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# FATIGUE QUALITY OF MAMMALIAN TENDONS

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## Summary

**When excised tendons are subjected to a prolonged load, whether constant or oscillatory, fatigue damage accumulates, leading eventually to rupture. 'Fatigue quality', assessed by the time-to-rupture under a given stress, was found to vary hugely among the tendons of a wallaby hind limb. This material property correlates with the varied stresses to which tendons from different anatomical sites are exposed in life. The correlation was demonstrated by subjecting each excised tendon to a load equal to the maximum isometric force that its muscle could have developed. The time-to-rupture was then approximately the same for each tendon, on average 4.2 h. A model is introduced in which damage is proposed as the trigger for adaptation of fatigue quality. The model aims, in particular, to explain why low-stressed tendons are not made of a 'better' material, although this clearly exists since it is used in high-stressed tendons. The principle of design to a minimum quality is viable in biology because of the availability of self-repair to balance routine damage. Clinical symptoms, to be included under the general heading of 'overuse injuries', will only arise when this balance fails.**

Key words: wallaby, tendon, creep, fatigue damage, stress-in-life, time-to-rupture, fatigue quality, Young's modulus, repair, biological design, *Macropus rufogrisea*.

## Introduction

All tendons transfer force between muscles and bones. However, the peak stress to which the tendon is thereby subjected varies according to its anatomical site and the species (Ker et al., 1988; Pollock and Shadwick, 1994b). To describe this quantitative functional characteristic, we define 'stress-in-life' as the stress in a tendon when its muscle is exerting maximum isometric stress. Among adult mammalian limb tendons, the range of stress-in-life is from approximately 10 MPa to at least 70 MPa, with the most common stress being approximately 13 MPa. The relatively few tendons with high values of stress-in-life include those, such as the human Achilles tendon (67 MPa), which act as springs to save energy during locomotion (Ker et al., 1988). Pollock and Shadwick (1994b) examined the hind limb tendons of a wider range of species than was used by Ker et al. (1988). In addition to variations according to the type of tendon (plantaris, deep digital flexor, gastrocnemius, common digital extensor), they showed that stress-in-life tends to increase with the mass of the animal (0.04–545 kg). The common digital extensor is the least stressed of these tendons. In the largest mammals, its stress-in-life is only approximately one-seventh of that of the most highly stressed tendon, which is the plantaris. At the opposite end of the size range, the factor is approximately one-quarter, with the most stressed tendon of small mammals being the gastrocnemius.

It seems possible, perhaps probable, that the material of tendons may differ to mirror these quantitative functional variations. However, such differences are not immediately obvious. Pollock and Shadwick (1994a) measured Young's modulus, $E$, and percentage hysteresis loss, $H$, for tendons from 18 species of mammal (mass 0.5–545 kg). (Here we are using the term 'Young's modulus' as an abbreviation for 'tangent modulus in the linear region of the stress–strain curve'.) Individual tendons differ substantially, with $E$ ranging from approximately 0.9 to 1.8 GPa and $H$ from 3 to 20 %. However, for both $E$ and $H$, the mean values do not differ significantly according to the type of tendon or the mass of the animal. The situation regarding strength is less clear. The data for ultimate tensile stress (UTS) in a ramp test to rupture reviewed by Elliott (1965) are mostly in the range 50–100 MPa. However, Elliott is careful to point out that clamping problems with tendon are such that *in vitro* measurements are (almost) inevitably underestimates. The data of Elliott (1965) and more recent data (Table 1), taken at face value, do not support the proposition that UTS varies with the anatomical site of the tendon or the size of the mammal in a similar way to stress-in-life. If anything, the opposite seems to apply: Achilles and calcaneal tendons (high stress-in-life) appear unusually weak, and the wallaby tail tendon (low stress-in-life) is strong.

However, as with many other materials, excised tendons rupture after prolonged application of tensile stresses far below their UTS (Wang and Ker, 1995; Wang et al., 1995;

Table 1. *Some values for the ultimate tensile stress of tendons published since Elliott (1965)*

| Reference | Mammal | Tendon | Ultimate tensile stress (MPa) |
|---|---|---|---|
| Benedict et al. (1968) | Human | Toe extensor | 92 |
| | | Toe flexors | 75 |
| Blanton and Biggs (1970) | Human | Toe extensors | 26 |
| | | Toe flexors | 31 |
| | | Other lower limb tendons | 20 |
| Yamada (1970) | Human | Achilles | 55 |
| | | Big toe and thumb flexors and extensors | 61–66 |
| | Various other mammals | Calcaneal | 35–82 |
| | | Flexor digitorum profundus | 41–57 |
| H. G. Vogel (1978) | Rat | Tail tendon | 96 |
| Butler et al. (1984) | Human | Gracilis | 112 |
| | | Semitendinosus | 89 |
| | | Patellar | 58 |
| Riemersma and Schamhardt (1985) | Horse | Hind deep toe flexor | 60 |
| | | Hind superficial toe flexor | 60 |
| Bennett et al. (1986) | Wallaby | Tail tendon | 107 |
| | Dolphin | Fluke tendon | 95 |
| | Sheep | Various | 90 |
| Shadwick (1990) | Pig | Toe extensors | 40–50 |
| | | Toe flexors | 80-90 |
| Wang and Ker (1995) | Wallaby | Tail | 144 |
| Thermann et al. (1995) | Human | Achilles | 41 |
| Schechtman and Bader (1997) | Human | Extensor digitorum longus | 100 |

As explained in the text, these values should be considered as minimum limits. The extent to which each is an underestimate will vary with the experimental technique and the characteristics of the tendon.

Schechtman and Bader, 1997; Ker and Zioupos, 1997). Prior to rupture, the damaged state of the tendon is indicated by loss of stiffness and of strength (Wang and Ker, 1995). How does this property correlate with stress-in-life? The spur for the present investigation was a calculation by Wang et al. (1995) based on their observations with wallaby tail tendons. They suggested that the human Achilles tendon would fail after only 1 h of running if it were made of the same material as the wallaby tail tendon. Our hypothesis to avoid this obviously incorrect 'prediction' is that the material from which the more highly stressed tendons are made is of higher quality.

To compare the time-dependent rupture properties of tendons, the tensile load may conveniently be either oscillatory, at a stated frequency, or constant. Both these regimes have the same qualitative consequences: (i) the mean length progressively increases (creep) and (ii) the material deteriorates (fatigue), leading ultimately to rupture. We chose to use constant loads. Oscillations introduce extra damage at a given average stress, so our tests give maximum values for time-to-rupture. (The appropriate averaging procedure is discussed in the Appendix to Wang et al., 1995.) Of course, we recognise that loads during life are not constant, but nor are they at any other fixed frequency. Wang and Ker (1995) used the term 'creep test' for a test at constant load. Here, we prefer the alternative 'static fatigue test' as being more appropriate when the emphasis is on damage. Creep curves are sometimes divided into three regions (see, for example, Teoh and Cherry, 1984). We are here concerned with 'tertiary' creep, whose characteristic is accelerating strain ending in rupture. For tendon, tertiary creep dominates the majority of the time-to-rupture (Wang and Ker, 1995).

For a flexible material, such as tendon, which cannot sustain a compressive longitudinal load, the mean value of any cyclic load is necessarily a positive tension. It is therefore impossible to study cyclic fatigue without involving a component of static fatigue. In contrast, static fatigue can be studied in the absence of cyclic fatigue. In this sense, static fatigue is the more fundamental phenomenon.

## Materials and methods

### *Wallabies*

Wallabies provide a suitable variety of tendons. To investigate time-to-rupture over a range of stresses, we needed large numbers of tendons with a similar stress-in-life. These came from the tail. To investigate variations with stress-in-life, we compared tendons from different leg muscles. (Fig. 1 in the Results section shows the range of stress-in-life available.)

Bennett's wallabies (*Macropus rufogrisea*) were obtained from Whipsnade Wild Animal Park, where they have free range over an area of 243 hectares. Carcases were stored at a temperature of −20 °C. The usual cause of death was necrobacillosis (Bourne, 1997). A few specimens had died following accidents and gave results similar to those from the other wallabies. The wallabies used for the key experiment (Fig. 5) were: A, female, mass 14.2 kg, age 2.5 years (accident); B, male, 17.2 kg, 4.0 years; C, female, 9.6 kg, 3.1 years.

### *Assessment of stress-in-life*

Values of stress-in-life were assessed from measurements, made during dissection, of the cross-sectional areas of the muscles and the tendons. The major assumption is that the muscles can all develop a similar maximum isometric stress: we use 0.3 MPa as representative of this stress (Wells, 1965). Maximum isometric stress can be exceeded if the muscle is stretched while it is active, but there are indications that this

does not apply during locomotion. The fascicles of the toe flexor and ankle extensor muscles are nearly isometric during the stance phase in running turkeys (*Meleagris gallopavo*) (Roberts et al., 1997) and hopping wallabies (*Macropus eugenii*) (Biewener et al., 1998). In any case, adjustment to higher stresses would leave the main conclusions of the present paper intact. With this assumption, stress-in-life, in MPa, is found by multiplying the ratio (physiological cross-sectional area of the muscle)/(cross-sectional area of its tendon) by 0.3. This definition slightly overestimates the stress in the tendon, since allowance has not been made for the effect of the non-zero angle of pennation, $\theta$ (Ker et al., 1988). The force in the tendon is less than that in its muscle by the factor $\cos\theta$. However, for wallaby limb muscles, $\theta$ is always less than 30 ° and therefore $\cos\theta > 0.86$. Within the accuracy achieved in the present study, $\cos\theta$ may be considered as effectively unity.

Gravimetric methods were used for measuring the areas of both muscle and tendon. The procedures described by Ker et al. (1988) were followed except for an improvement in the measurement of the physiological cross-sectional areas of muscles. Muscles, by their very nature, can be stretched and can contract through a range of perhaps 25 %. While this happens, the area changes inversely to the sarcomere length, so measurement of sarcomere length allows the position of the muscle within its range to be assessed. We measured the sarcomere length for a selection of fascicles from each muscle by laser diffraction. (Dimery, 1985, describes the use of diffraction for measuring sarcomere length.) The area was then adjusted to that which would apply with a sarcomere length of 2.2 μm, which is a standard length for vertebrate muscle. Tendon cross-sectional areas were measured by weighing a known length. This is not necessarily straightforward for non-uniform tendons, primarily the toe flexors, where the important cross section is that around which rupture occurs. Sometimes the tendon from one leg was tested while that from the other leg was used for area measurement, on the assumption that, on average, they both have the same area. With branched tendons (the toe flexors), we assumed that all branches carry the same stress. The branch to toe 4 is by far the thickest, and for that the error in this assumption cannot be large. The assumption is encouraged by noting that the sum of the areas of all the distal branches more-or-less equals the total area of the common, more proximal, region. (In making that statement, we are excluding regions at the calcaneus and the metatarsal heads where flexor tendons have intermediate links to bone.)

### *Clamping and mechanical tests*

Because the collagen fibres of a tendon are largely independent, effective clamping is difficult. Methods that hold only the outer fibres, such as using a glue, leave the inner fibres incompletely stressed during the test, and the material appears less stiff and less strong than it really is. Such inequalities of stress are most serious when the specimen is short and thick. Furthermore, cutting the specimen to a dumbbell-shape, as is a common practice in testing bone and engineering materials, is not an available option. The ideal of holding each tendon fascicle separately is achieved *in vivo*, but is unattainable *in vitro*. In our experience, the best technique is to air-dry the ends to be clamped, whilst the rest of the tendon is kept moist by being wrapped in a damp tissue (Wang and Ker, 1995). Drying reduces thickness, which is itself helpful, and makes the material less flexible, which presumably indicates better lateral stress transfer. Of course, not every problem is solved since stress concentrations are bound to arise where damp material merges with dry material. The difficulties of clamping vary with the shape of the tendon. The most troublesome of the wallaby limb tendons was the gastrocnemius, which, at the muscle end, spreads out in a fan of non-uniform thickness. We tried to force greater uniformity by repeatedly squeezing and releasing the portion to be clamped during the drying process. This was not fully successful.

The seriousness of the clamping problem depends on the measurement being made as well as the tendon being tested. It is most serious in attempts to measure ultimate tensile stress (UTS), where the stress of interest is the maximum attainable. For other measurements, including fatigue tests, useful results can be obtained with stresses well below the maximum.

Each dried end was clamped between flat steel plates screwed firmly together. With the thicker tendons, the plates had shallow transverse serrations. With the thinner tendons, both plates were smooth. Finding what works best is a matter of trial and error. The gastrocnemius and the toe flexor tendons were left attached to their respective distal bones. The bone was held by allowing its proximal surface to be pulled against a shaped aluminium plate. The alignment of the bone–tendon junction was maintained in a natural position. For the gastrocnemius, this required the calcaneus to be at an angle of approximately 90 ° to the length of the tendon. No failures occurred in the bone or at the tendon–bone junction.

Tests were carried out in a liquid paraffin bath, saturated with water, with the aim of maintaining a constant hydration of the tendon. The liquid paraffin is an inert immersion medium, which we preferred to saline because a tendon freshly removed from an animal swells when it is placed in saline. The solubility of water in liquid paraffin is small, but not zero. If pure liquid paraffin is used, a thin tendon tends to dry in a prolonged test. As with an air-dried tendon, it becomes stiffer against bending. When the liquid paraffin is saturated with water, the tendon remains fully flexible. The clamped ends remain apparently dry, presumably because the high pressure between the plates prevents the limited available water from entering. The temperature was held at 37 °C.

Loads were applied using an Instron 8500 dynamic testing machine. A small pre-load was required to enable the machine to be set to load control. This pre-load was often 4 N, or 8 N for the thicker tendons, and was always far too small for any significant fatigue damage to occur during setting-up. The load was increased to the target value in approximately 1 s and then held constant until the tendon ruptured. Throughout the test, creep was monitored by plotting the position of the actuator against time on a chart recorder. This plot was a useful indicator of how the test was progressing. Fig. 1 of Wang and

Ker (1995) shows the characteristic shape of a creep curve to rupture.

This test protocol was designed to find the time-to-rupture at a selected stress, but we were able to take advantage of the initial load-ramp to assess the stiffness of those tendons, mainly toe extensors, that were of uniform thickness. During the loading period, the displacement of the actuator and the output of the load cell were recorded using a high-speed digital recorder (Datalab 912). With the initial length taken to be the length at pre-load, the Young's modulus of the material was calculated as the slope of the linear region of the stress–strain curve.

In presenting the results, the units of time are s and of stress are MPa. Mean values are given ± the standard error of the mean (S.E.M.).

## Results

Fig. 1 demonstrates the range of stress-in-life values among the tendons of the wallaby limb and the tail tendon. There is a gap between approximately 30 and 40 MPa, but, none the less, the distribution is wider and more even than for many mammals. This was a major reason for choosing to use wallaby limbs. The values of stress-in-life lie within the general pattern observed for mammals (Ker et al., 1988; Pollock and Shadwick, 1994b). The only notable difference from quadrupedal mammals concerns the gastrocnemius. In Bennett's wallaby, the stress-in-life of the gastrocnemius is comparable with that of the plantaris, whereas in quadrupeds of similar mass it is definitely less. Fig. 1 is reasonably consistent with the few direct measurements of peak tendon stresses during vigorous activities that are available in the literature (for some kangaroo tendons, see Biewener and Baudinette, 1995; Bennett and Taylor, 1995; Kram and Dawson, 1998). These authors investigated the plantaris, deep toe flexor and gastrocnemius and found that, of these, the deep toe flexor is subject to the lowest stress, as in Fig. 1.

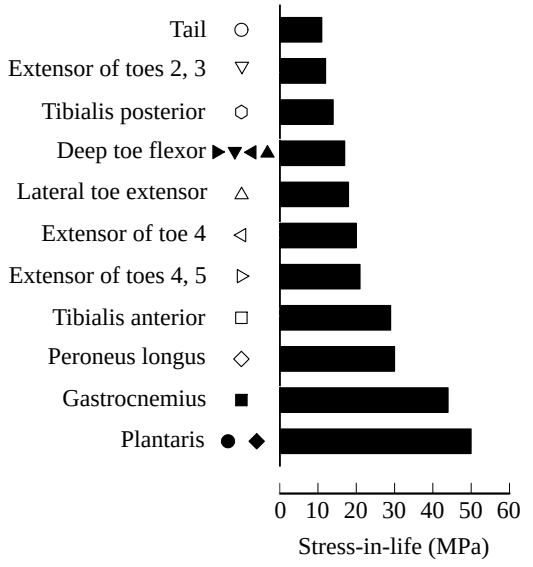


Fig. 1. Stresses-in-life for wallaby tendons. The bars show the stress on each tendon when its muscle is generating maximum isometric stress. The values are the averages for the three wallabies that contribute to Fig. 5. The symbols beside the names of the tendons are the key to those used in Figs 2–5, in which the results of mechanical tests are presented. The deep toe flexor and the plantaris (superficial toe flexor) both have branches to more than one toe, which were tested separately, and hence have more than one symbol. For the deep flexor, the four symbols are for the branches to toes 2, 3, 4 and 5 in that order from left to right. The plantaris lacks branches to toes 2 and 3, and the two symbols are for toes 4 and 5 respectively. Filled symbols are used for the tendons that bear the main load during the stance phase of locomotion. Of the rest, open triangles, in various orientations, are used for all four toe extensor tendons.

Fig. 2, a log–linear plot, shows the exponential reduction in time-to-rupture with increasing stress for tail tendons. Limb tendons gave similar results, with the additional feature that those subject to low stresses-in-life failed at shorter times, for any given stress, than those subject to high stresses-in-life. This is illustrated by Fig. 3, which was constructed by extracting from the full results the tests performed at or near 50 MPa. Fig. 3 shows that the times-to-rupture of the plantaris tendons were longer than those of the toe extensor tendons by a factor of approximately 100. We will use the term 'fatigue quality' to describe resistance to time-dependent rupture: the plantaris tendon has higher fatigue quality than any toe extensor tendon. The fatigue qualities of tendons can be compared by measuring either the time-to-rupture at a given stress or the stress required to achieve a given time-to-rupture.

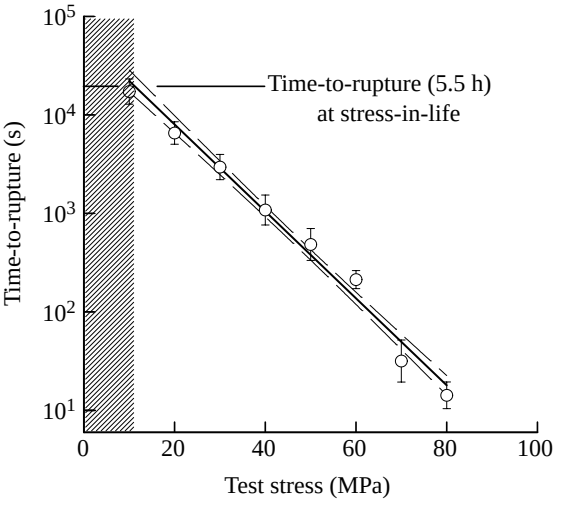


Fig. 2. Variation of time-to-rupture with stress for similar tendons. These data are for tail tendons from wallaby B (see Materials and methods). The hatched region indicates the range of stresses that can be applied to a tail tendon by its muscle. 95% confidence limits are used for the error bars and the linear regression. The regression line is $\log T = a + b\sigma$, where $a$ is 4.79, $b$ is –0.0442, $T$ is the time-to-rupture (in s) and $\sigma$ is the test stress (in MPa); $N$=90; $r^2$=0.93, $P$<0.001. Three very low outliers were discarded. Regression parameters for the two other wallabies that contribute to Fig. 5 are as follows: wallaby A, $a$=4.38, $b$=–0.0505; wallaby C, $a$=4.56, $b$=–0.0486.

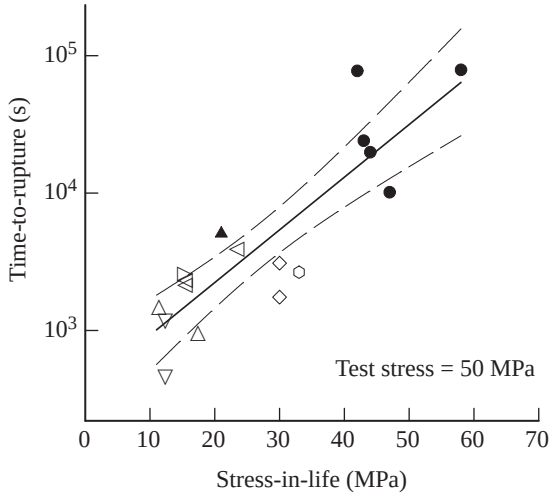


Fig. 3. Times-to-rupture with the same test stress (50 MPa) applied to different tendons. Time-to-rupture correlates with stress-in-life; $r^2$=0.75, $P$<0.001, $N$=17. The key to the symbols is given in Fig. 1. These results were extracted from a larger set of times-to-rupture covering a range of stresses. This plot uses all those in which the test stress was between 40 and 60 MPa inclusive. Those results not taken at 50 MPa have been adjusted to that value using data from the legend to Fig. 2 (average slope for all three wallabies –0.0478). Linear regression and 95 % confidence limits are shown on this log–linear plot.

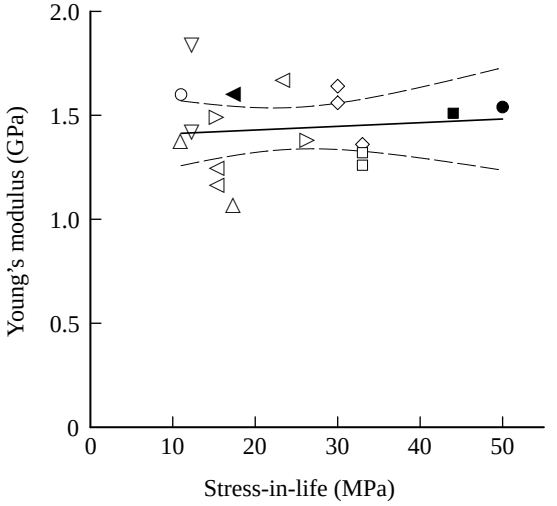


Fig. 4. Young's modulus for different tendons. No correlation with stress-in-life is observed: $r^2$=1.1×10$^{-2}$, $P$=0.69, $N$=18. Symbols are as in Fig. 1. The open symbols are data from the present study. The filled symbols are from Ker et al. (1986). Linear regression and 95 % confidence limits are shown.

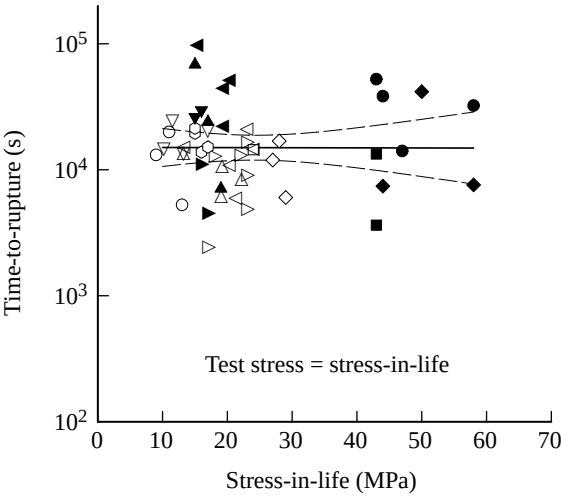


Fig. 5. Times-to-rupture at stresses related to those experienced in life. With the test stress applied to each tendon equal to its own individual stress-in-life, the time-to-rupture shows no significant variation between tendons, despite the wide range of stress-in-life: $r^2$=1.3×10$^{-3}$, $P$=0.98, $N$=47 (not including the tail tendon points). Symbols are as in Fig. 1. The gastrocnemius (filled squares) presented a difficulty because of its awkward shape. Proximally, it spreads out in a wide fan of non-uniform thickness. Our experience was that premature failure occurred in the clamp unless the test stress was well below the stress-in-life. For the two points plotted, the tests were at a stress of 30 instead of 45 MPa. The adjustment, applied as explained in the legend to Fig. 3, decreases log$T$ by 0.71. Linear regression and 95 % confidence limits are shown on this log–linear plot.

Fig. 3 shows that fatigue quality correlates with stress-in-life. In contrast, Fig. 4 demonstrates the absence of correlation between Young's modulus and stress-in-life for wallaby tendons. The present force–displacement data could only be converted to Young's modulus values in those cases in which the specimen was reasonably uniform and the stress was sufficient to reach the linear region of the stress–strain curve (Fig. 4, open symbols). The requirement of a uniform test specimen excludes those tendons held, in the testing machine, *via* the bone at their distal ends, i.e. the toe flexors and gastrocnemius. However, these are the very tendons for which data are available from Ker et al. (1986) (Fig. 4, filled symbols).

Tests at a given stress, as in Fig. 3, do not mirror the situation in life, where the various tendons experience very different stresses. To investigate the biological relevance of differences in fatigue quality, we carried out a series of tests on leg tendons from three wallabies, in which each tendon was tested at its stress-in-life. The results from the individual wallabies intermingle and the data have been merged in Fig. 5. The three sets of data, not surprisingly, cover similar stress-in-life values: comparison by one-way analysis of variance (ANOVA) gave $P$=0.647; $N$=13 for wallaby A, $N$=18 for B and $N$=16 for C. (The tail tendon results, open circles, are omitted from these comparisons.) Comparison of the three sets of log(time-to-rupture) data gave $P$=0.224 and are also not significantly different. The linear regression line in Fig. 5 represents an average of the results for the three wallabies. The slope is 0±4.0×10$^{-3}$ ($N$=47, $P$=0.98). (The first non-zero digit arising when calculating the slope is at a value considerably less than the standard error and thus is meaningless.) Fig. 5 shows very marked scatter. No doubt, this arose in part during the experiments, but it is likely also to reflect real biological

variation. At any given value of stress-in-life, some tendons are much more at risk from rupture than others. Nevertheless, the conclusion from Fig. 5 is clear: despite the widely different stresses to which they are exposed in life, all types of tendon are similarly prone to rupture. The overall average of log(time-to-rupture) is 4.18±0.049.

## Discussion

### *Variations in the material properties of tendons*

#### *Fatigue quality*

Figs 3 and 5 demonstrate the huge range of fatigue quality to be found among wallaby limb tendons. Previous reports on the fatigue rupture of tendons (Wang and Ker, 1995; Wang et al., 1995; Schechtman and Bader, 1997) do not reveal this range, because the tendons used, from wallaby tails and the extensor digitorum longus of the human foot, happen to be of fairly similar fatigue quality. Both are at the lower end of the range. Their values for stress-in-life are also similar: 11–13.5 MPa for the wallaby tail tendon (Fig. 1; Wang and Ker, 1995) and 11–13 MPa for the human extensor digitorum longus (Ker et al., 1988).

The magnitude of the result shown in Fig. 5 is most clearly brought out by the contrast with Fig. 2. If all the tendons of Fig. 5 were of similar material, the time to rupture would fall strongly with test stress (here equal to stress-in-life), as it does in Fig. 2. Compare the toe extensor tendons (open triangles) with the plantaris tendon (filled circles and diamonds). Both gave satisfactory experimental results. The extensor tendons are reasonably long and thin and clamp well. The plantaris tendon clamps well for a quite different reason. It divides into two branches, one of which inserts on toe 4 and the other on toe 5. Proximally, we clamped the significantly stronger common region. The two branches were tested separately (filled circles for toe 4 and filled diamonds for toe 5) with the distal end held by the relevant bone. The mean log(time-to-rupture) for the extensor tendons is 4.04±0.057 ($N$=19) and for the plantaris tendons is 4.33±0.136 ($N$=7), a difference of +0.29. A paired $t$-test gives $P$=0.048, and thus they are on the margin of being significantly different at the 5% level. Anyway, they are not much different, whereas in Fig. 2 a stress range from 18 to 49 MPa gives a difference in log(time-to-rupture) of −1.36, more than an order of magnitude. This comparison is between means. The range between the extremes of fatigue quality is greater: more than two orders of magnitude in Fig. 3. We have omitted the gastrocnemius from this comparison because its results are less reliable than those for the plantaris, as explained in Materials and methods section and in the legend to Fig. 5.

The deep flexors (filled triangles) are of low stress-in-life, like the extensor tendons, but appear in Fig. 5 to have somewhat higher fatigue quality. In Fig. 5, the branches of the deep flexor tendons that go to toes 4 and 5 have a mean log(time-to-rupture) of 4.53±0.142 ($N$=6). (The branches to toes 2 and 3 are exceedingly thin and are omitted in this comparison.) Compared with the extensor tendons, the deep flexor tendons and also, more marginally, the plantaris tendons appear of excessive fatigue quality. A reason for this may be that toe flexor tendons are more likely than toe extensor tendons to be subjected to stresses higher than those attributed in our calculations of stress-in-life. The flexor tendons are branched, and assigning equal stress to each branch may underestimate the maximum stress achieved in normal life. If a single toe lands on a stone, while the other toes are unsupported, its branch of the flexor tendon may be excessively loaded. Furthermore, although we have argued above that flexor muscles are unlikely to produce forces above their maximum isometric force in steady locomotion, they may well do so when running downhill or decelerating and when landing from a jump. Had we been able to allow for such factors in assessing the stress to be applied in the experiments leading to Fig. 5, the points for the flexor tendons would have moved to lower times-to-rupture. A modest shift in this way would serve to strengthen the main conclusion, which is that all tendons appear similarly prone to fatigue rupture, when tested under conditions related to those they experience in life.

#### *Young's modulus*

Fig. 4 is consistent with the results of Pollock and Shadwick (1994a,b). We agree with their inference that, where adjustments to structural stiffness are required, this is, on average, achieved by changing thickness rather than material stiffness. Equally, when stiffness differs, for example as a result of variations in the proportion of collagen, this can be allowed for in the structure by altering thickness (Riemersma and Schamhardt, 1985). Either way, thickness is the controlled variable.

#### *Ultimate tensile strength (UTS)*

Obviously, we could not measure the UTS in a ramp test at the same time as measuring fatigue quality. All we know from our tests is that the UTS is greater than the applied stress. In the tests with limb tendons, the minimum time-to-rupture was 450 s. Static fatigue is therefore clearly distinguished from the initial ramp, which took approximately 1 s.

Because of clamping problems, published UTS data (Table 1) should be considered to represent minimum values: the 'real' UTS values are at least as great. But even this minimum limit is useful. Consider, for example, the human extensor digitorum longus (EDL). It has a UTS of at least 100 MPa (Schechtman and Bader, 1997), but the maximum isometric tension from its muscle causes a stress of only 11–13 MPa (Ker et al., 1988). Under no circumstances can an undamaged EDL be ruptured in tension by a single pull, for the muscle will fail first. The EDL is far thicker than is required for adequate strength. Ker et al. (1988) suggest that the large thickness is required for optimum stiffness, and we assume that more-than-adequate strength is a consequence. The situation is quite different for the high-stress tendons, whose thickness may well be determined by the need for strength. Undoubtedly, the values for the human Achilles in Table 1 are underestimates for they are lower than the stresses that are

known to act in the Achilles tendon in life. Komi et al. (1992) measured a stress of 60 MPa when walking and up to 110 MPa when running at 6.5 m $s^{-1}$. Our experience with the wallaby gastrocnemius tendon is similar. It ruptured during the initial ramp when the target stress was the stress-in-life. In effect, we found an apparent UTS less than the stress that the gastrocnemius withstands in life! As explained in the legend to Fig. 5, we had to resort to using a lower target stress and adjusted the results according to the relationship between time-to-rupture and stress-in-life observed with the tail tendons.

*A priori*, an association between UTS and fatigue quality would seem entirely reasonable. At a fundamental level, it is difficult to distinguish a ramp rupture and a fatigue rupture. As the stress increases, the time-to-rupture reduces and must ultimately merge with the ramp duration. Conversely, every ramp takes a finite time and the ultimate failure must have a time-dependent element. Can UTS and fatigue quality really have different relationships to stress-in-life? All we can state at present is that evidence for a positive correlation between UTS and stress-in-life is lacking.

### *Variations in the structure of tendons*

Differences in physical and biochemical structures necessarily underlie observed differences in mechanical properties. Among tendons as a whole, major differences have been reported in (i) the diameters of collagen fibrils (for a review, see Parry, 1988) and (ii) the nature and amount of cross-linking between collagen molecules (for a review, see Bailey and Paul, 1999). The implications of these two possibilities will be considered in turn in the remainder of this subsection. But other structural possibilities remain. For example, the proportion of collagen in tendon undoubtedly varies (e.g. Riemersma and Schamhardt, 1985; Woo et al., 1982). The differences in collagen content are unlikely to be large in relation to the huge differences in fatigue quality. But, sometimes small changes can have very marked effects. In bone, Young's modulus is proportional to the fourth power of calcium content, expressed as fractional mass in dry defatted bone (Currey, 1999).

Parry et al. (1978) assume that a tendon with collagen fibrils of small diameter is likely to be resistant to non-recoverable creep. The rationale is that, with small fibrils, the total surface area of collagen is large, giving good opportunities for the transfer of stress between fibrils through the surrounding matrix. Thus, thinner fibrils are less inclined to slide relative to each other. They also assume that larger fibrils are stronger because of the increased opportunities for cross-linking between the larger number of nearby molecules (Parry and Craig, 1988). A bimodal mixture is observed with some adult tendons, in which most fibrils are either 'small' (diameter approximately 40 nm) or 'large' (approximately 200 nm). Parry et al. (1978) suggest that this distribution represents a balance between the need for strength and resistance to non-recoverable creep. It seems natural to associate Parry's 'non-recoverable creep' with fatigue, and it will be of great interest to determine whether small fibrils and high fatigue quality are correlated.

Table 2. *Comparison of collagen fibril diameter and the stress in the tendon when galloping for three tendons of the horse forelimb*

| Tendon | Mass-average diameter (nm)[a] | Stress (MPa)[b] |
|---|---|---|
| Deep digital flexor (DDF) | 202 | 45 |
| Superficial digital flexor (SDF) | 132 | 34 |
| Suspensory ligament (SL) | 114 | 26 |

[a]Patterson-Kane et al. (1998).
[b]Biewener (1998).

Patterson-Kane et al. (1998) examined the mass-average diameter of fibrils from three of the forelimb tendons of Thoroughbred horses. Biewener (1998) assessed the stresses to which the tendons of horses are subjected during galloping. These two sets of data are given in Table 2. The apparent correlation is that expected, according to the hypothesis of Parry et al. (1978), for strength rather than for creep-resistance. The largest fibrils go with the highest stress and therefore, on the basis of our results, the highest fatigue quality. Biewener (1998), using two horses, gives full data for muscle and tendon cross-sectional areas, so stress-in-life can be calculated according to our present definition. The average values are 45 MPa for the superficial digital flexor (SDF) and 67 MPa for the deep digital flexor (DDF). (The suspensory ligament, SL, lacks a muscle, so stress-in-life cannot be calculated.) In contrast, Ker et al. (1988) give stresses-in-life, for a single horse, of 75 MPa for the SDF and 38 MPa for the DDF. Large individual variations are a feature of stress-in-life (and many other aspects of tendon design), so Biewener (1998) and Ker et al. (1988) may both be right for their particular animals. The only clear conclusion is that too few data are currently available!

An interesting feature of the hypothesis of Parry et al. (1978), in the light of the section above dealing with 'strength', is that different mechanisms are ascribed to strength and to creep-resistance. This may help in understanding how fatigue quality and UTS might have different relationships to stress-in-life. Parry et al. (1978) involves the matrix in the mechanism of creep, as is also suggested by an observation of Wang and Ker (1995). They noted that, with wallaby tail tendons, reducing the test piece to a length below approximately 80 mm markedly increased the apparent fatigue quality. The implication is that the tendon is built up of 'structural units' with a length of the order of 80 mm. When both ends of a structural unit are held by clamps, the fatigue quality appears high. When only one end is held, structural units have the ability to slide relative to each other through the matrix.

Turning now to cross-links in collagen, Bailey and Paul (1999) show a clear relationship between the type and amount of cross-linking in a connective tissue and the age of the animal. The amount of cross-linking increases during growth, and stiffness and strength also increase (Viidik, 1982). Less is

known as to whether cross-linking differs between healthy mature adult tendons. Since wallabies continue to grow throughout life (Catt, 1981), the question arises as to whether the tendons we used are to be considered mature. The shift to maturity is gradual, and it seems probable our tendons are at least close to being fully mature. Their Young's moduli (Fig. 4) are appropriate for mature tendons. The tendons from a variety of immature animals have lower moduli (for example, H. G. Vogel, 1978; Viidik, 1982, for rat tail; Nakagawa et al., 1996, for rabbit Achilles tendon; Shadwick, 1990, for pig; Pike, 1998, for sheep). Similarly, stress-in-life values range up to 50 MPa in our wallabies, whereas the maximum is lower among the tendons of young mammals (at least for sheep; Pike, 1998). In any case, our main results, concerning the differences in fatigue quality among the tendons from a single animal, are not dependent on adulthood, but apply at whatever level of maturity appertains to that animal.

Davison (1989) makes an intriguing suggestion, which relates time-dependent damage to the impairment of cross-linking, at least for the tail tendons of young rats. Aldimine cross-links (see Bailey and Paul, 1999) are liable to dissociation by hydrolysis. When subject to mechanical strain, the dissociated parts tend to separate and the cross-link is broken. Davison (1989) calls this 'strain-catalysed hydrolysis'. The general principle of combining a chemical reaction with mechanical strain also applies to the fatigue of glass although, obviously, with quite different details. In the presence of water, the tip of a fatigue crack advances through glass because of chemical action at the point of greatest stress (Wiederhorn, 1972).

### *Routine damage and repair*

The average log(time-to-rupture) in Fig. 5 is 4.18, and the geometric mean time-to-rupture is therefore 4.2 h: $(10^{4.18})/3600=4.2$. Furthermore, the spread is wide, at least an order of magnitude at any given stress-in-life. The shortest times appear to be approximately 1.5 h. In contrast, wallabies in Whipsnade Wild Animal Park can live for more than 10 years (D. Bourne, personal communication). Of course, the muscles do not hold their maximum isometric forces continuously for 4.2 h, but fatigue damage accumulates, and it seems clear that, in the absence of repair, all tendons would rupture long before the wallaby was ready to die. Previous work using wallaby tail tendons (Wang and Ker, 1995; Wang et al., 1995) and the human extensor digitorum longus (Schechtman and Bader, 1997) came to the same conclusion: the maintenance of tendons must depend on ongoing repair.

Homeostasis requires that, on average, the rate of repair is equal to the rate of damage. The time-to-rupture in an *in vitro* test is an indicator of the rate of damage at the start of the test, in the sense that the higher the rate of damage, the shorter the time-to-rupture. (Wang and Ker, 1995, develop this argument through a mathematical model for wallaby tail tendons.) Fig. 5 therefore shows that the rate of damage, and hence in life the matching rate of repair, is independent of the anatomical site of each tendon. Routine repair is part of normal life and is required to prevent damage progressing to the point where symptoms of injury arise.

According to the hypothesis of Parry et al. (1978) (see above), damage would be represented by relative sliding of collagen fibrils. If damage involved breaking collagen cross-links, sliding would be on a smaller scale and within fibrils. Such mechanically non-recoverable sliding is 'damage' in the sense in which the word is used in the discipline of Damage Mechanics (see, for example, Krajcinovic, 1996). It involves breaking chemical links and, if not repaired, leads ultimately to rupture. The material can only maintain a constant state if it is continually rebuilt by the tendon cells. A prerequisite for repair is information about damage. It is known that a network of cell processes pervades tendons and seems to allow the possibility of communication between cells (Benjamin and Ralphs, 1997).

### *Material design*

Fatigue quality is, so far as we know, the only material property of tendon that correlates with stress-in-life, but it is not the only material property to show marked variations. Another is compressive stiffness. Most parts of most tendons are not subject to compressive loads and have no need for compressive stiffness. However, transverse compressive loads can arise, most notably at corners where tendons press against bony pulleys (Giori et al., 1993). Experiments have shown that, when any tendon with active cells is subjected to repeated compressive loads, the proteoglycan component is altered to increase the compressive stiffness (K. G. Vogel, 1995). Tendon becomes fibrocartilage. This example demonstrates the ability of tendon cells to respond to the mechanical environment and to adjust the material properties of their extracellular tissue.

Similar general considerations must apply to fatigue quality although, as explained above, we do not yet know the underlying changes in the structure of the material. High fatigue quality at high stress is obviously necessary to avoid damage at an excessive rate. But why not make all tendons from the best material and thereby reduce the need for ongoing repair? To explain the poor quality of low-stressed tendons, we propose a model of adaptation to fatigue in which the cells are sensitive to a change in the level of damage carried by the tendon. Only when measurable damage is present does the cell receive information concerning the condition of the extracellular material for which it is responsible. This model implies an equilibrium level of damage at which the rate of damage equals the rate of routine repair. If the habitual rate of damage is altered, equilibrium will be lost and the cells will respond by adjusting fatigue quality. Fig. 5, within the broad limits of its scattered points, is consistent with the concept of a 'target rate of damage'. The target may change during growth, because of changes in the rate of repair, but our present observations are for adult tendons only. This model is concerned with a limited aspect of tendon design. In particular, it makes no prediction of tendon thickness. The appropriate thickness for a tendon and therefore, with a given muscle, its stress-in-life depends on factors other than fatigue damage

(Ker et al., 1988). Whatever the pattern of stress-in-life, within a wide range, the fatigue quality is adjusted as required (Fig. 3). This adaptation may involve both genetics and epigenetics.

This model is potentially susceptible to experimental investigation. A change in the long-term average load applied to a tendon would affect the rate of damage and hence, ultimately, the fatigue quality. In a number of experiments, animals have been exercised by running and their tendons compared with those of non-exercised controls (for a review, see Archambault et al., 1995). A routine of steady running does not necessarily increase the peak tendon force, but will increase the time-average force: long-distance runners do not develop large muscles. The changes observed in the stiffness of the tendon or the elastic modulus of its material are either not statistically significant (for the rabbit Achilles tendon, see Viidik, 1969; for swine digital flexors, see Woo et al., 1981) or fairly small (for swine digital extensors, Woo et al., 1980). However, increased fatigue quality in the tendons of exercised animals would be expected, on the basis of our model, because the time-averaged stress is increased even if the peak stress is constant. This has not been investigated. If an experiment involves altering the maximum load on a tendon, the situation is more complicated and it is more difficult to attribute changes to specific triggers. The most extreme situation is that of complete stress deprivation (for a review, see Yasuda and Hayashi, 1999). In the rabbit patellar tendon, the control system seems to fail and many changes ensue, with increased collagen production, thickening of the tendon, less ordered collagen architecture and substantial reduction in elastic modulus. Reduction of fatigue quality is also to be expected, but it would be difficult to attribute this to specific triggers or structural changes.

These *in vivo* experiments cannot directly tackle questions concerning the mechanism of the cellular response. The best hope for progress in these complex matters lies in *ex vivo* experiments in which tendons are maintained in culture while being subject to tension (Slack et al., 1984; Hannafin et al., 1995; Banes et al., 1999). Even modest loading significantly increases the production of DNA and of proteins compared with controls (Banes et al., 1999). The increased cellular activity continues after the loading has ceased, which fits with the hypothesis that damage is the trigger (and, no doubt, also with other hypotheses!). Banes et al. (1999) found that application of a gap junction blocker, octanol, eliminated the response. This confirms the need for intercellular communication. *Ex vivo* experiments with whole tendons act as a bridge between the mechanical responses of animals and of isolated cells.

The situation in tendon may be compared with that in bone, which is also susceptible to fatigue damage. Prendergast and Taylor (1994) developed a model of bone in which a change to the level of damage is the signal for adaptation. At equilibrium, the rate of repair, which is determined by physiological factors, is equal to the rate of damage (Prendergast and Taylor, 1994; Taylor and Prendergast, 1997). In these respects, tendon is similar. Both bone and tendon carry a modicum of damage in the equilibrium state. However, there is a fundamental difference. In the model of Prendergast and Taylor (1994), the architecture of the bone, and in particular its thickness, is adapted, but in tendon the change is to a material property (fatigue quality) not to thickness. In bone, if the load stimulus (suitably integrated over time) is raised, the mass, in due time, increases so that the stress tends to return to its original level. The target is a ‘homeostatic stress’. This homeostatic stress is set at a level that ensures a sufficient safety factor against failure (Alexander, 1984). In tendon, a very wide range of stresses can be accepted, and at each stress the fatigue quality is adapted to give an appropriate rate of damage. The model of Prendergast and Taylor (1994) does not tie bone to a single stress because the homeostatic stress is site-specific. For example, in bending, which is an important mode of loading for bone, the stress near the neutral axis is low, but the bone does not disappear there. The fundamental difference is not in the variability of stress, but rather in the mechanism of the response to damage. In the bone model, the target rate of damage is achieved *via* a target stress by altering thickness: in tendon, a wide range of stresses are acceptable and the target rate of damage is achieved by altering the material.

Overuse injuries to tendons (Józsa and Kannus, 1997) are varied and, no doubt, have many causes. One of these causes may be a breakdown in the balance between fatigue damage and routine repair. If either the rate of damage increases too much or the rate of repair is for some reason diminished, damage will accumulate and, in due time, symptoms of injury will arise. Our observation that low- and high-stressed tendons are, in life, equally at risk explains why finger tendons can be susceptible to fatigue injuries, even though their stress-in-life is small compared with their UTS (Cutts et al., 1991). Furthermore, the model of adaptation of fatigue quality to the prevailing pattern of stresses explains why an abrupt increase in activity brings the risk of injury. This risk applies to all tendons, but the consequences are likely to be most dramatic for highly stressed tendons such as the human Achilles tendon. With a low-stressed tendon, a substantial amount of damage would have to occur before the tendon is so weakened that it can be broken in a single, final pull. Lesser symptoms will arise during this time, and the offending activity will be curtailed. With a high-stress tendon, it is much more plausible that almost the first symptom will be rupture.

The ability to repair is a fundamental feature of the living system and is one of the reasons why biological design differs from engineering design (S. Vogel, 1998). An engineer seeking competitive advantage has to aim for high quality, because his systems are not self-repairing. In contrast, the living world can accept a minimum quality at which repair can keep pace with damage. This concept may be applicable to a wide range of biological systems. Time-dependent damage to tendon provides a particularly clear example, because the stresses are relatively simple (longitudinal tension) and are limited by the size of the muscle. We were therefore able to assign values to stress-in-life more straightforwardly than could be done for

other systems such as ligament, cartilage or bone. Horses' hooves (Kasapi and Gosline, 1997) provide a contrasting example in which high quality is required, because the material cannot be repaired once it has reached its functional condition. Instead, like an engineering component, it is replaced.

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