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Rate Process Models for Thermal Welding

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ABSTRACT

Laser tissue welding is a thermal process for binding two tissues together. Optical and thermal models exist to calculate the temperatures of laser irradiated tissues. However, a rate process model is required to relate the time-temperature history to a weld strength. This paper proposes a first-order rate process model based on contraction during heating. The entropy and enthalpy associated with contraction of porcine intestine in a water bath was measured and used to calculate the fraction of altered molecules for both water bath and laser welding. Intestine was welded to intestine in a water bath at 60–80°C for seven minutes. Pulsed laser welding used 10–30 pulses and an exogenous chromophore. The yield strengths of the welds were measured and found to roughly correlate with the fraction of altered molecules estimated for both the water bath and laser welds.

Keywords: Indocyanine Green, Biomaterial

1. INTRODUCTION

Joining tissues with heat might be called "welding" or "fusion" or "adhesion" or "gluing" because the fundamental mechanism remains unelucidated. "Welding" has unfortunate associations with very high temperatures and metals, but will be used in this paper because it enjoys widespread use. This paper couples a simple thermal model with a first-order kinetic model to simulate the welding of tissue. The enthalpy and entropy of the thermal contraction process of porcine intestine is measured directly using a universal tester. These parameters are used to calculate the fraction of molecules participating in steady state water bath and pulsed laser welding experiments. These fractions are then correlated with the yield strengths of the two types of tissue welds.

2. THEORY

2.1. Arrhenius Model

A first-order rate process model was used by Henriques to determine the kinetic process of thermal damage to tissue.[1–6] The fraction of unchanged molecules is defined as

$$f \equiv \frac{n(t)}{n(0)} \tag{1}$$

where $n(t)$ is the number of unchanged molecules at time t and $n(0)$ is the initial number of molecules. The fraction f depends on the thermal history

$$-\ln f = \int_0^t \frac{RT(t')}{Nh} \exp\left[\frac{\Delta S}{R} - \frac{\Delta H}{RT(t')}\right] dt' \tag{2}$$

where R is the universal gas constant, N is Avogadro's number, h is Planck's constant, ΔS is the entropy of the reaction, ΔH is the enthalpy of the reaction, and $T(t')$ is the temperature.

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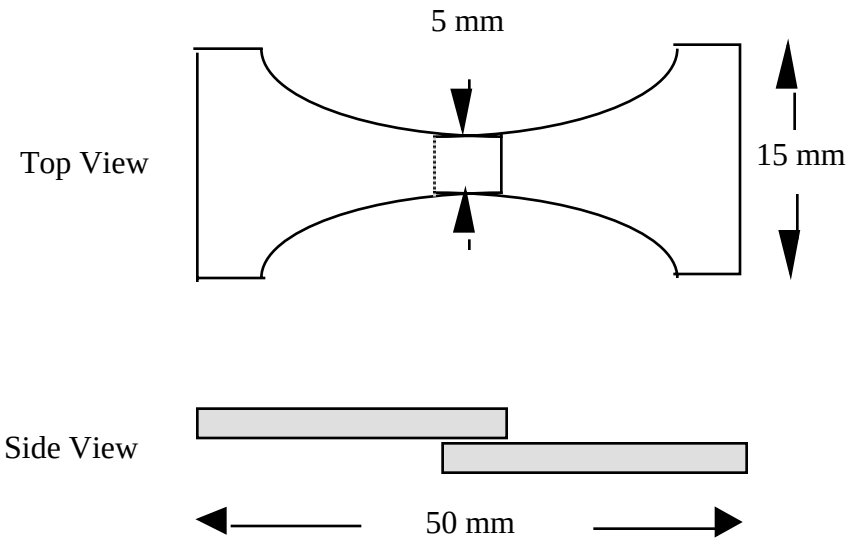

Figure 1. Dog bone shaped die mold used to section the aorta and intestine samples for mechanical testing.

2.2. Water bath Model

When the thermal history is a constant $T(t) = T_{\text{bath}}$, as one would obtain in a water bath, then the fraction f simplifies to

$$-\ln f = \frac{RT_{\text{bath}}t}{Nh} \exp\left[\frac{\Delta S}{R} - \frac{\Delta H}{RT_{\text{bath}}}\right] \tag{3}$$

and $\ln f$ decreases linearly with the time of immersion t. This formula may be rewritten as

$$\ln\left[-\frac{\ln f}{T_{\text{bath}}t}\right] = \left[\ln\left(\frac{R}{Nh}\right) + \frac{\Delta S}{R}\right] - \frac{\Delta H}{RT_{\text{bath}}} \tag{4}$$

to calculate the entropy and enthalpy of reaction from a set of measurements of f for different values of T_{bath} as a function of time t.

2.3. Laser Model

The fraction f remaining after pulsed laser heating is somewhat more problematic. A straightforward approach would assume that the absorption was uniformly distributed (as a function of depth) with an absorption coefficient μ_a. The temperature resulting from a thermally confined radiant exposure ψ would then be

$$T(x) = \frac{\mu_a \psi}{\rho c} \exp(-\mu_a x) \tag{5}$$

where ρc is the heat capacity of the tissue. This thermal distribution can be thermally propagated in time to get the full thermal history. This approach is too simple when temperatures in excess of 100°C are predicted because the phase change in water is ignored. One reasonable physical model for the thermal history is that the tissue temperature will rapidly rise to 100°C, at which point it will remain constant as excess energy is used to convert water to steam. The steam will later recondense as thermal conduction takes place, thereby keeping the temperature at 100°C for a duration longer than the original laser pulse.

An analytic version of this physical model clamps the surface temperature at 100°C until the total deposited energy in the tissue is equal to the laser pulse energy. At this point the boundary restrictions are removed and the temperature is allowed to naturally thermally relax.

The temperature in an infinite medium initially at a constant temperature T_{room} with the plane $x = 0$ maintained at T_{100° is

$$T(x,t) = T_{\text{room}} + (T_{100^\circ} - T_{\text{room}}) \operatorname{erfc} \frac{x}{\sqrt{4\kappa t}} \qquad \text{if} \qquad x \geq 0 \tag{6}$$

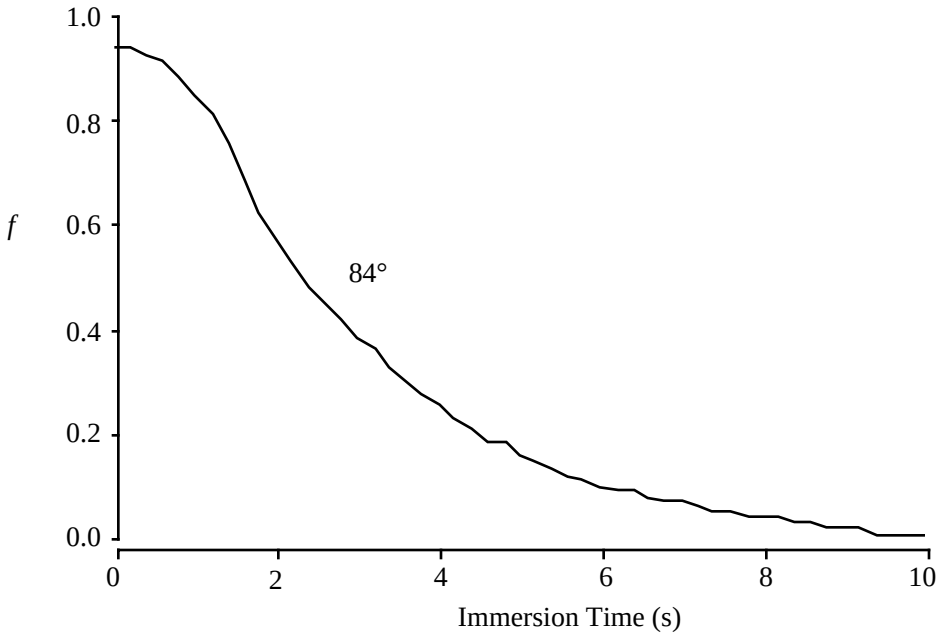

Figure 2. The normalized contraction of intestine at 84°C held at a constant force of 30 g. The contraction rate was faster at high temperatures and slower at lower temperatures.

The total energy deposited per unit area $q(t)$ in the total medium by a time t is

$$q(t) = 2\rho c \int_0^\infty (T_{100^\circ} - T_{\text{room}}) \operatorname{erfc} \frac{x}{\sqrt{4\kappa t}}\, dx = \frac{4\rho c\sqrt{\kappa t}(T_{100^\circ} - T_{\text{room}})}{\sqrt{\pi}} \tag{7}$$

The heating time t_h required to deposit an energy per unit area equal to the radiant exposure ψ is

$$t_h = \frac{\pi}{\kappa}\left[\frac{\psi}{4\rho c(T_{100^\circ} - T_{\text{room}})}\right]^2 \tag{8}$$

The temperature at time t_h and after is

$$T_{\text{laser}}(x,t) = T_{\text{room}} + \frac{(T_{100^\circ} - T_{\text{room}})}{\pi}\sqrt{\frac{4\pi}{\kappa t}} \int_0^\infty \operatorname{erfc} \frac{x'}{\sqrt{4\kappa(t-t_h)}} \exp\left[-\frac{(x-x')^2}{4\kappa(t-t_h)}\right] dx' \tag{9}$$

The plane $x = 0$ can be solved explicitly to obtain

$$T_{\text{laser}}(0,t) = \begin{cases} T_{\text{room}}, & \text{if } t \le 0; \\ T_{100^\circ}, & \text{if } 0 \le t \le t_h; \\ T_{\text{room}} + (T_{100^\circ} - T_{\text{room}})\dfrac{2}{\pi}\tan^{-1}\sqrt{\dfrac{t_h}{t-t_h}}, & \text{if } t_h \le t. \end{cases} \tag{10}$$

This temperature profile was used to calculate the fraction f in equation 2 for the laser welds.

Several assumptions are implicit in this simple model

- The optical penetration thickness is small compared to the thermal diffusion thickness.
- The laser pulse duration should be short compared to the time required for a boundary to deliver the proper amount of energy.
- The material over the sample has the same thermal conditions as the target.
- The material over the sample is sufficiently thick that an infinite sample approximation is reasonable.
- Sufficient laser energy is delivered to ensure that the equation (5) predicts temperatures in excess of 100°C.

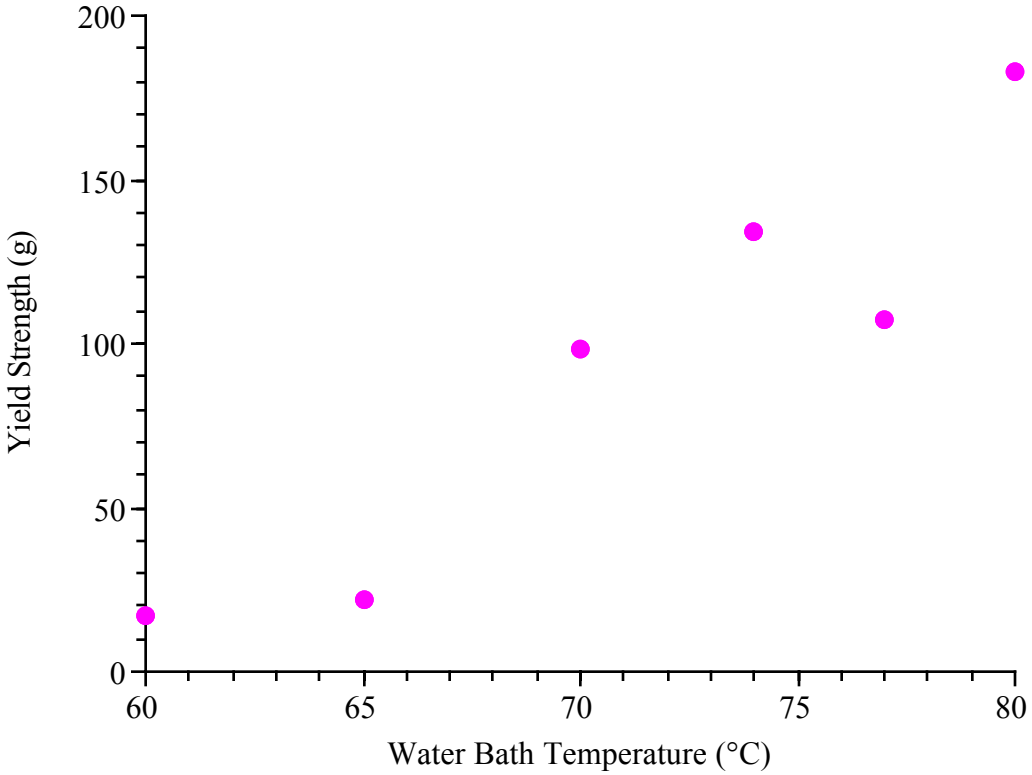

Figure 3. Weld strengths for intestine welded for 7 minutes in a constant temperature water bath.

3. MATERIALS AND METHODS

3.1. Tissue Preparation

Porcine intestine was obtained at Carlton Packing Co., Carlton, OR and placed on ice. The intestine came fresh in about 8 m lengths, and was cut in 10 cm sections before freezing in individual freezer bags. The tissue was kept frozen at −10°C until used. The intestine was thawed by placing the freezer bag in a beaker of room temperature water. Once thawed, the intestine was removed from the bag, rinsed with cool water, split open lengthwise with surgical scissors, and the inside wiped clean with gauze. Rectangular sections about 3–5 cm were cut into a dog bone shape using a cutting mold (see Figure 1). This mold is typical of mechanical testing shapes, and allowed the tested sample to fail in the center, rather than at the ends where the tester was attached. The cut samples were stored in gauze soaked with 0.9% NaCl to prevent drying.

The tissues used in the laser welding experiments were stained with 1.6 mM indocyanine green (ICG). ICG was added to 1 ml of deionized water in a small test tube. The test tube was vortexed for 2–3 minutes to completely dissolve the ICG and create a uniform green solution with no undissolved ICG granules. The tissue was laid flat on a cutting board, and the stain dripped on with a disposable pipette, left for 5 minutes, and blotted dry with a paper tissue. Staining was done on the serosal side of the intestine. To maintain an even ICG deposition, a large piece of tissue was stained before it was cut into smaller pieces for welding. The ICG stained depth was 25–50 μm and the absorption coefficient was estimated from transmission measurements as 200–400 cm^{-1}.

3.2. Weld Strength Testing

Yield strength tests were performed using the universal tester (Chatillon, V1000). This tester consisted of a computer-controlled motorized actuator in a vertical position, and load cells appropriate for the sample. The load cell was calibrated according to the manufacturer's instructions at the beginning of each day, or when a new load cell was

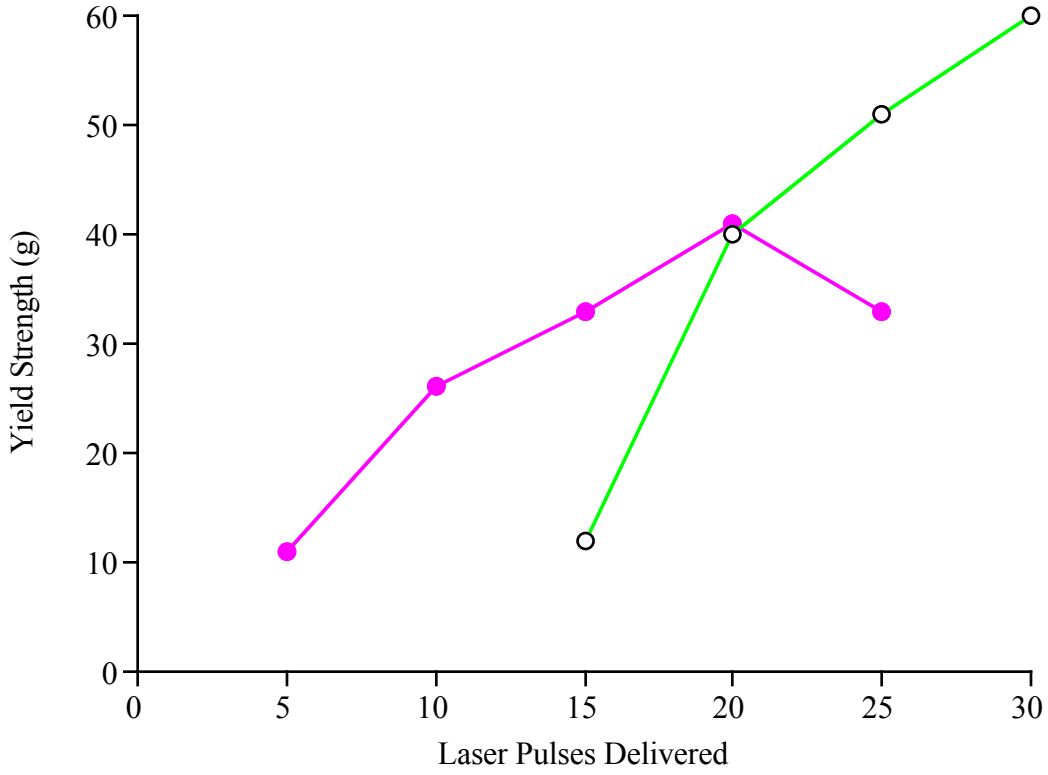

Figure 4. Weld strengths for intestine welded with different numbers of laser pulses. The radiant exposure was 42 mJ/mm^2 (filled circles) or 70 mJ/mm^2 (empty circles) and the absorption coefficient was 200–400 cm^{-1}.

used. The prepared welds were placed in the tester grips that consisted of two sliding metal plates backed with plastic screws to secure wide ends of the dog bone-shaped sample. A strength, or ramp test was performed by pulling on the sample at a constant speed of 200 μm/sec, and measuring the tension exerted by the sample. The yield strength was recorded when the weld failed.

3.3. Thermal Characterization

Denaturation and coagulation of tissue proteins cause tissue to contract or shrink. Each sample was pulled to about 10% of yield strength or 30 g with the universal tester. This force was maintained and the length of the sample was monitored over time. The sample was placed in the grips, a large beaker was placed underneath, and raised up over the sample. The sample was pulled to force, heated water was added to the beaker, and the change in length monitored at 5 samples/second. The temperature of the water bath was measured with a thermocouple. This test was repeated for temperatures ranging from 50–90°C. The position was normalized to give a fraction f that changed with time

$$f(t) = \frac{x(t) - x_{\text{end}}}{x_{\text{start}} - x_{\text{end}}} \tag{11}$$

where x_{start} was the length of the sample before immersion in heated water and x_{end} was the final length after three minutes of immersion. These values were used in Equation 4 to calculate the enthalpy and entropy of thermal contraction.

3.4. Water Bath Welding

Water bath welding experiments were performed using an water bath (Equatherm) that held temperatures constant to within one degree. Pieces of intestine were cut using the dog bone die and then divided in two. One half was

flipped over, and then overlapped with the other piece about 5 mm with serosal faces adjacent. This ensured that all welds had approximately the same surface area of 25 mm ^{2}. The overlapping tissues were sandwiched between 2×2 cm glass slides with 220 grit sandpaper in between the tissue and glass to hold the tissues in place. A small binder clip (ACCO) was used to apply approximately 800 N/cm^2 pressure to the weld site. Welds were immersed at temperatures of 60–80°C for 7 minutes, then removed from the water bath and placed in room temperature saline to cool. The clips and glass slides were removed, and the weld placed in the universal tester to measure the yield strength as described below.

3.5. Laser Welding

Our laser source was a pulsed diode laser at wavelength between 790–810 nm from Star Medical Technologies (Pleasanton CA). A condenser was fitted to the handpiece of the laser. The non-imaging optical condenser was made of polished copper that was shaped to collect the light from the diode array and redistribute it over a 6×6 mm square. The tip of the condenser was placed flush against the glass slide so that the laser light passed through one unstained intestine sample to reach the stained side of the other piece of intestine.

The laser parameters (radiant exposure, pulse length, pulse number, and repetition rate), ICG staining concentration, and staining time all affect the laser welding process.[7] A 5 ms laser pulse was used for all laser experiments; this pulse duration ensured thermal confinement of the laser pulse. Radiant exposures of 42 mJ/mm^2 and 70 mJ/mm^2 were used. We hand-pulsed the laser at about 3–4 Hz. The spot size was 6×6 mm. Two overlapping pieces of intestine were sandwiched between a glass slide and a 1 inch styrofoam layer. The laser welds had roughly the same welding area as the water bath welds (5×5 mm). The styrofoam layer helped keep the tissues stationary while under pressure. The sample was placed on a small digital scale, and the laser condenser placed on top. A pressure of 2 kg was applied by hand, and monitored with the scale. The yield strength was measured for samples irradiated by 5–30 laser pulses.

4. RESULTS

The contraction of intestine below 80°C was somewhat erratic and slow so only contraction data from 80–90°C was used in the analysis. Linear regression of the rates of contraction for seven intestine samples gave the following parameters for the entropy and enthalpy of reaction

$$\Delta S = 62.94 \pm 1 \text{ cal/mole°C}$$

and

$$\Delta H = 44.35 \pm 10 \text{ kcal/mole}$$

The enthalpy and entropy of thermal contraction of intestine are pretty close to the values of $\Delta S = 66.3$ cal/mole°C and $\Delta H = 44.6$ kcal/mole obtained for dog prostate.[8]

The yield strengths for water bath welds made at temperatures from 60–80°C for 7 minutes are shown in Figure 3. No welds was achieved at 55°C. The weld strength increased with temperature.

Almost all the strongest welds occurred at 42 mJ/mm^2 on samples stained with an ICG concentration of 1.6 mM, and more than 10 pulses. In these cases, parts of the stained layer remained fused to the unstained layer after the weld was pulled apart. Rarely was any bleaching of the stained layer noted for these strong welds. Weld strengths tended to increase with number of laser pulses.

Finally, the weld strength is plotted as a function of the calculated fraction of altered molecules for both the water bath and laser welds in figure 5.

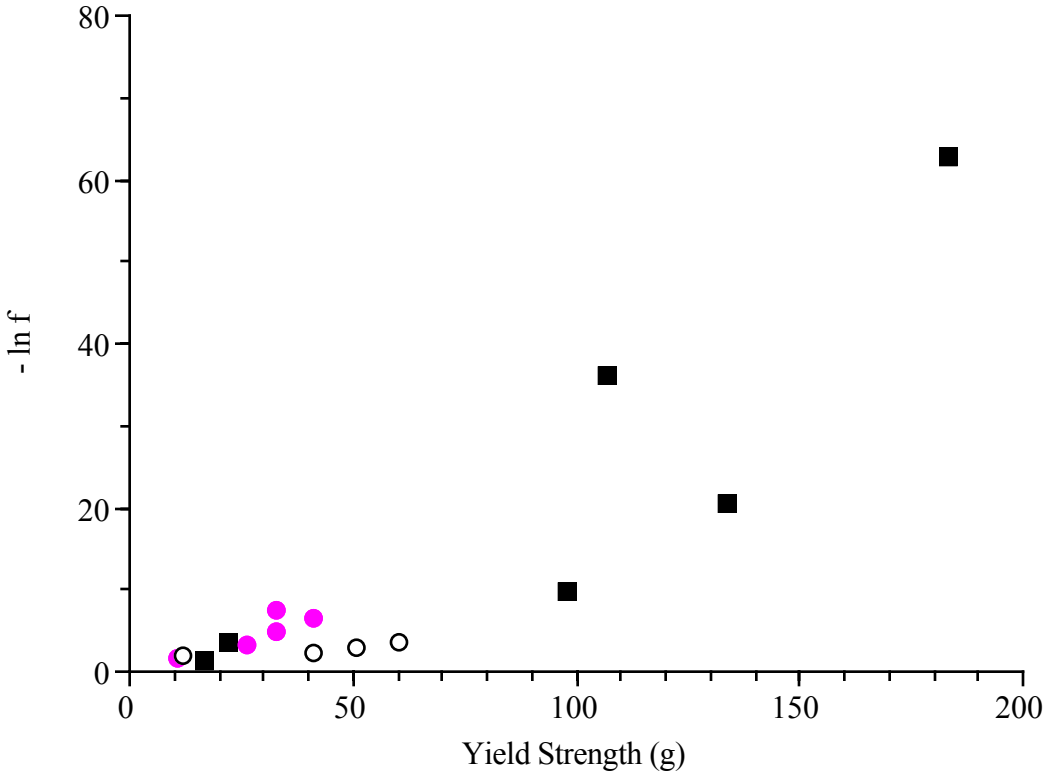

Figure 5. Correlation between the yield strength for water bath welds (solid squares) and laser welds (circles). The open circles are laser irradiances of 42 mJ/mm^2 and the solid circles are 70 mJ/mm^2.

5. DISCUSSION

Waterbath and laser welding are two different ways to obtain a bond between two tissue surfaces. However, is the actual mechanism for waterbath welding the same as the mechanism for laser welding? Past studies link collagen to the welding process,[9,10] where individual fibers unwind at temperatures above denaturation, and rebind with collagen fibers from the apposed tissue surface.[11] If this is the only source of a welding bond, then the huge discrepancy in welding times between waterbath (5–15 minutes) and laser (5–15 seconds) is somewhat of a mystery. Laser welding quickly heats an extremely confined area of the stained layer, whereas the waterbath slowly heats the entire tissue.

The first-order rate process model gives surprisingly good agreement between the predicted fraction of unaltered molecules and the weld strength. Thermal contraction of intestine occurs within the first ten seconds of immersion in a 80–90°C water bath. This contraction was used to determine the rate process parameters. The water bath welds took 420 s and had no free parameters in the calculation of the fraction of unaltered molecules. The 5 ms laser welds required a simple thermal model that used conservation of energy as its primary constraint. However, once the model was chosen, the calculation of the number of unaltered molecules was direct.

Figure 5 summarizes thermal processes that encompass more than five order of magnitude of time. While not conclusive, it certainly suggests that welding is primarily a thermal process and that it maybe characterized by first-order kinetics.

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