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Flexural fatigue behavior of rocking bioreactor films

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Flex Fatigue in Bioprocess Films

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Imagination at work.

GEHC Single-Use Disposable BioProcess Products

Xcellerex™ XDR, Wave™ & Xuri™ Bioreactors
(PL-01077/026, Bioclear 10 & 11)

ReadyToProcess™/ReadyCircuit™
(ReadyKleer)

Hyclone & PAA Media/Reagents
(CX-514, ReadyKleer, Flexboy)

Multilayer Bioprocess Films:
Range of use conditions pose unique challenges across product lines

- Xcellerex: Pressure
- HyClone/PAA/RTP: Abrasion
- Wave: Flex Fatigue

WAVE Bioreactor™ Products

Rockers, Pumps & Controls

Sensor-Enabled
Disposable CellBags

Rocking action enables gas exchange, fluid mixing & suspension for batch, fed-batch & perfusion culture of a wide range of cell types.

Flex Fatigue Resistance

Motivation

- Flexural fatigue of folded film during rocking → Film stresses can progress to loss of bag integrity
- Standard testing (Gelbo, tensile, etc.) do not reproduce fatigue mechanism
- Rare, but highly impactful failure mode

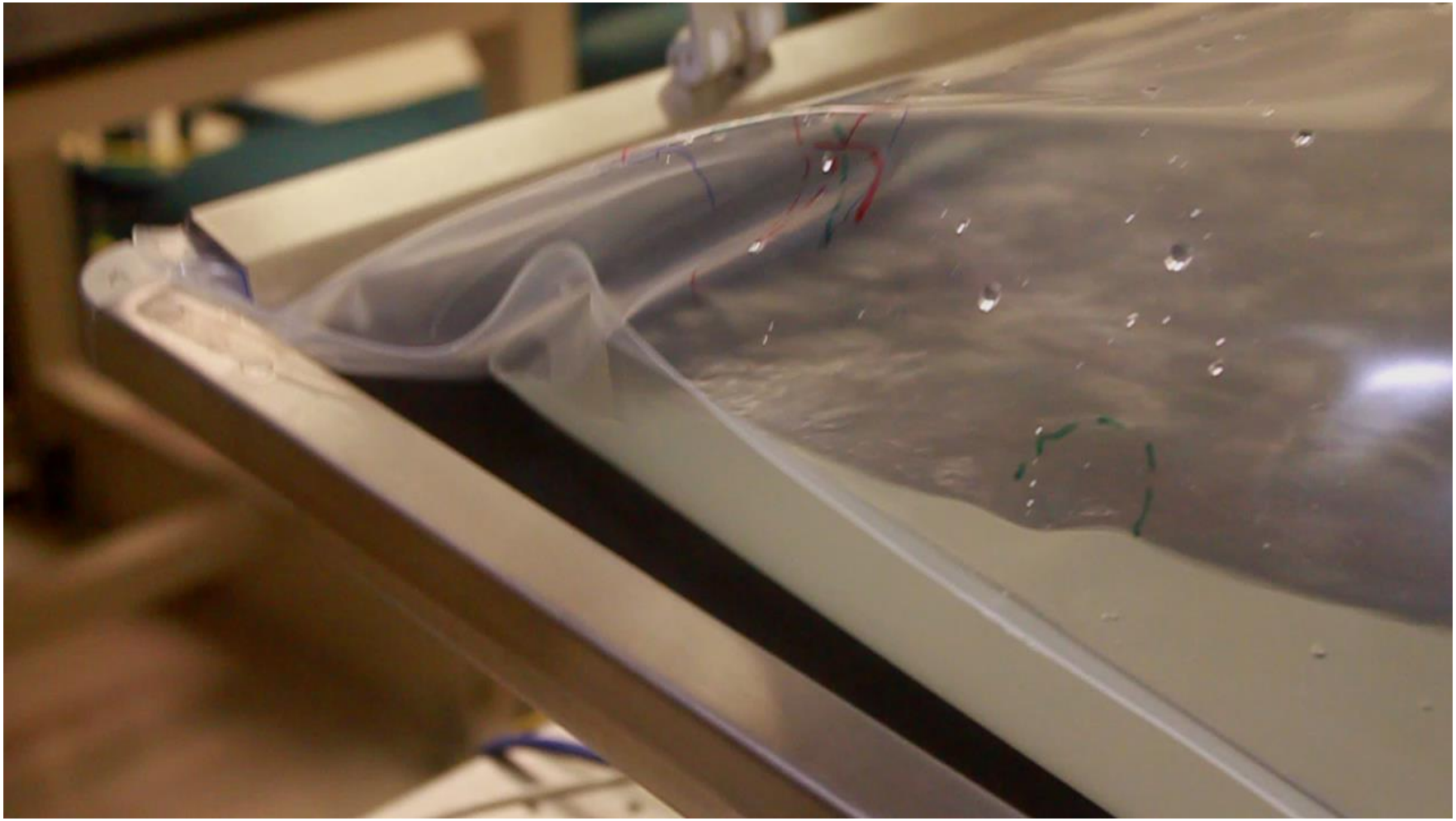
Test Method

- High Rock Rate/Angle (25rpm/9°)
- One 50L bag per rocker for >30 days
- Does not necessarily test bags to failure
- Low throughput, variable test

Goal: Develop a more rapid & reproducible flex fatigue test for Wave™ Bioreactor Films

Understanding Bag Mechanics on Wave Rocker

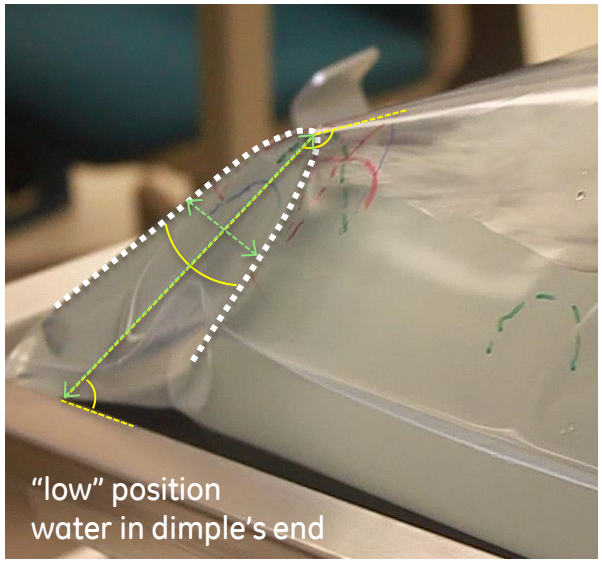
50L Cellbag™, 24L water, 25 rpm, ±10 °

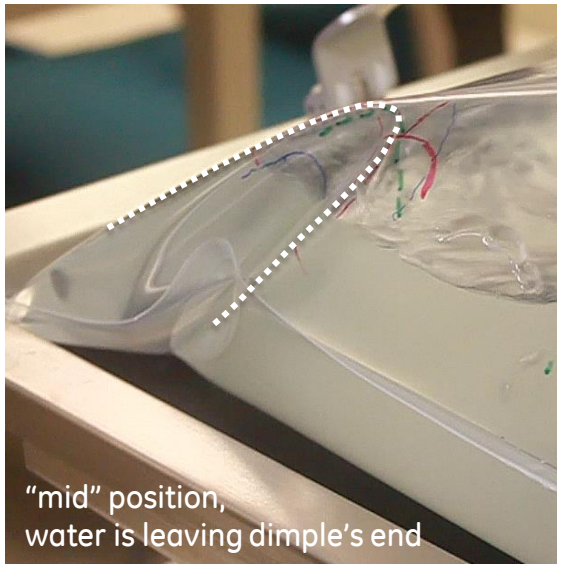


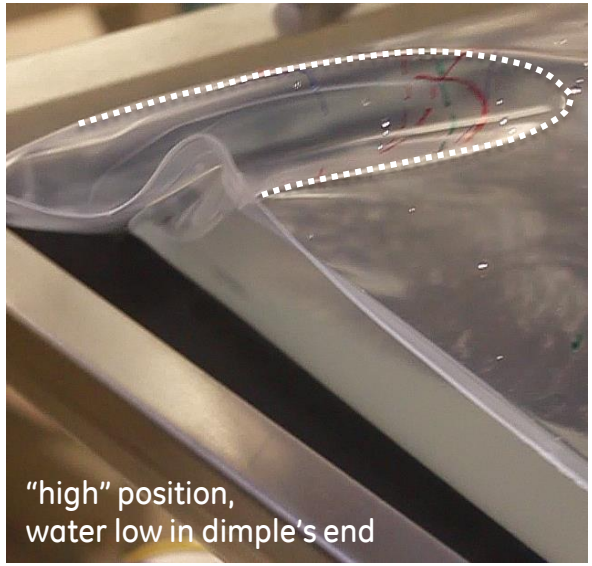
BioClear 10 50L WAVE CellBag

WAVE Rocker Testing

Analysis of real-world fold geometries on 50L WAVE CellBags







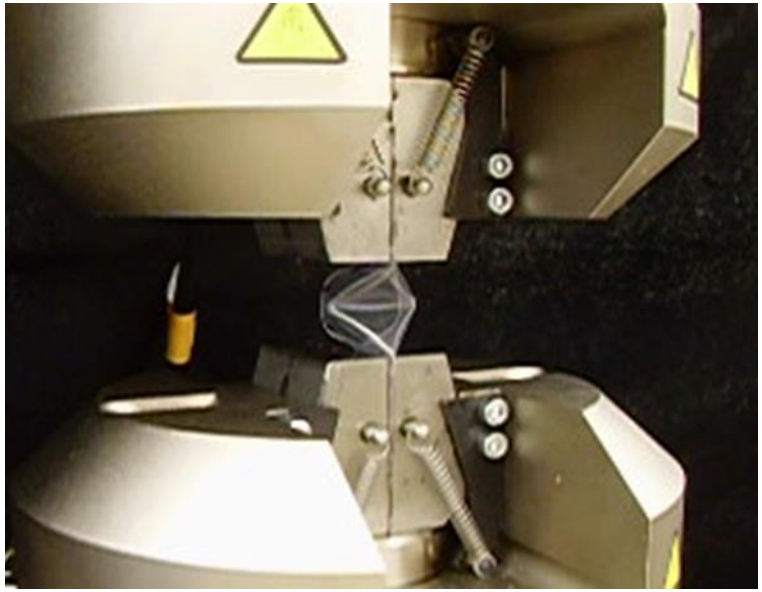
- Quantified static & rocking dimple geometries to understand film stresses
- Mechanism: Dimples roll, pivot & elongate during rocking generating local stresses in the film

Combined tensile + bending action on film results in fatigue

Flex Fatigue Test Method Evolution

Test Evolution

- Conventional flex tests are uncorrelated to rocker results
  - ASTM 2D, Gelbo, etc.
- Need greater constraint of ductile films to induce failure
- 3D "minibag" devised to reflect flex fatigue in Cellbags



GRC Flex Fatigue Test Approach:

- Reproducible dimple formation → fixed geometry
- More severe fold geometry → increased stress
- Rapid cycling of the fold (1Hz) → faster failure

Flex Test Progression:
Stages of Failure Seen in Wave Rocker Test and Flex Test

Rocker Test
(BioClear 10 film)

Flex Testing
(BioClear 10 film)

whitening

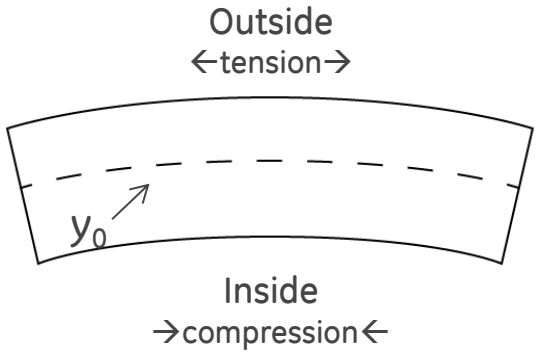
delamination
and/or crack

film break and leak

Flex Test Reproduces Sequence of Events in path to failure

Film Geometry

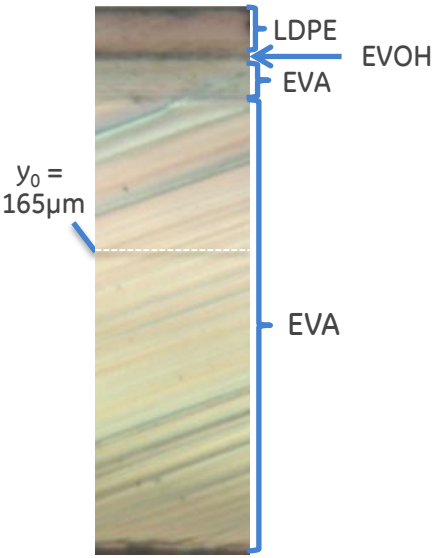
Neutral Plane: Film flexure causes tensile & compressive stresses, which are minimized near the neutral plane (y_0)



$$y_o = \frac{1}{2} \times \frac{\sum_{i=1}^{n} E_i \times \left(h_i^2 - h_{i-1}^2\right)}{\sum_{i=1}^{n} E_i \times (h_i - h_i)}$$

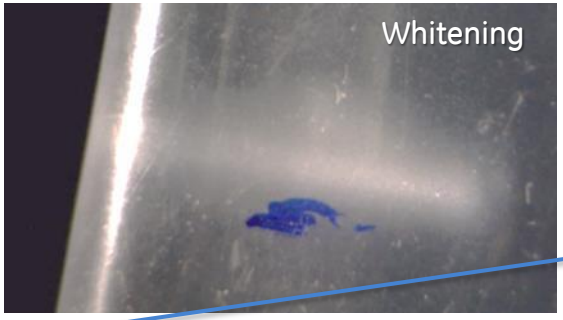
h - layer thickness
E – Young's modulus
y_0 – neutral plane

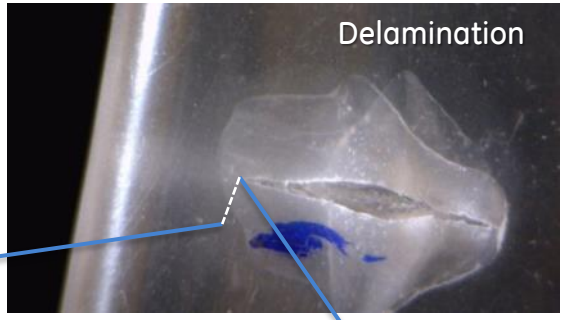
BioClear 10/11
(300µm)

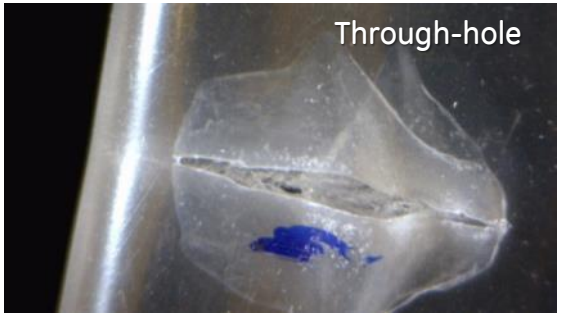


Flex Fatigue Failure Analysis – BioClear 10

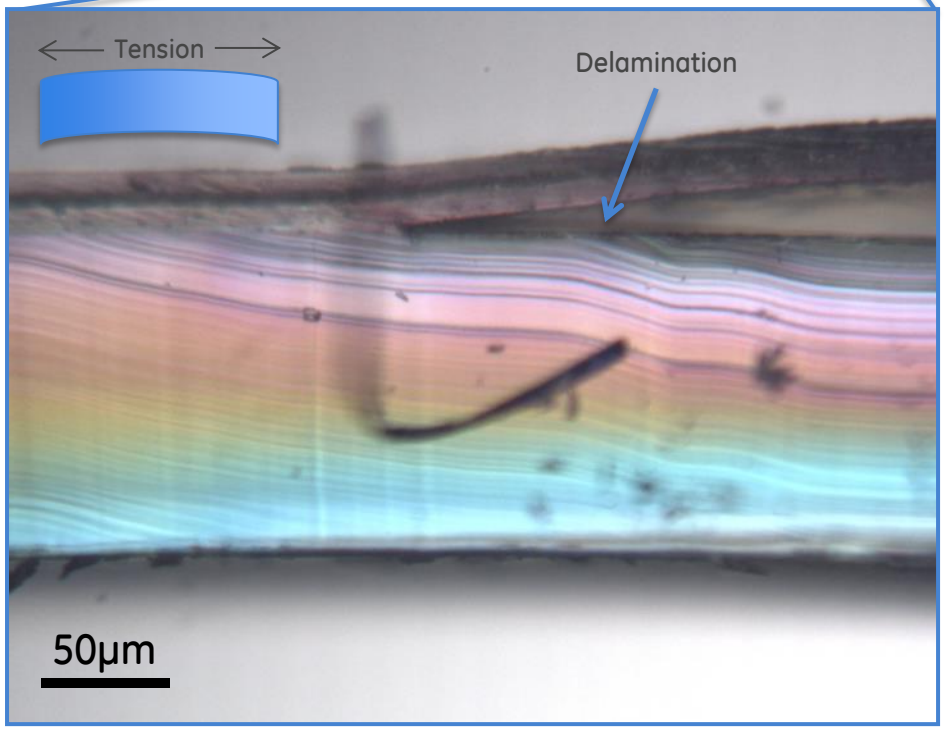
External View

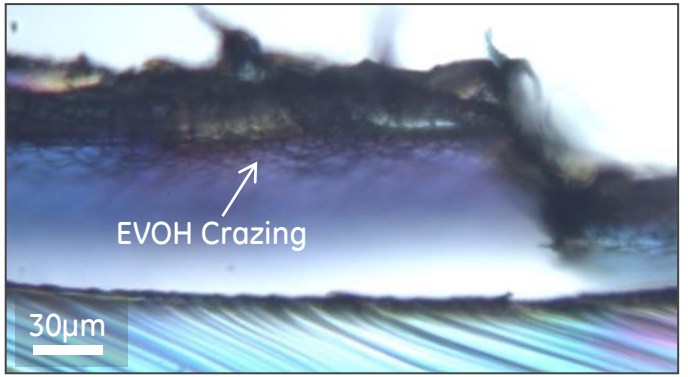






Cross-Section



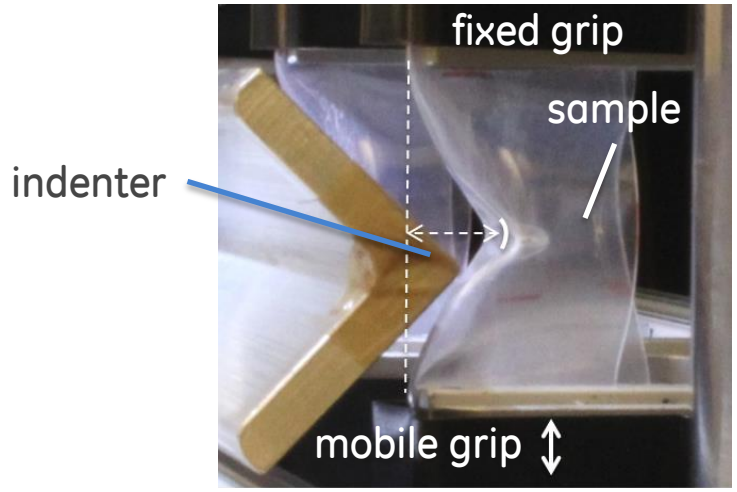


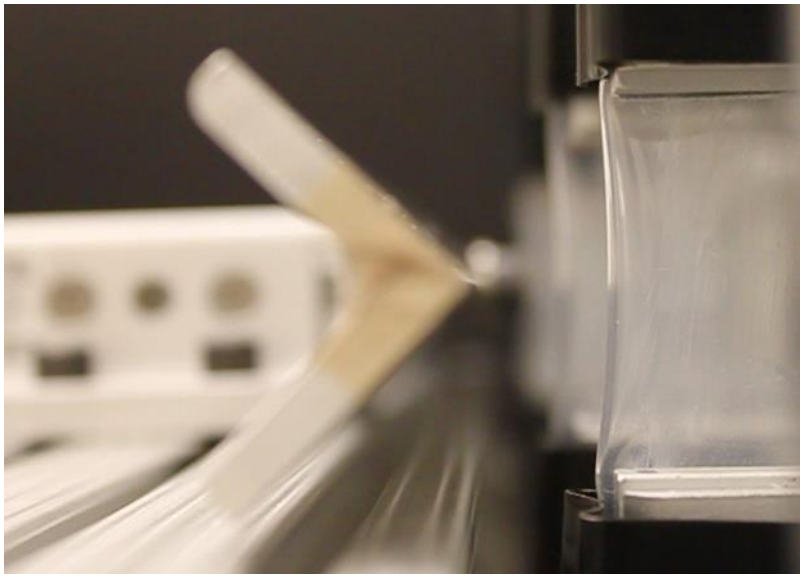
Test Parameters

Mounting
- Positioning – fixed grip distance
- Preload (2 lb. nominal)
- Gripping (mechanical or hydraulic)

Indent
- Depth & radius of curvature mimic, but exceed rocker geometry

Flexing
- Frequency: 1 Hz → 24 hr. test for current prototype films
- Flexing waveform: sinusoidal (analogous to Wave)
- Flexing amplitude: Exceeds dimple flex amplitude on rocker

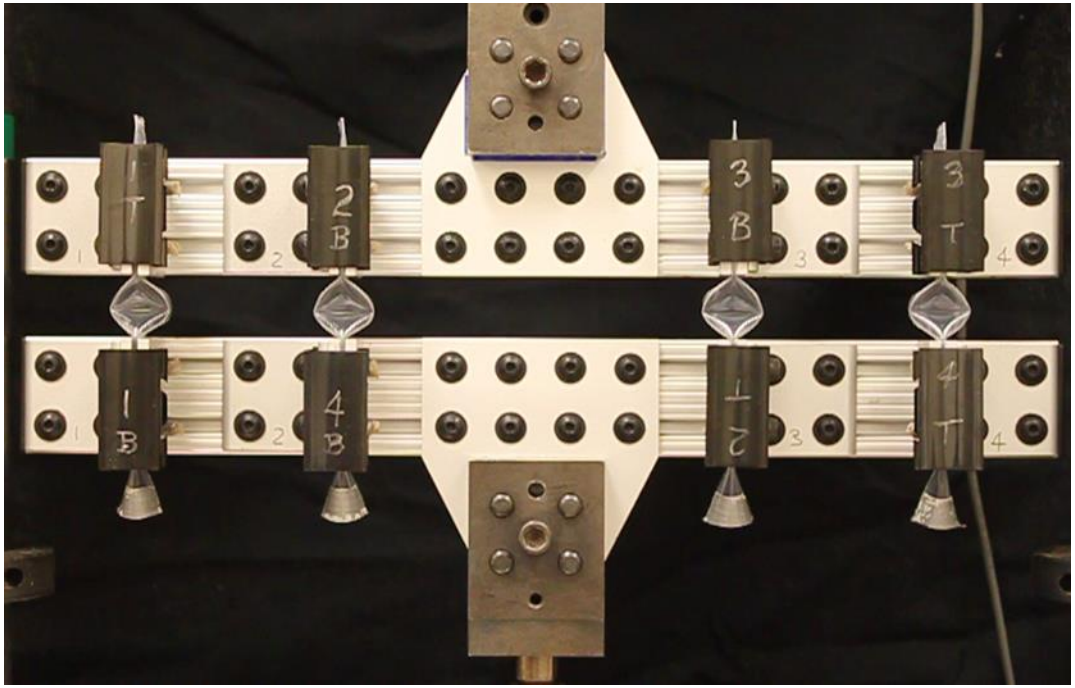




Set parameters to imitate rocker dimple, and to generate reproducible data

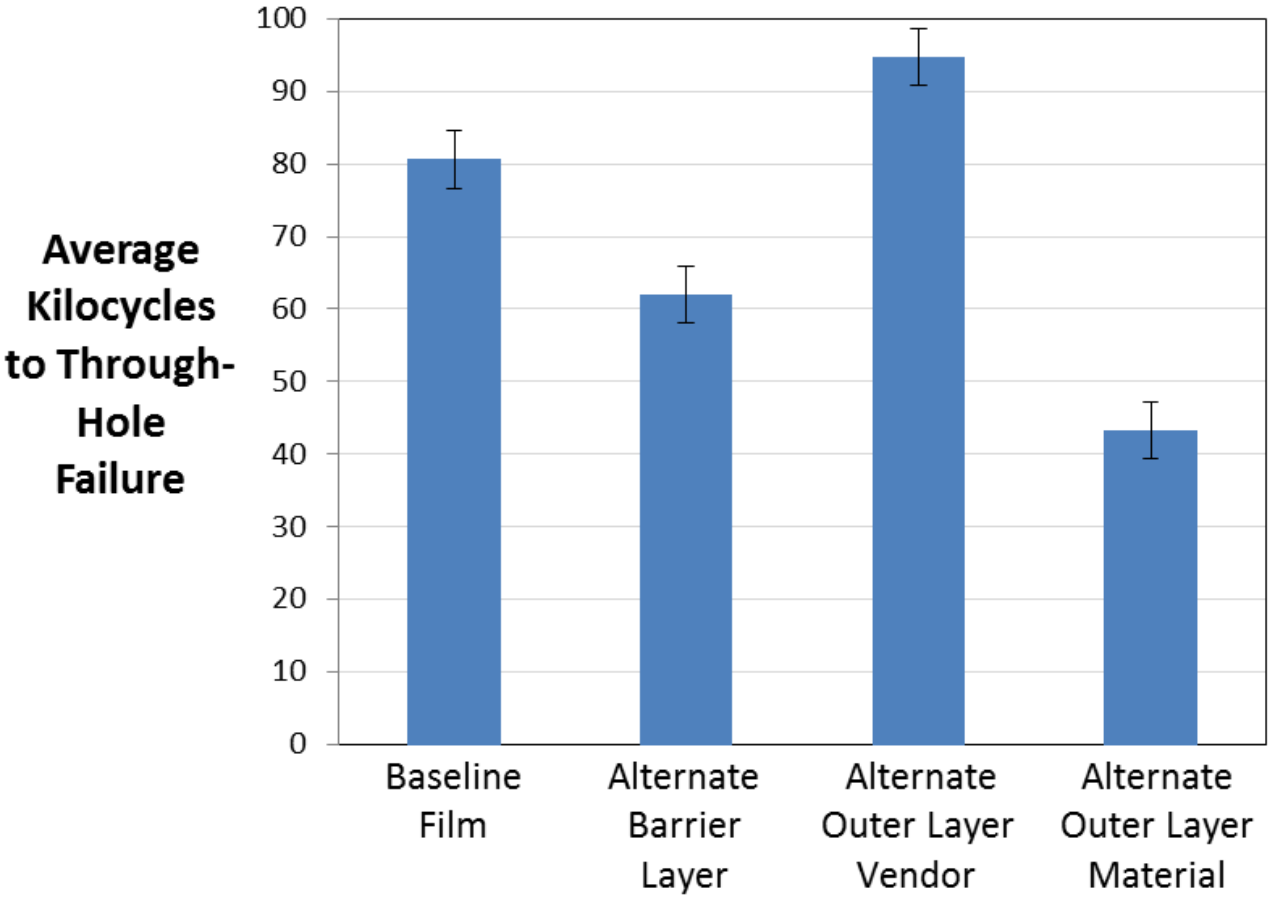
Parallel Testing: multi-sample "4X" Tester

- 4 samples mounted/ Indented/tested simultaneously
- Periodic dye test to detect through-holes
- Acquire fatigue data quickly to develop high level of statistical confidence



Research tool to assess flex fatigue resistance

4X Flex Fatigue Testing – Prototype Variants



Discriminates flex behavior of films to > 95% confidence

Summary

- A single film for use across a wide range of applications requires a balance of properties → need rapid assessment of prototype film performance
- WAVE is an extreme example of film flex fatigue (bulk liquid shipment, intermodal RTP shipment, STRs) → Films designed to exceed WAVE needs will exceed needs for other applications
- Developed a simple constrained flex test enabling discrimination of flex fatigue resistance in candidate films with high statistical confidence
- Cross-sectional microscopy elucidates failure sequences of different films, to guide decisions on structure optimization for flex fatigue
- Rapid screening of film candidates enables thorough rocker testing of promising candidates → reduce design cycle time & increase confidence