strength retention of the PLGA coated PGA nonwoven material(%) as output data.

2. Using the PGA individual fiber tensile strength retention(%), the fiber extraction force retention(%) and the PLGA coating strength retention (%) as input data, and the bursting strength retention of the PLGA coated PGA nonwoven material(%) as output data.
Based on the data selections listed above, two ANN models and two regression analysis models were developed.

For the models using data strategy 1, the only modification needed to be done to the model described in 4.8.1 was to change the input and output data: x was assigned to the PGA nonwoven material bursting strength retention(%), y to the PLGA coating strength retention (%) and z to the bursting strength retention of the PLGA coated PGA nonwoven material(%).

For the ANN model using data strategy 2, except for the switch of the data sets, an additional data input was needed. The scheme of the resulting network is shown in Fig.4.25.

In Fig.4.25 Input1 was the fiber tensile strength retention(%), Input2 was the fiber extraction force retention(%), Input3 was the PLGA coating strength retention (%) and the Output was the bursting strength retention of the PLGA coated PGA needle-punched nonwoven material (%).

For the regression analysis model using data strategy 2, a quadratic multinomial function
with three input data sets would bring more than 9 unknown parameters, making it impossible to calculate the absolute values. So instead, a trilinear interpolation with 8 unknown factors was used (Equ.4.5):

\[ axyz + bxy + cyz + dxz + ex + fy + gz + h = m \]  
Equ.4.5

Where x was the fiber tensile strength retention (%), y was the fiber extraction force retention(%), z was the PLGA coating strength retention (%) and m was the bursting strength retention of the PLGA coated PGA needle-punched nonwoven material (%).

Matrices A, B and C were defined as follows. A was an 8 x 9 matrix containing all input data and their combinations in Equ.4.5. B was a 1 x 9 matrix consisting of all unknown parameters and C was a 1 x 9 matrix containing all output data.

According to Equ.4.5, \( B \times A = C \). Since A and C contained only known experimental results, B could be calculated using Matlab.

\[
A = \begin{bmatrix}
  x_1 & y_1 & z_1 & x_2 & y_2 & z_2 & \ldots & \ldots & x_9 & y_9 & z_9 \\
  x_1 & y_1 & x_2 & y_2 & \ldots & \ldots & x_9 & y_9 & \\
  y_1 & z_1 & y_2 & z_2 & \ldots & \ldots & y_9 & z_9 & \\
  x_1 & z_1 & x_2 & z_2 & \ldots & \ldots & x_9 & z_9 & \\
  x_1 & x_2 & \ldots & \ldots & x_9 & \\
  y_1 & y_2 & \ldots & \ldots & y_9 & \\
  z_1 & z_2 & \ldots & \ldots & z_9 & \\
  1 & 1 & \ldots & \ldots & 1
\end{bmatrix} ; \quad B = [a \ b \ c \ d \ e \ f \ g \ h] \\
C = [m_1 \ m_2 \ m_3 \ m_4 \ m_5 \ m_6 \ m_7 \ m_8 \ m_9]
function regression3()

% 9 output values;
output = \[m_1 m_2 m_3 m_4 m_5 m_6 m_7 m_8 m_9\];
% 9 input values;
input = \[x_1 \; x_2 \; x_3 \; x_4 \; x_5 \; x_6 \; x_7 \; x_8 \; x_9\]
\[y_1 \; y_2 \; y_3 \; y_4 \; y_5 \; y_6 \; y_7 \; y_8 \; y_9\]
\[z_1 \; z_2 \; z_3 \; z_4 \; z_5 \; z_6 \; z_7 \; z_8 \; z_9\]

% assign initial matrix A containing only 1s for the input matrix
a = ones(8, 9);

% trilinear interpolation is used
% assign xyz for the first line
a(1, :) = input(1, :).* (input(2, :).*input(3, :));
% assign xy for the second line
a(2, :) = input(1, :).*input(2, :);
% assign yz for the third line
a(3, :) = input(2, :).*input(3, :);
% assign xz for the 4th line
a(4, :) = input(1, :).*input(3, :);
% assign x and y and z for the 5th 6th and 7th line leave 8th line unchanged
a(5:7, :) = input(:, :);

% compute transfer matrix via pseudo inverse method
b = output*transpose(a)* (a*transpose(a))^-1;
% display the transfer matrix B and the predicted values
disp('prediction value of the model:');
disp (b*a);
disp('transfer matrix B:');
disp (b)
end

After the calculations and training were completed, the model parameters are shown below:

**ANN model using PGA nonwoven strength:**

Bias: Bias1= -1.2955, Bias2=0.4141, Bias=0.757

Weights: W11=-0.0325, W12=1.0992, W21=2.1282, W22= 0.022, W1=03448, W2=0.9303

**ANN model using fiber tensile strength and fiber extraction force:**

Bias: Bias1= -1.1598, Bias2=-1.9476, Bias=0.564
Weights: $W_{11} = 0.1419, W_{12} = -0.8278, W_{21} = 1.0842, W_{31} = 0.6702, W_{32} = 1.394, W_{1} = 1.3894, W_{2} = 0.1477$

Regression analysis model using PGA nonwoven strength:

$$0.0211x^2 - 0.0416xy + 0.0124y^2 + 2.3463x - 0.5757y + 3.9175 = z \quad \text{Equ.4.6}$$

where $x$ is the PGA nonwoven material strength retention (%) and $y$ is the PLGA coating bursting strength retention (%) and $z$ is the bursting strength retention of PLGA coated PGA nonwoven webs (%).

The regression analysis model using fiber tensile strength and fiber extraction force:

$$0.0001xyz - 0.0049xy + 0.0122yz - 0.0017xz + 0.1947x - 0.081y - 0.5141z + 10.7771 = m \quad \text{Equ.4.7}$$

where $x$ is the fiber tensile strength retention(%), $y$ is the fiber extraction force retention(%), $z$ is the PLGA coating strength retention (%) and $m$ is bursting strength retention of the PLGA coated PGA needle-punched nonwoven material (%).

Similarly, precise results were obtained from the mathematical models designed to predict the strength loss of the PLGA coated PGA nonwoven webs. The main contribution to the average error came from the predicted value of Day24 for the first three models. For the regression analysis model developed using the mechanical properties of the PGA fibers (3 inputs), the trilinear interpolation function with no quadratic component was applied. This gave a similar result for the performance of the bilinear interpolation function developed in Section 4.8.1.1, which when compared to the ANN model, achieved a relatively low approximation accuracy in terms of $R^2$. 

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Table 4.4 Evaluation of mathematical modeling results for bursting strength of PLGA-coated PGA nonwoven material

<table>
<thead>
<tr>
<th>Duration (Days)</th>
<th>Coated material bursting strength retention (%)</th>
<th>Neuron using PGA bursting data (2 inputs) error %</th>
<th>Regression using PGA bursting data (2 inputs) error %</th>
<th>Neuron using fiber tests data (3 inputs) error %</th>
<th>Regression using fiber tests data (3 inputs) error %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100.00</td>
<td>100.06</td>
<td>100.24</td>
<td>100.02</td>
<td>100.02</td>
</tr>
<tr>
<td>2</td>
<td>60.87</td>
<td>60.20</td>
<td>59.85</td>
<td>60.78</td>
<td>55.10</td>
</tr>
<tr>
<td>4</td>
<td>35.78</td>
<td>37.31</td>
<td>35.87</td>
<td>35.84</td>
<td>34.35</td>
</tr>
<tr>
<td>6</td>
<td>17.77</td>
<td>17.60</td>
<td>19.48</td>
<td>18.42</td>
<td>18.63</td>
</tr>
<tr>
<td>7.5</td>
<td>13.33</td>
<td>11.38</td>
<td>13.14</td>
<td>11.73</td>
<td>12.67</td>
</tr>
<tr>
<td>9</td>
<td>9.46</td>
<td>9.37</td>
<td>9.15</td>
<td>9.46</td>
<td>8.15</td>
</tr>
<tr>
<td>12</td>
<td>4.08</td>
<td>4.44</td>
<td>4.26</td>
<td>4.45</td>
<td>4.05</td>
</tr>
<tr>
<td>15</td>
<td>2.91</td>
<td>3.30</td>
<td>3.98</td>
<td>3.12</td>
<td>3.78</td>
</tr>
<tr>
<td>18</td>
<td>1.36</td>
<td>1.95</td>
<td>42.82</td>
<td>-129.87</td>
<td>1.24</td>
</tr>
<tr>
<td>Average</td>
<td>9.68</td>
<td>20.86</td>
<td>12.65</td>
<td>8.57</td>
<td></td>
</tr>
<tr>
<td>(R^2)</td>
<td>0.99959</td>
<td>0.99952</td>
<td>0.99967</td>
<td>0.99834</td>
<td></td>
</tr>
</tbody>
</table>

In summary, all the mathematical models developed in this study were purposefully and appropriately designed, and offered a straightforward soft computing technique for both research use and industry quality control. The function approximations were accomplished with high coefficients of determination and within tolerable errors. The mathematical models developed using ANN structures achieved better approximations while the regression analysis models with quadratic components generated higher accuracies than multilinear interpolation functions.
CHAPTER 5

CONCLUSIONS AND FUTURE WORK

5.1 Conclusions

Chapter 1 of this thesis outlined the primary goals and objectives in undertaking this study. Following completion of the experimental and modeling stages, this project has successfully measured the effect of *in vitro* degradation of resorbable PGA nonwoven webs with and without a resorbable PLGA coating while incubating the samples for periods of up to 24 days under controlled conditions of pH and temperature. The performance parameters of the individual PGA fiber tensile strength, of the PGA fiber extraction force, of the bursting strength of the PGA nonwoven web as well as the strength contributed by the PLGA coating have all been used as inputs and outputs to build mathematical models using ANNs and regression analysis techniques. To be more specific, the following conclusions summarize the findings of this study.

1. The *in vitro* degradation of the resorbable PGA material took place primarily in terms of hydrolysis of the ester bonds since there was clear FTIR spectral evidence after 9 days in PBS buffer solution of increasing amounts of carboxylic acid and hydroxyl end groups at the expense of losses in the concentration of the ester bonds.
2. During the initial period of about 18 days, the DSC results suggest that degradation occurred primarily in the amorphous regions since the degree of crystallinity steadily increased during this period. It was only after the first 18 days that erosion of the crystalline regions was observed and the resorbable PGA material showed the appearance of surface cracks, fiber breakage and rapid degradation.

3. From the SEM images, fiber failure could be observed in the nonwoven material after 12 days of degradation. Then after 24 days, all the PGA fibers broke into small fragments and the nonwoven web lost its textile structure and integrity. The resorbable PLGA coating provided a certain level of adhesion by holding the PGA fibers together and offering extra fiber-fiber interactions. As a result, after 24 days of \textit{in vitro} hydrolysis, the PLGA coating held the broken fiber fragments together, hence maintaining a certain level of integrity of the nonwoven web structure despite eventually being resorbable.

4. A new and novel individual fiber extraction test was developed in an attempt to measure the extent to which fiber entanglements within a needle-punched nonwoven web contribute to the overall bursting strength of the nonwoven structure. This fiber extraction test showed a linear reduction of fiber interactions from an initial value of 10.5 gf before PBS exposure to 3.3 gf after 9 days of resorption. The extent to which individual fibers failed during the extraction process also suggested that fiber entanglements contributed to the strength of the resorbable nonwoven webs primarily during the first 6 days of resorption. After the first 6 days of PBS incubation, it appeared that individual fiber strength was a more important factor in predicting the
bursting strength of resorbable PGA nonwoven webs.

5. Individual fiber tensile strength decreased linearly after a stable initial “incubation” period of 2 days. Furthermore, they became the limiting factor for predicting the bursting strength of a resorbable PGA nonwoven web after 7.5 days. The load-displacement curve showed a reduction in both the yield point and Young’s modulus after 12 days of hydrolysis.

6. The decrease in bursting strength of the resorbable PGA nonwoven web exposed to PBS buffer followed an approximate biquadratic multinomial function. The nonwoven web strength dropped from its initial value of 285 N to 99 N at Day4 with only 35% strength remaining. The resorbable PLGA coated PGA sample showed a similar behavior. No statistically significant differences were observed between the coated and uncoated samples after 6 days of in vitro degradation, which is an observation consistent with the limited theory described above.

7. There was a marginal increase in the bursting strength of the PGA nonwoven web brought about by the addition of a resorbable PLGA coating. The bursting strength decreased by 43% from 58 N to only 25 N within 6 days. However, the variation in the data was high due to the relatively small absolute values.

8. A series of mathematical models was developed using regression analysis and artificial neural network (ANN) techniques to predict the change in bursting strength of the resorbable PGA nonwoven materials with and without a PLGA coating. The various models showed a high degree of agreement with coefficients of determination (R^2 values) higher than 0.998. Mathematical models developed using the ANN
technique achieved better approximations while the regression analysis models with quadratic components performed with higher accuracy than with multi-linear interpolation functions.

5.2 Future work

During the course of this study, it became clear that progress on generating an effective and reliable model was limited by a lack of practical experimental techniques to measure the performance and contribution of individual fibers within a needle punched nonwoven structure. Here are some suggested topics for future work that would assist in measuring and understanding the role of individual fibers within a nonwoven web.

1. Analyzing a nonwoven structure using 3D imaging techniques in order to explore the contribution of fiber entanglements in a more direct manner.

2. Develop a well-defined standard method to determine the individual fiber extraction force from the load-displacement curve.

3. Develop a non-manual technique for obtaining a fiber end without causing damage to the fiber, so as to extend the measurement range and generate more reliable results.

4. To undertake molecular weight measurements on the resorbable PGA polymer fibers through gel permeation chromatography (GPC) and/or intrinsic viscosity tests, so as to better understand the \textit{in vitro} degradation process at the molecular scale.

5. To undertake degradation experiments on nonwoven webs with different needle-punching densities, different types of resorbable polymers, and fibers with different
lengths and linear densities, so as to extend the input data sources for the predictive models.

6. Develop more complex ANN structures by using the data generated from 5 above. This will improve the performance of current models and enable them to be applied to a wider range of polymers, fibers and nonwoven structures.
References


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