Aims
Loosening is a well-known complication in the fixation of fractures using devices such as locking plates or unilateral fixators. It is believed that high strains in the bone at the bone-screw interface can initiate loosening, which can result in infection, and further loosening. Here, we present a new theory of loosening of implants. The time-dependent response of bone subjected to loads results in interfacial deformations in the bone which accumulate with cyclical loading and thus accentuates loosening.

Methods
We used an ‘ideal’ bone-screw system, in which the screw is subjected to cyclical lateral loads and trabecular bone is modelled as non-linear viscoelastic and non-linear viscoelastic-viscoplastic material, based on recent experiments, which we conducted.

Results
We found that the interfacial deformation in the bone increases with the number of cycles, and the use of a non-linear viscoelastic-viscoplastic model results in larger deformations, some of which are irrecoverable. There is an apparent trend in which interfacial deformations increase with increasing porosity of bone.

Conclusion
The developed time-dependent model of the mechanical behaviour of bone permits prediction of loosening due to cyclical loads, which has not been possible previously. Application of this model shows that implant loosening will be accentuated by cyclical loading due to physiological activities, and the risks of loosening are greater in osteoporotic patients.

Keywords: Cyclic loading, viscoelastic-viscoplastic, Bone volume ratio, Irrecoverable strain
has been reported frequently, and it has previously been noted that this is usually initiated by mechanical forces before any contribution from biological processes.\textsuperscript{2} It has been suggested that screw loosening and failure, observed clinically, probably results from bone-screw separation events and from elevated strains.\textsuperscript{3} The bone yields locally at the interface due to high stresses or strains, and this initiates loosening, which may lead to infection, and further loosening.\textsuperscript{4-6}

Most orthopaedic implants have some form of load-sharing arrangement with the bone which cause cyclical stresses and strains at the bone-implant interface due to physiological activities. Experimental investigations have shown that the separation is a function of the number of cycles for a range of implants, including pedicle screws,\textsuperscript{7,8} dynamic hip screws,\textsuperscript{9} and the fixation of distal tibial\textsuperscript{10,11} and distal radial fractures.\textsuperscript{12} A study on dental implants drew attention to the fact that repeated loading-unloading cycles result in alternating compression and separation of the bone-screw interface.\textsuperscript{3} The nature of migration suggests that it is a mechanical phenomenon, or at least mechanically triggered, rather than a purely biological process.\textsuperscript{2}

In computational modelling, loosening at the interface has, in the past, been examined by evaluating the level of strain after using time-independent elastic\textsuperscript{7} or elastoplastic\textsuperscript{5,8} constitutive models for bone. On the other hand, it is recognized that the response of bone to loads is time-dependent\textsuperscript{9} and some permanent deformation arises even at low levels of strain (<3000 µε).\textsuperscript{10,11} It has also been shown that, similar to time-independent material properties such as Young’s modulus, time-dependent properties are also related to the bone volume fraction (BV/TV).\textsuperscript{12,13} However, these time-dependent mechanical properties of bone are not generally incorporated in modelling.\textsuperscript{14}

The aim of this study was to examine possible loosening due to cyclical loading in an idealized bone-screw system in which trabecular bone is assigned time-dependent non-linear viscoelastic and non-linear viscoelastic-viscoplastic properties. The properties which were used are based on recent experiments and constitutive models.\textsuperscript{15} Our hypothesis was that bone-screw systems used in the fixation of fractures can become loose when subjected to cyclical loading due to time-dependent mechanical properties of bone, and the rate of loosening is associated with the BV/TV.

### Materials and Methods

In designing the study, we considered a screw inserted in a block of bone subjected to lateral cyclical loads, as shown in Figure 1a, which also shows the dimensions. The dimensions of the screw are similar to those used in locking plates. Taking advantage of symmetry, only half of the bone block-screw system was modelled (Fig. 1b). Exact fit between the screw and the bone was considered at the interface due to high stresses or strains, and this initiates loosening, which may lead to infection, and further loosening.\textsuperscript{4-6}

All external faces of the block were assumed to be fully restrained except for the face with the screw hole, and symmetry boundary conditions were applied at the symmetry surface (Figs 1a and 1b). Triangular cyclic forces with an amplitude of 300 N and a frequency, 1 Hz, as shown in Figure 1c, were applied to the external end of the screw (Fig. 1a). The models were permitted 1000 seconds of recovery after 500 complete cycles, as shown in Figure 1c. We chose 500 cycles as we were mainly interested in evaluating the trends, though this choice was also partly dictated by the computational resources required for this highly non-linear problem.

The screw and the cortical bone were modelled as linear elastic time-independent materials, with Young’s moduli of 180 GPa and 20.7 GPa, respectively,\textsuperscript{16} and a Poisson’s ratio of 0.3. Trabecular bone was modelled
using two models: a non-linear viscoelastic (VE) model and a non-linear viscoelastic-viscoplastic (VEP) model. The mathematical details of these models are provided as supplementary information, which include data for each of the three BV/TV values considered.

The screw-bone system was modelled in Abaqus (v6.12; Dassault Systèmes Simulia, Providence, Rhode Island), using 13,182 3D finite elements (brick, C3D8 and tetrahedron, C3D10M). Mesh convergence studies were performed and they showed that further refinement resulted in a change of peak displacement of bone by < 0.5%.

Results
Trabecular bone displacements and strains in the region around the screw were compared at three stages for different cycles: timepoints when the load is at its peak (300 N); timepoints when the load is zero; and at the end of the recovery (at the end of 1000 seconds after loading is stopped). In Figure 2, the rows present displacement contours at different stages and cycles. The columns are for different samples of bone, with numerals indicating BV/TV percentage of the samples, and for the two time-dependent material models used (VE and VEP). For each case, contours along the length of the screw (Fig. 1a) and at the symmetry surface, section A-A (Fig. 1b), are shown in Figure 2. The displacements were magnified ×150, and the section plots are superimposed with undeformed geometry for better comparison with its original shape. Seven representative cycles (1, 5, 10, 50, 100, 300 and 500) were selected for examining variations of displacement.

In all cases, the peak trabecular bone displacements occurred at the interface in the middle region of the screw hole at the top, and the entrance of screw hole at the bottom for all three stages. The peak displacements of trabecular bone at section A-A at selected cycles for all six models were extracted and are shown in Figure 3.

The maximum and minimum principal strain contours are shown in Figure 4 for VEP models at seven representative cycles.

Peak loading timepoints. At the peak loading timepoints, the difference in displacement between the samples with different BV/TV is apparent. The lower BV/TV samples undergo larger interfacial displacements than higher BV/TV samples, as seen from the displacement contours (Fig. 2a), peak displacements (Fig. 3a) and principal strain contours (Figs 4a and 4b).

At peak loading timepoints, similar displacement contours were observed for models which included VEP and those that were modelled using VE alone. Small differences were, however, observed after the samples had experienced a relatively larger number of cycles and for trabecular bone with low BV/TV. Thus, 15 VEP had slightly higher displacement than the 15 VE cases. The differences between VE and VEP models were negligible at the highest BV/TV considered in the study, as between 35 VE and 35 VEP. As expected, Figure 3a shows that the maximum displacement experienced by trabecular bone increases with the number of cycles. However, this increase was found to be small; the largest increase for the lowest BV/TV sample with a VEP model was 15%. Lower BV/TV in conjunction with viscoplasticity produced larger maximum displacements.

By examining the maximum and minimum principal strain contours (Figs 4a and 4b), we observe that the strain experienced by trabecular bone increases with the number of cycles. It is worth noting that the magnitude of strains in bone during the loading phase were generally below 0.5% and 0.7% for tension and compression, respectively, which are the typically reported yielding strains in the literature. Another observation is that trabecular bone experiences higher strain in compression than in tension (Figs 4a and 4b). As in the observation about displacements, the magnitude of strain increases with a decrease in the BV/TV of trabecular bone.
Zero loading timepoints. In the initial cycles, most of the deformation is recovered upon unloading (Fig. 2b). However, as the number of cycles increase, deformations accumulate with increasing number of cycles at zero load timepoints. This indicates the development of a gap between the screw and the bone. This is also seen when comparing peak displacements, as shown in Figure 3b. As expected, the VEP models have much larger peak deformation upon unloading than VE models, especially for lower BV/TV samples (Fig. 3b). Similar to the loading phase, the displacements of trabecular bone at zero loading timepoints were related to trabecular bone’s BV/TV; the deformations were found to increase with a decrease in BV/TV. The largest increase for the lowest BV/TV sample with a VEP model (15 VEP) was > 700% from cycle 1 to 500. It is important to note that at zero load timepoints, there are residual displacements of bone not only when using viscoplastic models but also when using viscoelastic models. These residual displacements cannot be obtained if time-independent elastic properties are used, which require the deformation to recover instantaneously upon unloading.

Figures 4c and 4d show the maximum and minimum principal strain upon unloading with increased number of cycles for VEP models. Most strain is recovered upon unloading (note the difference in scale of the contour plots for peak loading and zero loading timepoints), but residual strains accumulate with the number of cycles and the residual strains are associated with the bone BV/TV. We also found that the accumulation of principal strains, both maximum and minimum, is more rapid for bone with lower BV/TV.

Recovery. All six models were allowed to recover for 1000 seconds under zero force after 500 cycles of loading. As expected, the VE models showed almost complete recovery of displacement, whereas there was residual displacement with VEP models (Fig. 2c). These irrecoverable deformations were found to be related to BV/TV (Fig. 2c); they increased with decreasing BV/TV. The highest irrecoverable deformation was found for bone with
lower BV/TV (Fig. 3b), and irrecoverable deformation was found to be negligible for bone with the highest BV/TV (Fig. 3b). This is also apparent from principal strain contours in Figures 4e and 4f. Bone with lower BV/TV experiences a relatively higher irrecoverable minimum and maximum principal strain, showing that viscoplasticity plays an important role.

Discussion

We found that, in a bone-screw system subjected to cyclical loading, the inclusion of time-dependent properties for trabecular bone predicts separation between the screw and bone, which increases with an increasing number of cycles. Incorporation of viscoplasticity results in larger deformation, some of which is irrecoverable. Interfacial deformation was found to follow a trend based on BV/TV, with porous bone having larger deformations, or larger separation between the screw and the bone.

Numerical simulation of loosening due to mechanical forces in a bone-screw system subjected to cyclical loading has not been possible previously, as a time-dependent material constitutive model of bone has not been included before. A recent multiple-load-creep-unload-recovery experimental study,13 followed by the development of time-dependent constitutive models15 for trabecular bone, has permitted their use in this clinically-relevant study. A number of previous studies, both clinical21 and experimental,22,23 have reported that the migration of an implant or loosening of a screw is a function of time, some which is irrecoverable. Interfacial deformation was found to follow a trend based on BV/TV, with porous bone having larger deformations, or larger separation between the screw and the bone.

During the loading phase, the deformations in the bone are forced to follow those of the screw. Consequently, bone deformations only show a small increase with an increasing number of cycles as the time lag between the bone response and the instantaneous response of the screw increases. At peak loading in the first cycle, there is no difference between deformations from VE and VEP models (Fig. 3). However, with increasing numbers of cycles, differences emerge. Thus, we found that the inclusion of viscoplasticity produces larger deformations not only at zero loading timepoints, but also at peak loading timepoints.

The strong positive relationship between the BV/TV of trabecular bone and its time-independent properties has been previously reported;19,24 In general, bone with higher BV/TV has a larger stiffness and yields at larger loads, though it is recognized that the bone’s microstructure also has an important role. In other words, denser trabecular bone has a better ability to resist the applied forces and undergoes lower deformations. This trend was consistently observed with the three samples we considered. The deformations at different stages followed a clear trend based on trabecular bone’s BV/TV. Porous bone, with lower BV/TV, has higher deformation compared with less porous bone. This is true for loading and unloading timepoints and even for recovery modelled using viscoplasticity. It has also been reported in various studies that implants are more likely to be unstable in bone with low density, such as due to osteoporosis. These studies include in vitro experiments,22,25,26 finite element simulations27,28 and clinical findings.29 Basler et al22 found that displacement was strongly correlated with the initial BV/TV (r² = 0.95), which implies that it is also related to implant migration. Consistent results are seen in the current study. Screws are more likely to be unstable in bone with a low BV/TV which has higher interfacial deformation, compared with denser bone. In addition, the deformation increases more rapidly with increasing numbers of cycles.

We considered primary stability soon after the operation and before any biologically driven remodelling of bone occurs in a manner similar to several previous computational4,7 and in vitro22,23 studies. Primary stability relies on interlocking and frictional bone-screw contact phenomena. The cycle-dependent deformation results in the screw hole become enlarged. This causes the frictional resistance at the bone-screw interface to reduce with increasing loading cycles. Donaldson et al4 reported that, in unilateral external fixators, there exist push-in and pull-out forces that accompany axial loading. These forces, in conjunction with increasing diameter of the screw hole and decreasing frictional resistance, can result in an increased risk of loosening, particularly in low BV/TV bone.

It has been suggested that bone ingrowth and ongrowth occur if the micromovements are < 40 µm to 50 µm.20 If physiological loads give rise to bone-implant
micromovements of the order of 100 µm to 200 µm, they inhibit the ingrowth of bone, resulting in the formation of fibrous tissue around the prosthesis and eventual loosening. Some previous experiments have shown that the threshold value of micromovement for osseointegration is between 30 µm and 150 µm. Although we considered an idealized system, with a screw inserted in a block of bone, it is tempting to examine quantitative values of the interfacial movements. They are smaller than the threshold value of micromovement required in the formation of a fibrous tissue layer. However, it is important to note that in the idealized system used in this study, the offset at which the load is applied is perhaps similar to that in a locking plate, while devices with a larger offset, such as unilateral fixators, will result in much larger forces at the bone-screw interface. Moreover, it has been shown that deformations increase non-linearly as the external plate or frame bends, a phenomenon not included in this study. We only applied 500 cycles, as non-linear simulation takes considerable computational resources. Nonetheless, the trends show that the separation continues to increase. While the magnitude of the maximum and minimum principal strains is generally lower than the typically reported values for yield, they are not too far from yield values after 500 cycles of load application, particularly for the lowest BV/TV sample considered. It is also important to note that, while minimum principal strain occurs primarily in a direction radial to the screw, maximum principal strain is in the hoop direction. Steiner et al. reported that damage to the bone may occur due to the process of inserting the screw itself, with most damage occurring within a 300 µm radial distance of the screw. In this study, we assumed that the screw was inserted into bone without any damage. Consequently, this study is valid with respect to trends rather than actual quantitative values.

This study had limitations. We used single frequency of 1 Hz. It is reasonable to expect that the quantitative results will vary with the choice of frequency. However, the trends in the range of frequency that are not too dissimilar to the one selected here, are likely to be maintained. We found a clear trend with variation in BV/TV, but we only considered three samples. A statistical analysis that considers the influence of different BV/TV was not possible. So, while we expect the trend to be generally followed, we deliberately did not develop a relationship with respect to BV/TV. Previous studies on time-independent mechanical properties of bone have shown that, in addition to BV/TV, microstructure plays an important role. We expect microstructural anisotropy, in particular, will have a role in time-dependent properties. As the focus of this study was to examine the radial separation at the bone-screw interface, and not slippage due to pull-out forces, the threads of the screws were not included. The threads are likely to reduce loosening due to slippage when pull-out or push-in forces are applied. However, they generate stress/strain concentrations at the interface which may also accentuate loosening. We only applied 500 cycles; a larger number of cycles would increase the predicted separation. Lastly, time-independent elastic material properties were used for cortical bone and screws. The time-dependent effect on the screw is negligible, but cortical bone will also have time-dependent behaviour. Inclusion of time-dependent behaviour for cortical bone is likely to accentuate screw loosening even further.

The current study is more advanced than the conventional finite element analyses of the mechanics of the bone-screw interface, in which only time-independent material properties that are either elastic or inelastic, or assigned to bone. However, it does not consider a full bone-fixator construct. The importance of time-dependent effects at the bone-screw interface was discussed at least two decades ago, but these have not been previously included in models, due to a lack of experimental data and an absence of time-dependent constitutive models for bone. The developed non-linear viscoelastic-viscoplastic constitutive models permit the simulation of time- and cycle-dependent responses to be included in the analysis of bone-screw systems.

We can conclude that the loosening of an implant due to physiological activities can be predicted computationally by employing models that incorporate the time-dependent behaviour of bone. Implants are at a great risk of loosening in osteoporotic patients with a lower BV/TV. We know that secondary healing can be promoted by the application of cyclical loads that cause interfragmentary movement between fractured segments. Clinically, this implies that the need for the application of cyclical loads must be balanced against the risk of loosening before healing occurs.

**Supplementary material**

Details of the non-linear viscoelastic and non-linear viscoelastic-viscoplastic computational models used, as well as data for each of the three BV/TV values considered.

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Author Contributions
S. Xie: Designing and conducting the study, Analysing the data, Drafting the manuscript.
K. Manda: Developing the algorithm used in the study.
P. Pankaj: Designing the study, Analysing the data, Critically revising the manuscript.

Conflict of Interest Statement
None declared

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