Predicting and Designing Integrated Safety Syringe for Shelf Life Using Advanced Nonlinear Constitutive Models in ABAQUS

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***Abstract**: The Medical device industry is a highly regulated industry with patient safety being paramount. Ensuring the highest quality and patient safety demands that the device performs as desired from the time it is manufactured, through the shelf life of the product, and during use. Plastics used in medical devices can undergo degradation in mechanical properties over time during the product shelf life depending on the design of the device. It is therefore important to take this aspect of plastic behavior into account during material selection and device design. Plastics under constant load for long periods of time exhibit creep deformations. Testing devices for creep can be a lengthy process often leading to delay in design iterations to yield the optimum design and subsequently time to market. Computational modeling and FEA simulations with advanced material models can predict material behavior with a high degree of accuracy and can provide deep insights into how the device will perform over time resulting in valuable feedback for design iterations and often reducing design iteration cycles. In this paper, the short term and long term behavior of polycarbonate is modeled using hyperelastic-nonlinear viscoelastic model based on the parallel rheological framework. Constitutive model is calibrated against uniaxial tension and long term creep test data, is used to predict strain as a function of time in polycarbonate components of the Unifill Finesse™ Integrated Safety Syringe. Model predictions are validated against long term real time as well as accelerated aging test data. Typically these tests run for months. In summary, through this work, time consuming expensive design iterations through testing were reduced to a few cycles with accurate modeling and material creep strain predictions making use of advanced nonlinear constitutive models in ABAQUS demonstrating how FEA simulations can be leveraged as an effective tool in product development process to save time and cost and in bringing high quality products faster to the market.*

***Keywords**: Polycarbonate, Medical Devices, Syringe, Creep, Shelf Life , Hyperelastic, Nonlinear Viscoelastic*

1. Introduction

The use of polymers in medical devices is on the rise in the recent years and this is attributed to the versatility of polymers. The ability to engineer and customize polymers, in accordance with varied application needs, creates opportunities for greater usage of plastics in medical devices. As medical devices need to be increasingly smaller, more highly functional, and aesthetically pleasing, device developers and manufacturers look for ways to gain performance advantage,

reduce weight, and lower cost. As such polymers can be used to meet these needs with exceptional durability, flexibility, strength and good sterilization capability. With respect to mechanical behavior of polymers, shelf life, and aging capabilities, polymers can be very attractive when choosing the appropriate plastic material for use in medical devices. Both short term and long term mechanical behavior of polymers need to be considered when designing plastic parts in medical devices where accurate prediction of product shelf life performance is critical. Medical grade polycarbonate is often used in medical devices for its chemical and impact resistance and superior mechanical properties within the range of their application. In this paper, design for, prediction and validation of shelf life of medical grade polycarbonate components in the Unifill Finesse™ Integrated Safety Syringe, is presented. The short term as well as the long term behavior of polycarbonate is modeled using hyperelastic-nonlinear viscoelastic model based on the parallel rheological framework in ABAQUS. Model predictions are validated against long term real time as well as accelerated aging test data. The method described in this paper has also been successfully used in predicting creep behavior of other polymer resin components in the Integrated Safety Syringe as well as Wearable Injector platforms at Unilife Medical Solutions. However, in this paper, test data and validation has been presented for parts made of polycarbonate resin.

1.1 Product and Application Interest

Unifill Finesse™ Integrated Safety Syringe shown in Figure 1 is a primary container, drug delivery system and sharps containment system – all rolled in to one.

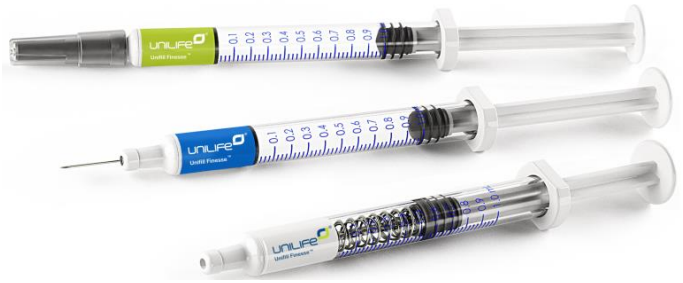


Figure 1. Unifill Finesse™ Integrated Safety Syringe

Automatic, user controlled retraction directly from injection site avoids exposure to a contaminated needle. Figure 2 shows end of dose configuration of the syringe with needle fully retracted into the glass barrel.

Figure 2. Automatic User Controlled Retraction at End of Dose

The needle retraction mechanism inside the Unifill Finesse™ Syringe is a spring loaded system in which functional plastic components are under constant load from compressed springs from the time it is manufactured to the time the device is used. This constant load during the shelf life results in creep deformations in the plastic components and it's critical that this creep behavior is taken into account during design to ensure the device will function as intended when used by the customer at any time within the product's shelf life. Aging testing of medical devices is time consuming often requiring months of testing to obtain results to inform subsequent design iterations. The testing approach can be effective but is time consuming and can extend time to market. FEA simulations with advanced material models can predict long term material behavior with high degree of accuracy and can provide valuable feedback for design iterations, saving on time and resources by substantially reducing the number of design iteration cycles (redesign, prototype and testing).

2. Material Characteristics

In this work, the focus is on unfilled polycarbonate (PC) resin Lexan 141R from Sabic Innovative Plastics. Plastic components in the Unifill Finesse™ Syringe are a medical grade variation of the Lexan 141R polycarbonate resin. Lexan 141R is an amorphous thermoplastic with exceptional mechanical and thermal properties. This resin exhibits excellent mechanical property retention over a wide range of temperatures as shown in Figure 3.

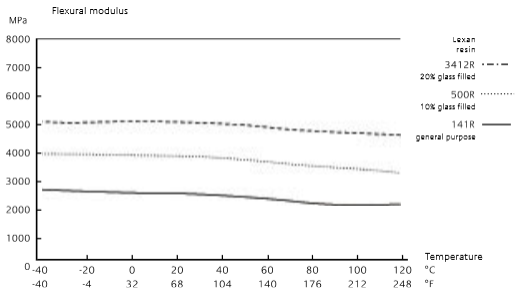


Figure 3. Flexural Modulus of Lexan Resin Grades as a Function of Temperature. (Reference 2)

Figure 4 shows nominal stress vs. strain curves for Lexan 141R resin for various temperatures. The tests were based on ISO 527. The stress strain behavior is nonlinear and it is important to capture this in the material model to predict the correct strain level in the part as soon as the part is loaded, for subsequent creep strain calculations. This behavior is typically captured by hyperelastic models as illustrated in material model section of this paper.

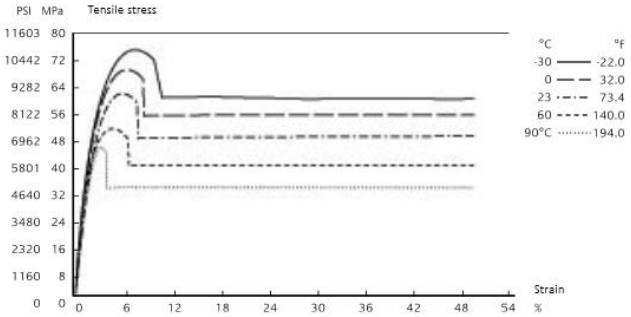


Figure 4. Stress-Strain Curves for Lexan 141R (ISO 527) at Various Temperatures. (Reference 2)

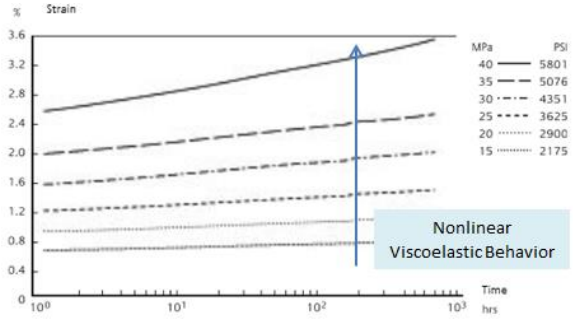


Figure 5. Creep of Lexan 141R Resin at 23^0C (ISO 899-1) (Reference 2)

Creep behavior of Lexan 141R resin based on ISO 899-1 at 23^0C at various stress levels is shown in Figure 5. As can be seen in the plot, the material has low creep behavior even at higher loads and this is due to its amorphous structure and this makes it a suitable material. The spacing between the strain vs. logarithmic time plot is not uniform between various stress levels suggesting that the material exhibits nonlinear viscoelastic behavior. In other words, the creep compliance is stress dependent. See Figure 6. The creep behavior of this material is dependent on the temperature however the temperature dependence is not considered in this work due to lack of test data at temperatures in the range of interest for the design.

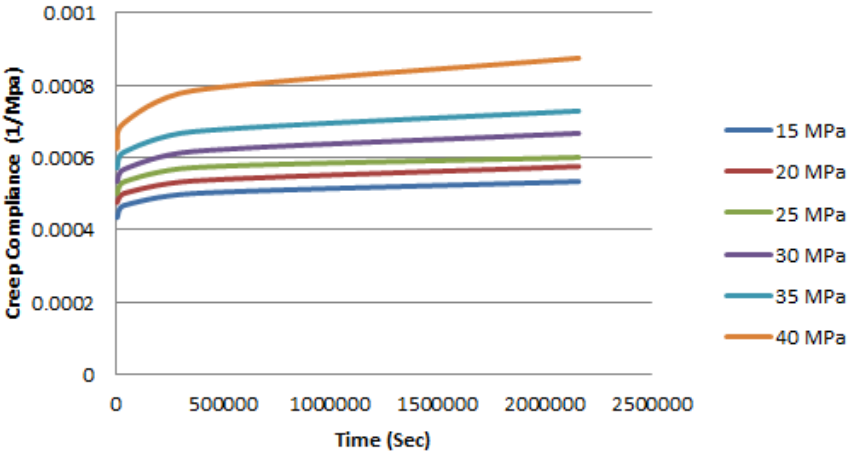


Figure 6. Creep Compliance as a Function of Time and Stress

3. Material Model

The material behavior of interest for the polymer resin considered in this work is the static nonlinear stress strain behavior and the nonlinear viscoelastic behavior. The constitutive model based on the parallel rheological framework in the ABAQUS material library is intended for modeling polymers that exhibit nonlinear viscous behavior and undergo large deformations and this model is chosen to model the material behavior of Lexan 141R resin.

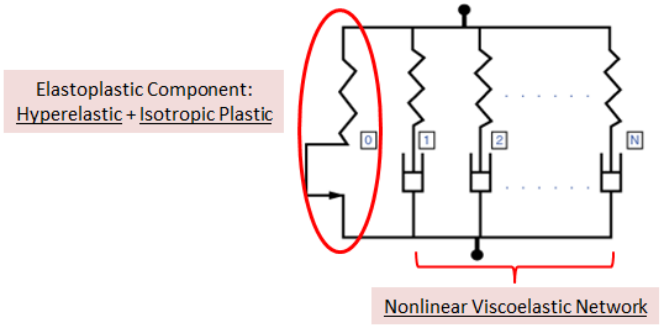


Figure 7. Parallel Rheological Framework

The model consists of multiple viscoelastic networks and an elastoplastic network in parallel. The elastoplastic component consists of hyperelastic model to capture nonlinear large deformations and an isotropic plastic component to capture yielding in the material. The viscoelastic network captures long term creep response of the material.

3.1 Hyperelastic Model

The nonlinear elastic large deformation exhibited by the material is modeled using a 3rd order reduced polynomial strain energy function also known as the Yeoh model. The strain energy potential of a reduced polynomial model is shown in Figure 8.

$$U = \sum_{i=1}^{N} C_{i0}(\bar{I}_1 - 3)^i + \sum_{i=1}^{N} \frac{1}{D_i}(J^{el} - 1)^{2i}$$

$C_{i0}, D_i, and\ N$: *Material parameters*
$\bar{I}_1$: *First deviatoric strain invariant*
J^{el}: Elastic volume ratio

Figure 8. Strain Energy Potential of a Reduced Polynomial Model

The model is calibrated using the static stress strain data at 23^0C presented in Figure 4. Figure 9 shows model prediction compared to test data.

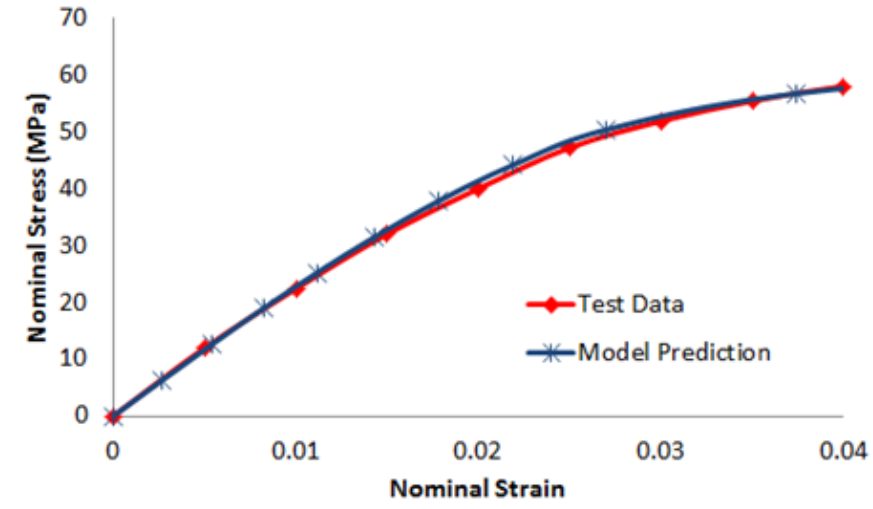


Figure 9. Model Prediction Compared to Test Data at 23^0C

3.2 Nonlinear Viscoelastic Model

Viscous behavior for the viscoelastic network is modeled assuming a multiplicative split of the deformation gradient and existence of a creep potential. Flow rule is derived from the creep potential and evolution law for the equivalent creep strain rate $\dot{\bar{\varepsilon}}^{cr}$ is a power law strain hardening model and stiffness ratios for each network is provided. Evolution law for the creep strain rate is shown in Figure 10.

$$\dot{\bar{\varepsilon}}^{cr} = (A\tilde{q}^n[(m+1)\bar{\varepsilon}^{cr}]^m)^{\frac{1}{m+1}}$$

$\bar{\varepsilon}^{cr}$: Equivalent creep strain
$\tilde{q}$: Equivalent deviatoric Kirchoff stress
$A, m, and\ n$: $Material\ parameters$

Figure 10. Evolution Law for the Creep Strain Rate

Model is calibrated using the strain vs. time data presented in Figure 5. Number of networks considered is 2. Figure 11 shows model prediction compared to test data.

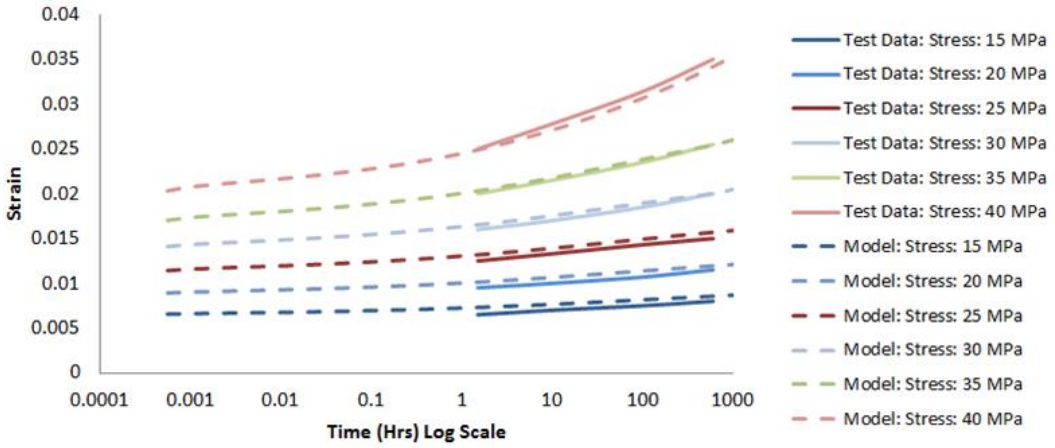


Figure 11. Model Prediction Compared to Creep Test Data at 23^0C

4. Shelf Life Prediction

The part shown in Figure 12 is an active component in the retraction mechanism of the Unifill Finesse™ syringe and is under constant spring load until the retraction mechanism is activated at end of dose of syringe. This component undergoes creep deformation during shelf life.

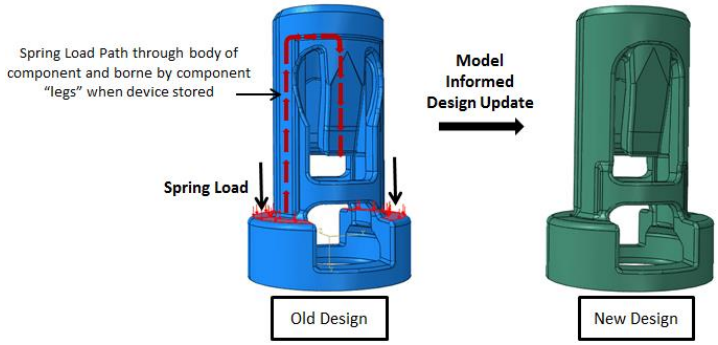


Figure 12. Active Component in the Retraction Assembly of the Syringe

Analysis is performed using ABAQUS/Standard as a two-step process. Step 1 is a static loading of the part to mimic part behavior immediately after installation and step 2 is a creep analysis to analyze part behavior during shelf life. The material model is the parallel rheological model described in the paper. Principal stress and principal strain in the old and new design at time=0 (i.e., immediately after installation) are shown in Figure 13 and Figure 14 respectively.

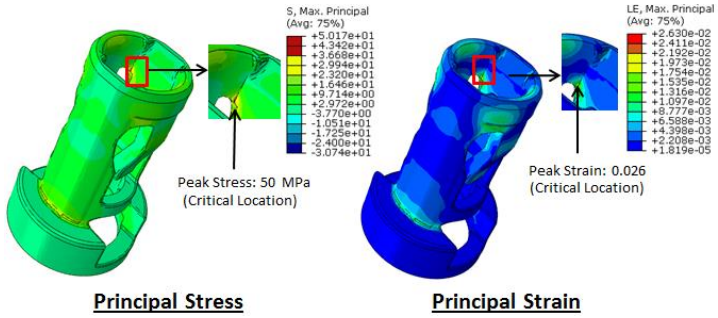


Figure 13. Principal Stress and Strain in Old Design Immediately After Installation

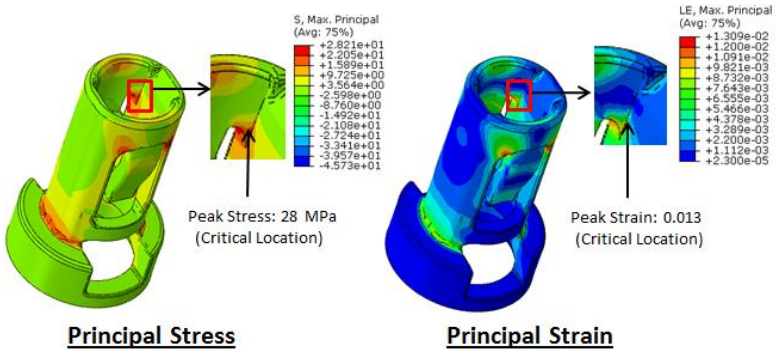


Figure 14. Principal Stress and Strain in New Design Immediately After Installation

The results shown in Figure 12 and Figure 13 show the critical locations within the part which are considered as the areas of greatest stress concentration. These critical locations will therefore be the area of interest for the creep analysis. Principal stresses and strains are considerably lower in the new modified design compared to old design. While the maximum principal stress in the old design is well within the elastic range (suggesting stress level is acceptable), the creep calculations at the critical location (Figure 13) identified in the model predicted failure of the part during shelf life. See strain vs. time plot in Figure 16.

Creep analysis in step 2 is performed using *VISCO procedure in ABAQUS/Standard and the time period used in this analysis is seconds equivalent of 4 years to mimic shelf life of the device for 4 years. Results from creep analysis yields strain as a function of time at any location of the part. The objective is to design the part such that the max strain in the part at the end of 4 years is well below the yield strain of the material ensuring the part stays intact and does not fail during installation or during shelf life. Figure 15 shows creep analysis results of the final design of the part and as can be seen in the results, max principal strain is ~30% of the yield strain.

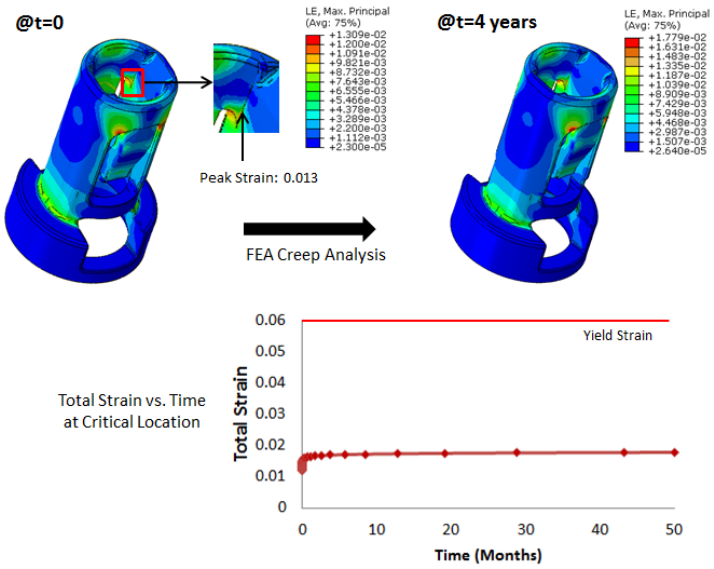


Figure 15. Creep Analysis Results for the New Design

Figure 16 shows a comparison of total strain as a function of time plot for the old and the new design. As can be seen in the plot, the total strain exceeds the yield strain of the material for the old design and this is assumed as failure strain as per design requirement. As predicted by simulation, the parts during accelerated shelf life testing were indeed observed to fail with cracks originating at the critical locations.

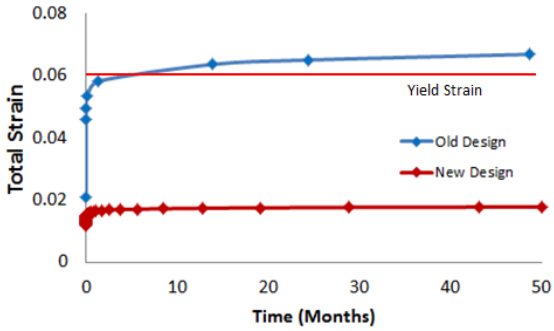


Figure 16. Total Strain vs. Time Comparison for Old and New Design

For creep analysis, alternatively, since the part is load controlled (through a constant force application from compressed springs which does not degrade over time), strain as a function of time at the critical location of interest can also be calculated analytically based on the strain value immediately after installation and using the Bailey Norton power law to characterize creep strain as a function of time at the stress level estimated immediately after installation. This is illustrated in Figure 17.

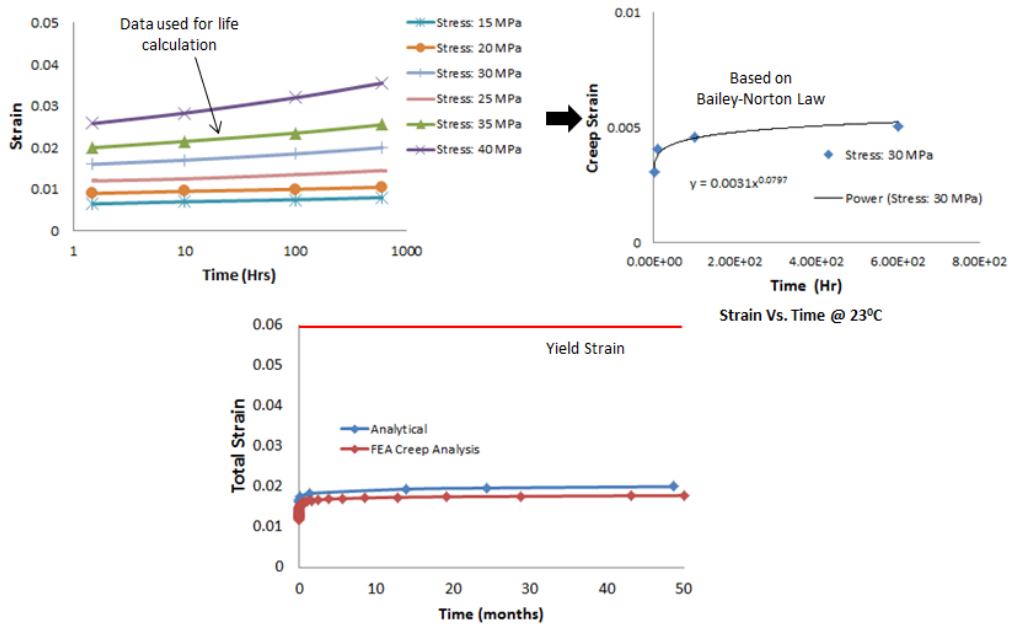
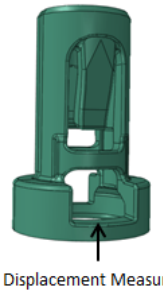


Figure 17. Analytical Calculation of Total Strain as function of Time

Total strain as a function of time predicted by the analytical method matches very well with FEA prediction and this compliments each method. There is a slight difference in the results and this is due to the fact that the analytical calculations are performed at 30 MPa whereas the actual stress is 28MPa which is correctly accounted for by the nonlinear viscoelastic model. For the analytical calculations, creep curves at stress levels not readily available as a test data require an additional extrapolation step to estimate creep rate at the desired stress level. This process can be tedious and yields only approximate results. However, creep rate as a function of stress is directly captured by the nonlinear viscoelastic model, and furthermore any stress change due to creep deformations in the part is directly accounted for during creep analysis. Using the material model, strain state as a function of stress and time at any location on the part is readily available from FEA results.

5. FEA Validation with Test Data

The simulation result and prediction are well supported and validated by long term real time as well as accelerated aging testing. Devices were tested at various time points (6 months, 12 months, 18months etc.) for the components, sub-assemblies as well as full device performance. Real-time aging for components and sub-assemblies is performed at controlled room temperature of 20^0C - 25^0C per USP 659 general notices and requirements and accelerated aging is performed at 40 ± 2°C, 75 ± 5% RH per ICH Q1A. Figure 18 shows the axial displacement of the lower platform at time t=0 sec and at time t=12 months. FEA predictions correlate very well with test data.



	Test Data	FEA Prediction
@t=0 After Assembly	1.02 mm	1.03 mm
@t=12 months After Storage	1.09 mm	1.11 mm

Figure 18. FEA Prediction Compared to Component Level Test Data

Axial displacement correlation provides a good validation for simulation results. In addition to quantifying displacement within the test devices, the part integrity and full device (i.e., assembled syringe) performance were evaluated. A visual inspection of the part first shown in Figure 11 was completed. As predicted by FEA (see Figure 19) no visual defects were observed in N=60 samples tested after being aged for 7 months real time (i.e., 7 months real time at 20^0C - 25^0C conditions) Additionally as predicted by FEA with only small changes in geometry predicted by the creep analysis, the N=60 samples were tested for proper function in device activation.

	Aging Time	Samples	Result
Unfilled	7 months	30	100% Pass
Filled	7 months	30	100% Pass

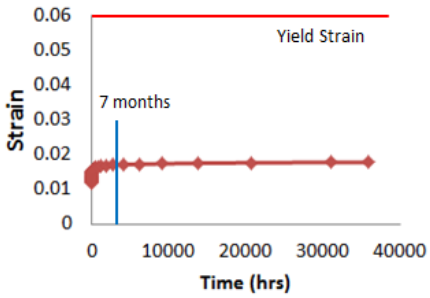


Figure 19. FEA Prediction Compared to Full Device Test Data

To further validate this method, simulation was performed on Unifill® Syringe which uses the same Lexan resin material and is subjected to similar stress levels as the Unifill Finesse™ Syringe. Simulation predicts that total strain levels at the critical locations are well below the yield strain limit immediately after installation as well as during long term storage. See Figure 20. These results are in very good agreement with test data. Real time testing shows no visual defects observed in 2000 real time 30 months aged samples and all samples performed as intended.

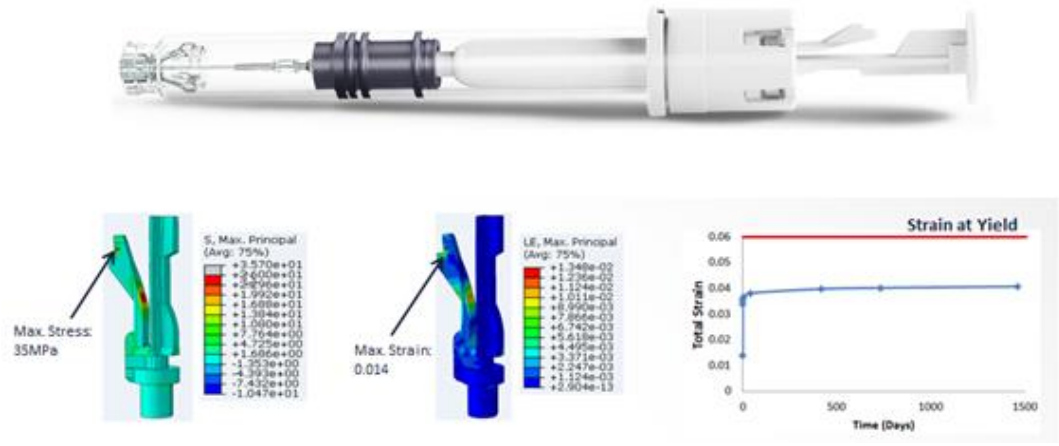


Figure 20. Creep Analysis on Unifill® Syringe

6. Summary

Nonlinear viscoelastic material model based on parallel rheological framework has been successfully used in designing polycarbonate components in Integrated Safety Syringe products at Unilife Medical Solutions. Similar methodology and constitutive models has been successfully used in reliable design of other polymer resin components in the Integrated Safety Syringe as well as Wearable Injector platforms. Through simulation, design iterations running into months of design-prototype-testing cycles has been reduced to 1 cycle and components optimally designed for performance, assembly and manufacturability have been performing as desired at various stages of shelf life testing. Further, effects of creep combined with geometric tolerance on components have been successfully integrated into FEA simulations to study variation in user profile force as well as activation force. Unilife product development teams have immensely benefited from using advanced FEA, CFD as part of design work resulting in robust elastomeric, plastic as well as metal components for various drug delivery platforms at Unilife. Integrating FEA simulations early in the product development cycle and using advanced modeling methods have resulted in reliable high quality products and with significant savings in time and cost.

7. References

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