ELASTIC MOLECULAR MACHINES AND A NEW MOTIVE FORCE IN PROTEIN MECHANISMS

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Abstract:

It is demonstrated that the polypentapeptide, (Val\textsuperscript{1}-Pro\textsuperscript{2}-Gly\textsuperscript{3}-Val\textsuperscript{4}-Gly\textsuperscript{5})\textsuperscript{n} when \(\gamma\)-irradiation cross-linked, can perform work on raising the temperature from 20° to 40°C. This is due to an inverse temperature transition leading to a regular helical structure called a dynamic \(\beta\)-spiral which exhibits entropic elastomeric force. Processes which alter the hydrophobicity of a peptide segment can shift the temperature of an inverse temperature transition. When the hydrophobicity is changed reversibly as is possible with 20% Glu\textsuperscript{4}-polypentapeptide, the temperature for the onset of the inverse temperature transition can be reversibly shifted from being initiated at 37°C at pH 2 (COOH) to being initiated at 50°C at pH 7 (COO\textsuperscript{−}). Presumably therefore once a synthetic elastomeric matrix is formed from 20% Glu\textsuperscript{4}-polypentapeptide, it should be possible at 50°C to turn "on" elastomeric force by changing the pH from 7 to 2 and to turn "off" elastomeric force by returning the pH to 7. This is called mechanochemical coupling of the first kind, and, in addition to ionization and deionization, it should be possible similarly to turn off and on elastomeric force by phosphorylation and dephosphorylation, respectively.

When the elastomeric state is arrived at by means of a regular transition from a more ordered state (e.g., \(\alpha\)-helix) to a less ordered state (e.g., a \(\beta\)spiral) on raising the temperature and a chemical process can change the temperature of the transition, this is referred to as mechanochemical coupling of the second kind. Mechanochemical coupling on going from an ordered state to a disordered state has often been considered. The work on the polypentapeptide brings consideration of an inverse temperature transition for the first kind and of a less-ordered but non-random state for mechanochemical coupling of the second kind. It is proposed that these new considerations are relevant to mechanisms for the turning on and off of elastic forces in protein mechanisms as varied as those of enzymes and muscle contraction.
I. The Polypentapeptide of Elastin as an Elastic Molecular Machine

By definition a machine is a device for doing work and work is performed when a force acts against resistance to produce motion in a body. Consider as a specific example a weight suspended from the synthetic elastomeric polypentapeptide band at 20°C in water (see Figure 1A). The band is formed on γ-irradiation of (Val-Pro-Gly-Val'-Gly)n where n is greater than 100, and the composition is approximately 40% peptide, 60% water by weight (1,2). On raising the temperature to 40°C, the weight (300 grams/cm² elastomer cross-section) is raised against gravity as the synthetic elastomeric band shortens to 70% of its 20°C length (3). For a band 10 cm long, the weight would be raised 3 cm against the pull of gravity. The same qualitative result is obtained with the entropic elastomer, latex rubber, but for this classical rubber the length change is much less only about 5% instead of 30% (3). Both elastomers are molecular machines but the polypentapeptide elastomer is a more effective machine for moving an object when changing the temperature from 20° to 40°C. What occurs as the result of this temperature change in the polypentapeptide is an enhanced effect due to an inverse temperature transition wherein the polypentapeptide wraps up into a helical structure, i.e. a β-spiral, on raising the temperature from 20° to 40°C (4). The helical structure is the result of optimizing intramolecular hydrophobic interactions. The heat absorbed during this inverse temperature transition occurring between 20° to 40°C, is approximately 1 cal/gram of the polypentapeptide in water. The class of β-spirals to which the elastomeric polypentapeptide belongs is shown in Figure 2 (5-8) and the length change under zero load is from 100% to 40% on going from 20° to 40°C (see Figure 1B). At fixed length, development of elastomeric force (f) correlates with structure development (4) and as shown in Figure 3, the structure so formed exhibits entropic elastomeric force (9). As will be further discussed below, the polypentapeptide forms an entropic anisotropic elastomer.
II. Entropic Elastomeric Force Resulting From an Inverse Temperature Transition

Previously entropic elastomeric force has been taken to require that the polymeric system be a network of random chains in adherence to the classical theory of rubber elasticity (10). When elastin fibers were shown to give a result like that in Figure 3 for the polypentapeptide of elastin in the temperature range above 40°C, the conclusion was "A network of random chains within elastin fibers, like that in a typical rubber, is clearly indicated" (11). In a typical rubber, the decrease in entropy on deformation is taken to be due to the displacement from a random distribution of end-to-end chain lengths (12,13). But a random distribution of end-to-end chain lengths is not the product of an inverse temperature transition. An inverse temperature transition involves an increase in polymer order on increasing the temperature. For the polypentapeptide of elastin, it is demonstrated in Figure 3 that entropic elastomeric force occurs above 40°C on completion of the inverse temperature transition, that is, once the increase in order has occurred. This is because the elastomeric force, \( f_e \), is the sum of two components: \( f_e \), an internal energy component and \( f_s \), the entropic component. When \( \ln[\text{elastomeric force}/T(\text{OK})] \) is plotted versus temperature, a zero slope is taken to mean that \( f_e/f = 0 \), that is, the elastomer exhibits dominantly entropic elastomeric force (14). As shown in Figure 3 (solid curve), the cross-linked polypentapeptide exhibits a dominantly entropic elastomeric force above 40°C (15,16).

Numerous physical characterizations of the polypentapeptide of elastin in water have shown that on raising the temperature from 20° to 40°C, there is an increase in molecular order. Those physical characterizations include: i. light and electron microscopy demonstrating on increasing the temperature a
self-assembly into fibers, comprised of parallel aligned fibrils which in turn are comprised of parallel aligned filaments (7,17,18); ii. light scattering following the aggregation with increase in temperature (2); iii. circular dichroism showing an increase in intramolecular order with occurrence of regularly recurring β-turns (19); iv. the nuclear Overhauser effect demonstrating the intramolecular hydrophobic interactions attending the inverse temperature transition (20); v. composition studies showing the phase transition to a unique composition of polypentapeptide plus water (2); vi. nuclear magnetic resonance relaxation studies showing a decrease in backbone mobility on raising the temperature through the inverse temperature transition (21,22); vii. dielectric relaxation studies showing the development of an intense, low frequency, high amplitude, localized, Debye-type relaxation on raising the temperature through the inverse temperature transition (23,24); viii. and the above noted temperature dependence of elastomer length (3). Having demonstrated an increase in order on arriving at 40°C, thermal denaturation can be demonstrated on raising the temperature above 60°C. This has been demonstrated reversibly by composition studies where a transition with expulsion of water occurs on raising the temperature from 60°C to 80°C (2) and by circular dichroism showing the decrease in intramolecular order on standing at 80°C (2); and thermal denaturation has been demonstrated directly in the loss of elastomeric force and elastic modulus on heating at 80°C (25). These are not the properties of random chain networks. Accordingly a new understanding is required for the decrease in entropy on deformation and it is one of a damping of internal chain dynamics on deformation called the librational entropy mechanism of elasticity (9,26,27). A new understanding of entropic elastomeric force has emerged from which interesting new possibilities arise.
III. Effect of Changing Hydrophobicity of Polypeptide Elastomers

The fact that the elastomeric force development occurs with shortening by means of an inverse temperature transition (3,4) gives interesting new potential to the polypentapeptide and like elastomers as molecular machines. It has been shown (28,29) that changing the hydrophobicity of the repeating unit in the elastomeric polypeptide changes the temperature range of the inverse temperature transition which gives rise to regular structure; that changing the hydrophobicity changes the temperature range over which elastomeric force develops, and that changing the hydrophobicity changes the range over which the elastomer shortens. For example, increasing the hydrophobicity of the polypentapeptide (VPGVG)$_n$ as in the Ile$^1$-polypentapeptide, (IPGVG)$_n$, analog (28) lowers the temperature range over which the transition occurs by some 20°C from a midpoint of near 30°C for (VPGVG)$_n$ to near 10°C for (IPGVG)$_n$. Furthermore when the hydrophobicity is decreased as when the Val$^4$ residue is removed as in the polytetrapeptide (VPGG)$_n$, the product is an elastomer but the development of elastomeric force is now shifted to 50°C (29). Thus by changing the hydrophobicity, the midpoint temperature of the inverse temperature transition for the development of elastomeric force has been shifted over the temperature range from 10°C to 50°C. Increase the hydrophobicity and the inverse temperature transition occurs at a lower temperature; decrease the hydrophobicity and the inverse temperature transition occurs at a higher temperature. Even the magnitudes of the shifts are calculable from the change in hydrophobicity (29,30,31).

When temperature is limited as a variable, therefore, as for example in the case of living organisms, varying the hydrophobicity would be a useful way to perform work. Decreasing hydrophobicity which, of course, is equivalent to increasing hydrophilicity can be achieved by hydroxylation. Accor-
dingly, it has been shown, by chemically introducing hydroxyproline in place of proline and by direct hydroxylation of \((VPGVG)_n\) using the enzyme prolyl hydroxylase, that the temperature range of the inverse temperature transition can be raised in proportion to the amount of replacement or conversion of proline to hydroxyproline (32). When the ratio of \((Val-Pro-Gly-Val-Gly)\) to \((Val-Hyp-Gly-Val-Gly)\) was 9:1 in the polymerizing mixture, the resulting polymer exhibited a transition midpoint that was shifted 7°C to higher temperature; for \((Val-Hyp-Gly-Val-Gly)_n\) itself the transition midpoint was above 65°C (32). What would be of particular interest would be to shift reversibly the temperature of the inverse temperature transition and thereby to turn "on" and "off" the elastomeric force. One means would be protonation or deprotonation of a functional side chain; another might be enzymatic reactions wherein there is an interconversion between charged and uncharged states of a side chain; and yet another could be the phosphorylation and dephosphorylation, for example, of a serine or threonine side chain. The use of pH is briefly considered below.

IV. Reversibly Changing Hydrophobicity of the Polypentapeptide as a Means of Turning Elastomeric Force "On" and "Off"

As shown in Figure 4, the inverse temperature transition can be followed by means of the temperature profiles for aggregation for the polypentapeptide and its 20% Glu⁴ analog. Changing one in five Val⁴ residues to a Glu⁴ residue, when the pH is 2 where the side chain is the carboxyl, changes the onset of the inverse temperature transition from 25°C to 37°C. On ionization of the side chain to form the carboxylate anion at pH 6, the onset of the inverse temperature shifts further to 49°C. Once the 20% Glu⁴-polypentapeptide is cross-linked to form the elastomeric matrix, it is expected that the elastomer can most effectively at 50°C be turned "on" at pH 2 and "off" by
changing the pH to 7. This would be a chemomechanical transducer. If 50°C were not the desired temperature, for example, if lower temperature were desired, then more hydrophobic residues could be used place of Val¹ and Val⁴. Starting with Ile¹-polypentapeptide which has a transition midpoint of about 10°C (28), inclusion of a more polar residue, such as Glu, Asp, His, Lys, or Tyr for example in every third pentamer at position four would raise the temperature of the transition toward 30°C for the non-ionized state. The appropriate mix of Ile¹ and Val¹ and of Val⁴ and the more polar side chain at position four would allow the midpoint of the transition to be selected over a temperature of 10°C to above 30°C. On ionization the transition would shift to a higher temperature yet. Suppose that the non-ionized analog exhibited a transition midpoint near 30°C and that the β-spiral structure were formed and the development of elastomeric force were essentially complete by 37°C, as in the solid curve of Figure 3, then on ionization (e.g., on raising the pH above the pK of the ionizable function) the transition midpoint would shift to a higher temperature; the structure would unwind and the elastomeric force would be turned off as in the dashed curve of Figure 3. Lowering the pH to below the pK would cause the elastomeric force to turn back on. A change in the activity of the hydrogen ion becomes the switch. A number of other switches could be devised.

V. Mechanochemical Coupling

Previously, developments of elastomeric force with increase in temperature have been conformed to considerations of the classical theory of rubber elasticity with consideration of an order to disorder transition. In one proposed mechanism for the power stroke of muscle contraction in the S-2 fragment of myosin, an α-helix to random coil transition provides an interesting possibility to consider (33,34). The polypentapeptide data, in which the
elastomeric state is a non-random \( \alpha \)-spiral structure, indicate that random coil is not a necessary consideration and even suggests that it could be incorrect since the elastic modulus on thermal randomization of the polypentapeptide of elastin and of elastin itself becomes so low as to be of little relevance to the elastic forces of muscle contraction (16,25). Accordingly analysis in terms of an \( \alpha \)-helix to spiral transition seems warranted. Thus the situation could be one as shown in Figure 5 in which an \( \alpha \)-helix with 1.5A/residue converts to a spiral with about half the translation per residue, e.g., 0.7A/residue as in the \( \beta \)-spiral of Figure 2. This would be consistent with the pitch estimated for the \( \beta \)-spirals of the polypentapeptide with about 15 residues/turn of spiral (8), of the polytetrapeptide with about 16 residues/turn (35), of the polyhexapeptide with about 12 residues/turn (36) and of the polynonapeptide with about 18 residues per turn (Chang, Trapane and Urry, in preparation). With heptamer repeats in myosin grouped as 28mers (37) some fourteen residues per turn would be reasonable for a spiral structure. Whatever the details of the situation, one looks for a chemical process to shift the temperature of the transition such that at a given temperature the elastic contraction could occur as the result of a chemical process.

There have now been discussed two kinds of mechanochemical coupling. Mechanochemical coupling of the first kind in which an inverse temperature transition from a higher to a lower entropy structure is the transition for the development of elastomeric force, and mechanochemical coupling of the second kind which utilizes a standard transition from a lower entropy state to a higher entropy state. The structural transitions for these two kinds of coupling are shown schematically in Figure 6. A key element of these considerations is that there exist structures intermediate in entropy between the \( \alpha \)-helix, \( \beta \)-sheet and collagen triple stranded (ordered and relatively rigid)
structures on the one hand the random chain networks or random coil structures on the other hand. That such regular structures of intermediate entropy exist has been shown with the sequential elastomeric polypeptides of elastin as well as in the series of helical structures that can exist for the polydipeptide gramicidin A (9).

VI. Entropic Motive Force in Protein Mechanisms

Having demonstrated entropic elastomeric force to be due to internal chain dynamics in non-random polypeptide systems, it seems appropriate to note situations in which protein elastic processes may be viewed in terms of this new perspective. Several examples will be briefly noted below.

Elastin: The most striking primary structural feature of porcine and bovine elastin is the polypentapeptide considered above. It is not surprising therefore that similar physical characterizations of elastin have shown it to be an entropic elastomer which forms its elastic structure by means of an inverse temperature transition (15,16,38). Accordingly it is expected that increased hydrophilicity such as prolyl hydroxylation would raise the temperature of the inverse temperature transition and limit fiber formation. This has been observed in cell culture (39) and has been proposed to be the reason for the near absence of elastic fibers in the scar tissue of wound repair (40). Of further medical significance is that by the foregoing reasoning, any oxidative process should shift the inverse temperature transition, that gave rise to elastin fibers, to higher temperature and cause an unwinding of the spiral structures in elastin. A loss of elastic recoil and elongation has been looked for and observed using a superoxide generating system with bovine ligamentum nuchae elastin (38). Elastin fiber oxidation has been proposed in the initiation of pulmonary emphysema (38) which is characterized by disrupted elastic fibers and loss of elastic recoil of the
lung (41). Oxidative loss of elastic recoil can also be considered in the sagging and wrinkling of skin with age.

**Titin (the elastic [third] filament of muscle):** The elastic and third most prevalent filament in muscle is a megadalton protein called connectin or titin (42-44). In the sarcomere a single titin polypeptide chain is thought to extend from the Z line to the M-line (Wang, private communication), a length of 1.2 \( \mu \text{m} \) with a width of 4 to 5 nm (45). This filament is thought to be largely responsible for the resting tension of muscle and for the passive tension when the thick and thin filaments are pulled beyond overlap (42,45). It would not be an easy task to force this highly anisotropic protein to conform to the isotropic network of random chains required in the classical theory of rubber elasticity. As it has been shown to exhibit an entropic elastomeric force (44), displacement from a random distribution of end-to-end chain lengths seems an unlikely description. It is expected instead that changes in internal chain dynamics would be the source of elastomeric force.

**Entropic Elastomeric Force in Enzyme Catalysis:** In globular proteins that catalyze chemical reactions, it is difficult to utilize the random chain network perspective of elastomeric force. With internal chain dynamics as a source of entropic elastomeric force, however, a single short peptide segment can exert an entropic elastomeric force and what better way to induce strain in a scissile bond (46-48) to achieve a reaction with a low internal energy of activation. If during substrate binding the induced fit process (49) resulted in a small chain extension of a polypeptide segment contiguous with a critical electrostatic interaction of the catalytic mechanism (50), then that segment could exert a strain in the scissile bond increasing the probability of achieving the transition state complex (39).
Modulation of Channel Activity: In an analysis of the open-closed equilibrium of the sodium channel, Rubinson (51) provides an argument for a rubber-like (entropic) elastic peptide segment undergoing deformation due to structural coupling to the transmembrane potential to provide the on-off mechanism. Also cyclic AMP dependent kinase and protein kinase C are thought to modulate channel function by changing the state of phosphorylation of the channel (52). In terms of mechanochemical coupling of the first kind, increasing the hydrophobicity of an elastic polypeptide chain segment jutting into the aqueous cytoplasmic side of the membrane could increase the temperature of the inverse temperature transition giving rise to the elastic structure and could cause a relaxation of the elastic structure and/or a relaxation of the elastic force constraining additional structural features. In terms of mechanochemical coupling of the second kind, phosphorylation could shift the temperature for the transition from a lower entropy to a higher entropy elastic structure; for example, it could induce an α-helix → elastic spiral structure interconversion. Similarly phosphorylation/dephosphorylation could be used to alter the functional state of globular enzymes and of fibrillar proteins in muscle contraction (53) and cell motility (54-57).

VII. Summarizing Comments

The general implications of the foregoing considerations are several:

i. Elastic processes in polypeptides and proteins need not be described in terms of networks of random chains or random coil structure; indeed it may be incorrect to do so.

ii. Entropic elastomeric force can be exhibited by a short anisotropic peptide segment due to internal chain dynamics (the librational entropy mechanism of elasticity). Random chain networks are not required.

iii. Whether in a short peptide segment of a globular protein or in
a fibrillar protein, it is expected that elastomeric force can be turned "on" and "off" by reversibly changing the hydrophobicity of the polypeptide. A most obvious means of doing so would be phosphorylation and dephosphorylation. And iv. It should be possible to design a wide range of polypeptide elastomeric biomaterials that could function in thermomechanical, chemomechanical and electromechanical transduction.

ACKNOWLEDGEMENT

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References:


6. G. J. Thomas, Jr., Betty Prescott and D. W. Urry, "Raman Amide Bands of Type-II β-turns in Cyclo-(VPGVG)₃ and Poly(VPGVG), and Implications for Protein Secondary Structure Analysis," Biopolymers (in press).


Figure Legends:

Figure 1: The polypentapeptide of elastin as an elastic molecular machine. High molecular weight (Val-Pro-Gly-Val-Gly)_n with n greater than 100 is γ-irradiation cross-linked when in a viscoelastic state of 40% peptide, 60% water by weight to form an insoluble band of material.

A. A weight of 300 gms/cm² of band cross-sectional area measured at 40°C is applied. At 20°C in water, the length is taken as 100%. On raising the temperature to 40°C, the band shortens to 70% lifting the weight. The work performed is mgh. B. A band of cross-linked polypentapeptide is depicted at 20°C in water in the absence of any load. On raising the temperature to 40°C, the sample contracts to approximately 40% of its original length. The heat absorbed during this inverse temperature transition is approximately 1 cal/gm polypentapeptide. This shortening of the sample is due to the winding up of the polypentapeptide chain into a helical structure, termed a β-spiral, as shown in Figure 2.

Figure 2: Molecular conformation of the 40°C state of the polypentapeptide of elastin in water.

A. The β-turn perspective of the pentamer, showing the Val¹ C-O --- HN Val⁴ ten atom hydrogen bonded ring with Pro²-Gly³ at the corners. Adapted with permission from reference 5. Raman studies indicate that the β-turn is present before and after the transition observed in Figure 1B on going from 20° to 40°C (6). B. On raising the temperature, the largely extended series of β-turns wrap up into a helix in which the
\(\beta\)-turns function as spacers between turns of the helix as shown in C. The helix with \(\beta\)-turns spacers is called a \(\beta\)-spiral and it is the wrapping up into a \(\beta\)-spiral that is responsible for the dramatic contraction of size seen in Figure 1B. The length change for the depicted \(\beta\)-spiral to become an extended series of \(\beta\)-turns is close to a factor of 3; interestingly, a not unreasonable factor of 2.5 is observed (see Figure 1B). (B., C. and D. reproduced with permission from reference 7.) D. and E. are stereo pair perspectives of the detailed \(\beta\)-spiral seen in axis view (D) and side view (E). The interturn contacts are hydrophobic and result from the optimization of intramolecular hydrophobic contacts developed during the inverse temperature transition. Between the \(\beta\)-turns are suspended segments running from the Val\(^4\) \(\alpha\)-carbon to the Val\(^1\) \(\alpha\)-carbon in which the peptide moieties can undergo large amplitude, low frequency librational motions. On stretching these librational motions become damped which is a decrease in entropy that provides the resistance to and the restoring force from deformation. This is called the librational entropy mechanism of elasticity (7). E. is reproduced with permission from reference 8.

**Figure 3:** Thermoelectricity data on the \(\gamma\)-irradiation cross-linked polypentapeptide of elastin (solid curve). The observation that the slope of the \(\ln[(f/T^0K)]\) versus temperature curve at fixed extension is near zero above 40°C is the basis for arguing that the elastomeric force is dominantly entropic. The data (9) is
used in the present context to demonstrate the effect of decreasing the hydrophobicity, i.e., increasing the hydrophilicity, as for example by ionization of a residue within the polypentapeptide, such as an occasional glutamic acid residue or by a phosphorylation of a serine or threonine residue. The effect of making this polymer more polar would be to raise the temperature midpoint of the inverse temperature transition that is responsible for the observed development of elastomeric force. The expected result is the dashed curve. The perspective is, therefore, that the elastomeric force is turned on at 37°C when the polypeptide is neutral and is turned off when the polypeptide is more polar or charged.

Figure 4: Temperature profiles of aggregation showing the temperature dependence of the intermolecular aspect of the inverse temperature transition. This also coincides with the intramolecular component of the inverse temperature transition. Curve a: the polypentapeptide of elastin; curve b: 20% Glu⁴-polypentapeptide at pH 2 where the polar side chain is the COOH moiety; and curve c: 20% Glu⁴-polypentapeptide where the side chain is ionized (COO⁻) at pH 6. The solid curve in Figure 3 showing the development of force with temperature corresponds to curve a. On the basis of this, it is expected that the 20% Glu⁴-polypentapeptide cross-linked matrix would develop elastomeric force with a midpoint temperature near 40°C when at pH 2 and that force development would shift to a midpoint temperature of near 55°C when at pH 7. Therefore at 50°C, changing the pH from 2 to 7 should turn off elastomeric force and the reverse should turn on elastomeric force.
Figure 5: Proposed α-helix to spiral structural transition for the turning on of elastomeric force with the result of lifting a weight. The α-helix is shown with a graded instability such that the lower end would first convert to spiral on raising the temperature as in B and then as the temperature increased further, the conversion would continue on up the chain as shown in C. The graded instability with respect to temperature would facilitate reversibility in a condensed matrix.

Figure 6: Structural Transitions for Mechanochemical Coupling

A. Type 1. The structural transition is from a higher entropy to a lower entropy state with increase in temperature, that is, it is an inverse temperature transition. The example involves a largely extended high entropy series of β-turns that wrap up to form an elastic β-spiral. A β-spiral is defined as a helical arrangement of β-turns. The result of the inverse temperature transition is the optimization of intramolecular, interturn hydrophobic interactions. Increasing hydrophobicity lowers the temperature of the transition and decreasing hydrophobicity increases the temperature of the transition. The development of elastomeric force at fixed extension occurs as the result of the inverse temperature transition and therefore by this analysis, elastomeric force can be turned on and off by varying the temperature of the transition, that is, by reversibly changing the hydrophobicity of the polypeptide. At a fixed temperature, increase the polarity of the polymer, for example by ionization of a side chain; the result is that the temperature for the transition is raised above the fixed
temperature and elastomeric force is turned off. Deionization would lower the temperature of the transition to below the fixed temperature and would turn elastomeric force back on. Enzymatic phosphorylation and dephosphorylation at constant temperature and constant pH would be another means of reversibly shifting the temperature of the transition by reversibly changing the hydrophobicity of the polypeptide.

B. Type 2. The structural transition is from a lower entropy state to a higher entropy state with increase in temperature, that is, this is a standard transition. The example is the conversion of an α-helix to an elastic spiral wherein changes in internal chain dynamics give rise to an entropic elastomeric force. The relaxed state of the spiral has a lower axis translation per residue (0.5Å/residue) than the α-helix (1.5Å/residue) such that the structural conversion results in a contraction. Any chemical process which shifted the temperature of the transition by changing the relative free energies of the structure could turn on or off the elastomeric force of the spiral structure. Possible chemical processes would be changes in pH, changes in calcium ion concentration or phosphorylation/dephosphorylation. This mechanism, Type 2, has been generally considered to be mechanochemical coupling. The element introduced by the work on polypeptide elastomeric biomaterials is the consideration of a spiral structure instead of a random coil.
A. with load

20°C

40°C

B. without load

20°C

40°C

100%

70%

100%

40%

FIGURE 1
FIGURE 2

A) β-turn perspective

B) β-spiral of the polypentapeptide of elastin

C) schematic representations

D) axis view

E) side view

F) twisted filament (super coiled) representations

G)
FIGURE 3

ln (f/T(e^x))

Temperature, °C

-3
-4
-5
-6

non-ionized (less polar)
ionized (more polar)

FIGURE 3
% Normalized Turbidity, 300 nm

Temperature, °C

FIGURE 4

a. polypentapeptide
b. 20% Glu<sup>4</sup> -polypentapeptide (COOH)
c. 20% Glu<sup>4</sup> -polypentapeptide (COO<sup>-</sup>)
Structural Transitions for Mechanochemical Coupling

A. Type 1

- largely extended
- series of $\beta$-turns

$\beta$-spiral
(helical arrangement of $\beta$-turns)

B. Type 2

Chemical process

$\alpha$-helix

Spiral

FIGURE 6
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