Best Practices for Glass Primary Containers; 09-Oct-2019; Mainz, Germany

Strength and reliability of glass containers used in the pharmaceutical industry

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Parenteral Drug Association

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Outline

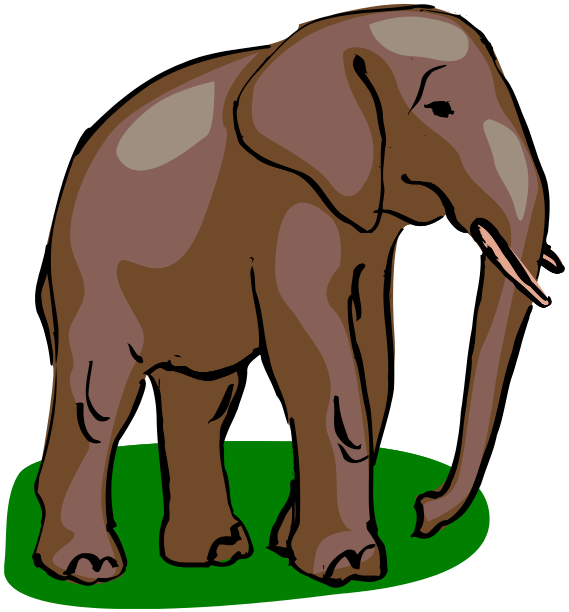
- Glass Breakage – Fundamentals
- Assessment of flaws
- Fractography – Fundamentals

Glass Breakage – Fundamentals

“Crackademy“

Glass breakage

- Or – what does glass have in common with an elephant?



Root cause for glass breakage

- Simultaneous presence of
  - Flaw (critical in terms of mechanical strength)
  - Mechanical load (tensile stress) at flaw
- Interaction of critical flaw and mechanical load (“stress intensity”) reaches critical value
  - “Breakage resistance”

Glass breakage: *Surface flaw × tensile load ≥ breakage resistance*

stress intensity

Different cases

- No breakage if no or only one factor is present
- Flaw and mechanical load occur simultaneously
  - Impact
- Flaw is created prior mechanical load
  - Depyrogenization/heat sterilization
  - Lyophilization/freeze drying
  - Auto-injector
- Flaw is introduced while mechanical load is already present
  - Residual stresses
  - Constant internal pressure

Definition of “flaw”

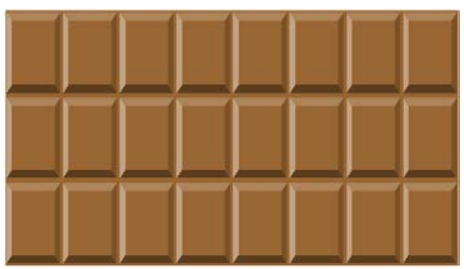
- Any type of discontinuity within the isotropic, monolithic structure of the glass (including the surface) can act as flaw
  - Foreign material
  - Voids
  - Surface irregularities
- Discontinuities act as concentrators for mechanical stresses
- Also variations in geometry
- Size (dimension) and shape (geometry) of discontinuity affect criticality
  - Large flaws can exhibit low criticality
  - Small flaws can exhibit high criticality

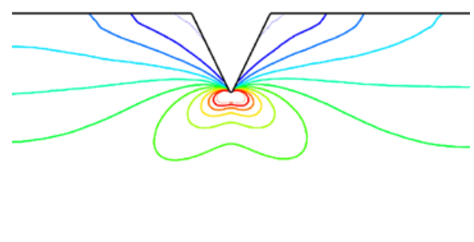
Any type of discontinuity within the isotropic monolithic structure of a glass (including the surface) can act as flaw and become critical in terms of strength

- Criticality affected by size and shape

Intensification of stresses

- Discontinuities act as concentrators for mechanical stresses
- Example: Bar of chocolate
  - Notches act as stress concentrators (“surface flaws”)
  - Contribution of notches to stress intensity factor ≈2 higher than for plane bar
  - Lower tensile loads (≈1/2) for breakage required



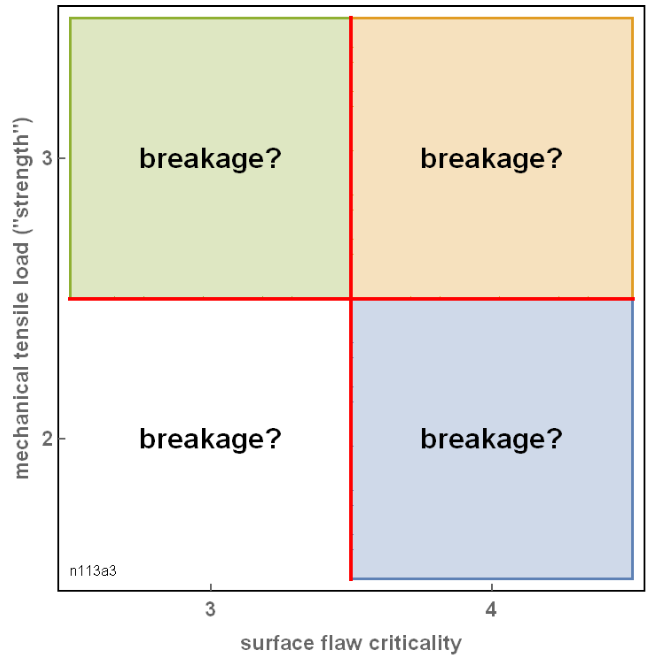


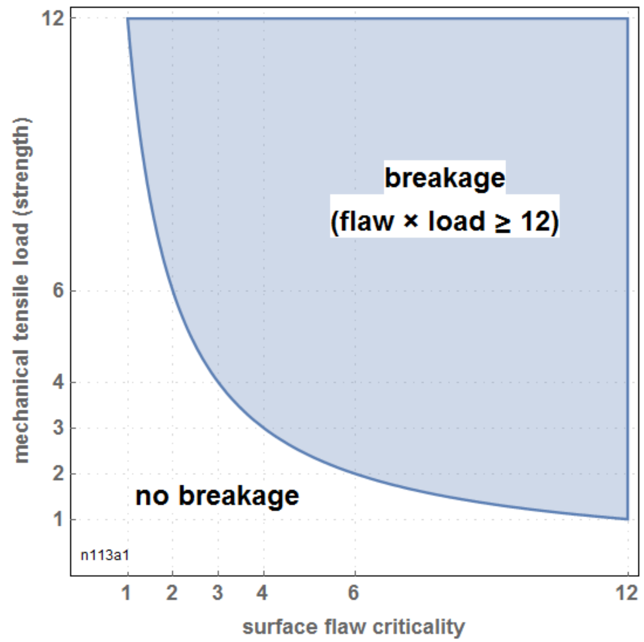
	surface flaw	×	tensile load	≥	breakage resistance
plane	1	×	12	≥	12
notched	2	×	?	≥	12

„strength“

Determination of failure criteria

- Definition of strength: Mechanical resistance against breakage
  - Value/magnitude of mechanical load at which breakage occurs





Determination of failure criteria

- Definition of strength: Mechanical resistance against breakage
  - Value/magnitude of mechanical load at which breakage occurs

Glass breakage: Stress intensity ≥ breakage resistance

- Strength depends on combination of flaw and load contribution

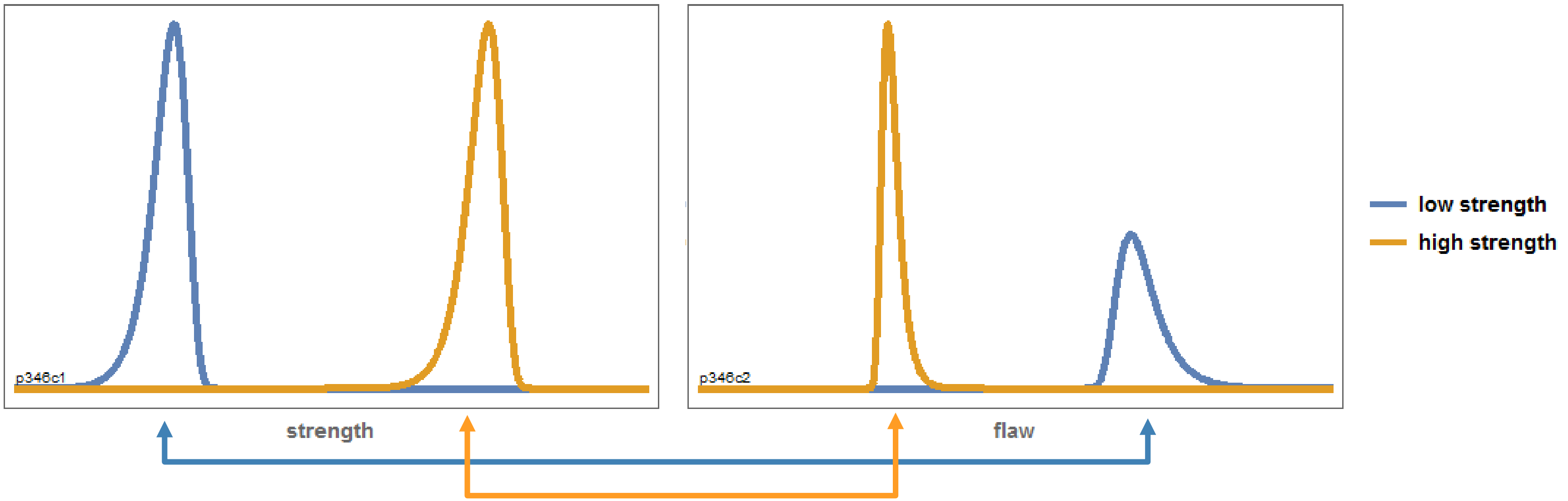
The strength of glass is *not* a material constant

The strength of glass is a projection of its surface quality

- Surface quality defined by flaw size (distribution)

Determination of failure criteria

- Flaw size distribution → strength distribution
  - Large flaws → low strength
  - Small flaws → high strength



Determination of failure criteria

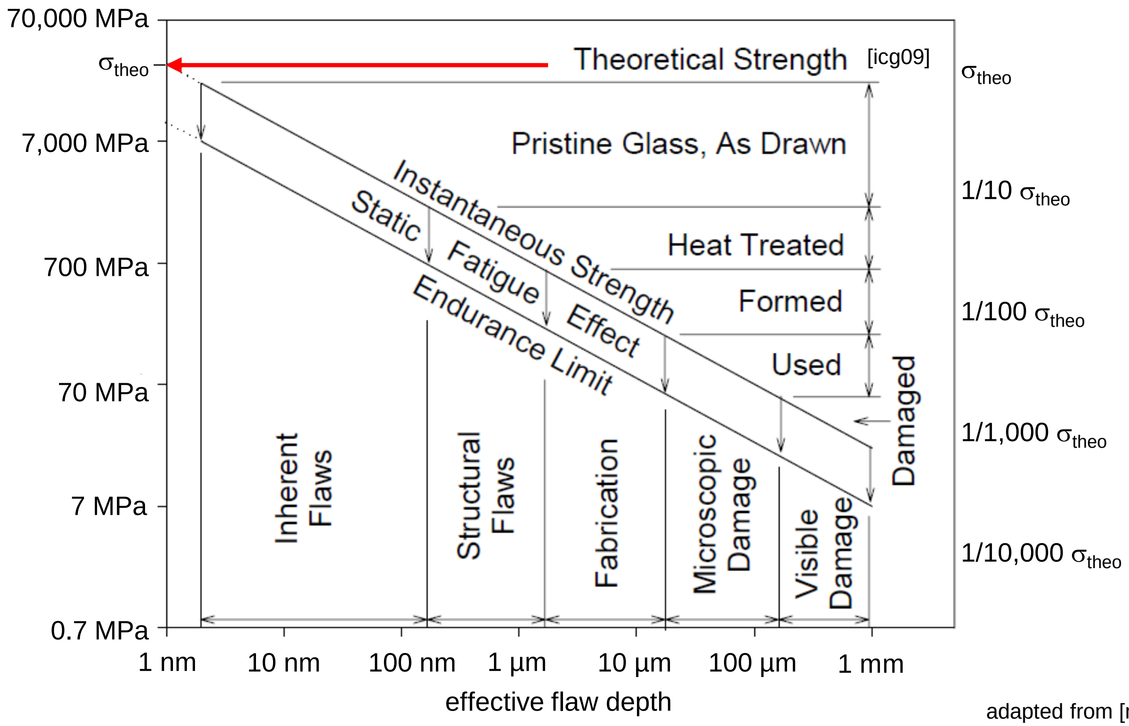
- The surface quality of glass is defined by the
  - Type(s)
  - Criticality (shape)
  - Size distribution(s)
  - Number/amount

  of surface flaws
- Every glass surface contains flaws
- A perfect glass surface without any flaws does not exist

Consequence: Flaws limit the strength of a glass solid

Reduction of strength

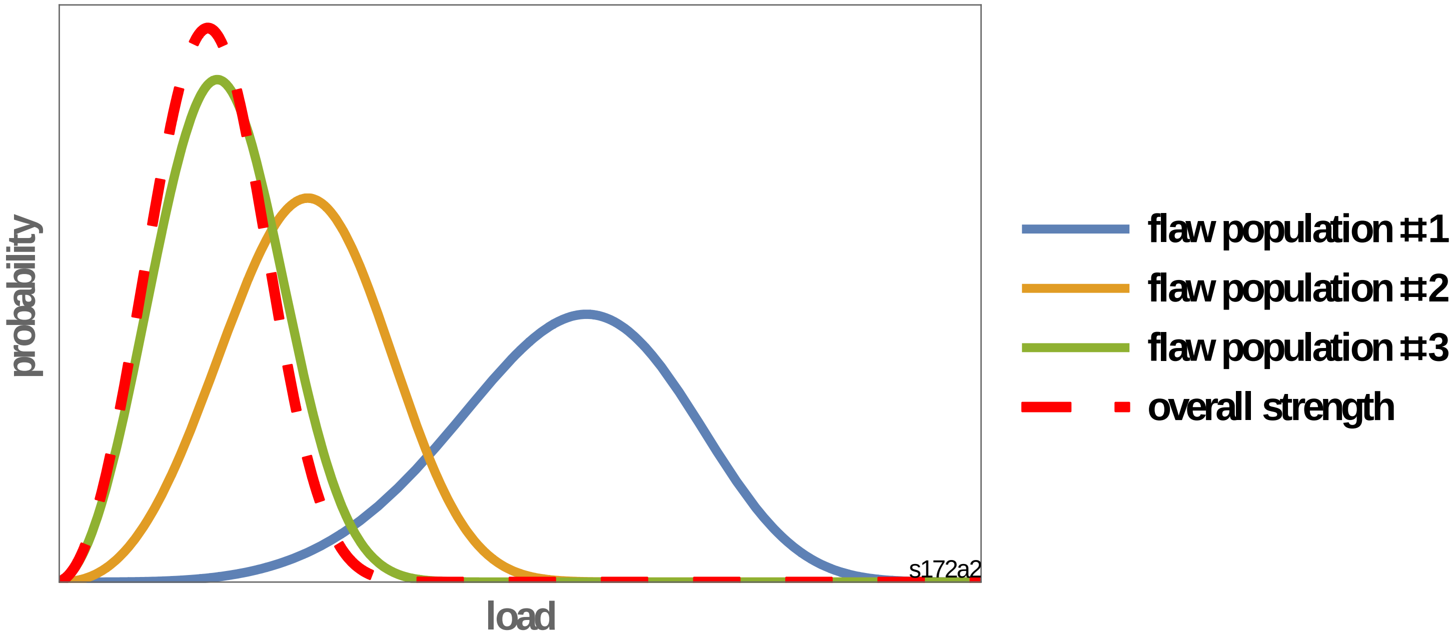
- Increase in flaw size (depth) reduces strength



adapted from [moul67]

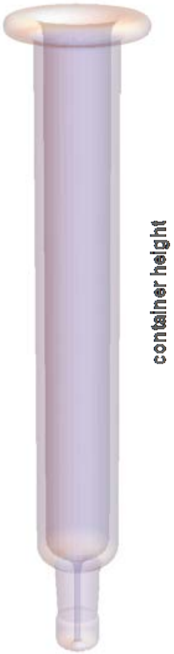
Multiple flaw populations

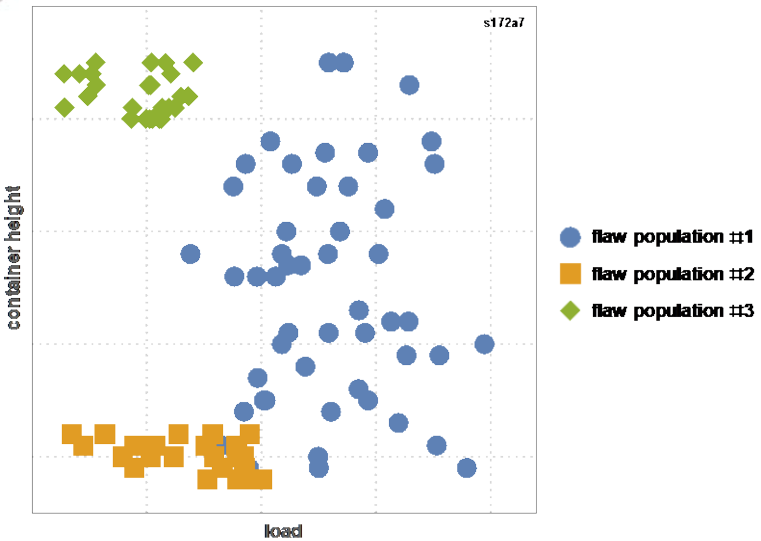
- The distribution of the most critical defects dominate the overall strength



Multiple flaw populations (example)

- Reference sample: after process step
- Damaging during process step
- Burst-pressure strength experiments
- Fractographic examinations
- Location of fracture origin



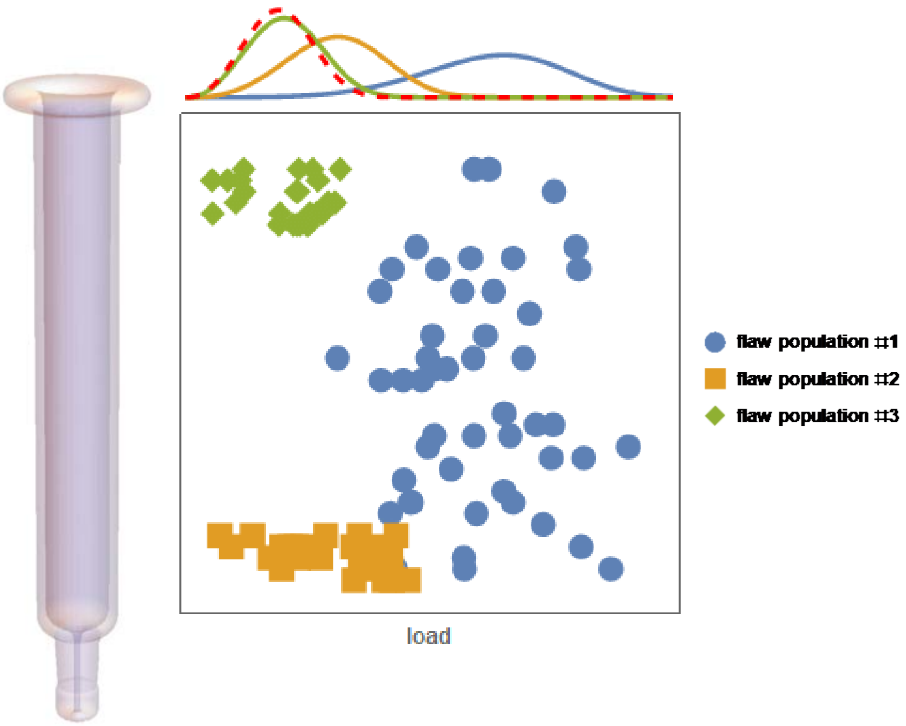


Most important requirement for smart/gentle strength improvement: Identification of most critical flaws

Multiple flaw populations (example)

- Systematic strength improvement
  - Identification and quantification of most critical flaw
- Stepwise elimination of damage mechanisms
  - Stepwise improvement of strength distribution

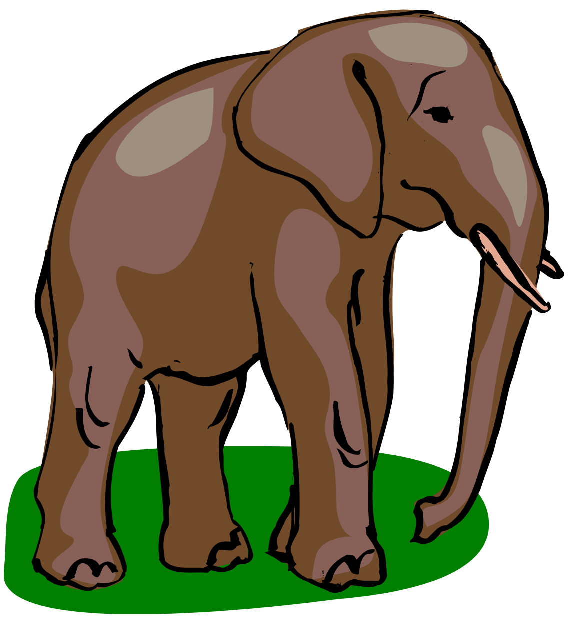
A systematic elimination of defect mechanisms approaches recovery of initial strength distribution



Glass breakage

- So what does glass have in common with an elephant?
- Both do not forget and do not forgive any mistreatment!

Overall summary: Treat your glass (and your elephants) right!



Assessment of flaws

Assessment of flaws (in terms of breakage criticality)

- Different publishers
  - PDA Technical Report #43 [pda43]
  - Editio Cantor Verlag [harl16]
  - Container vendors [pt07]
  - Company-internal
- Defect catalogues
  - In general: No distinction between cosmetic and strength-affecting flaws
  - Characterization and assessment of flaws only by (lateral) dimensions
- Required information for assessment of criticality
  - Flaw shape/geometry, container shape/geometry → (three-dimensional) geometry information
  - Flaw dimension → flaw size (“depth”)

Assessment of flaws (in terms of breakage criticality)

- Are optical techniques capable to acquire information about (three-dimensional) flaw geometry and depth?
  - Manual (human eye)?
  - Automated (camera/software)?

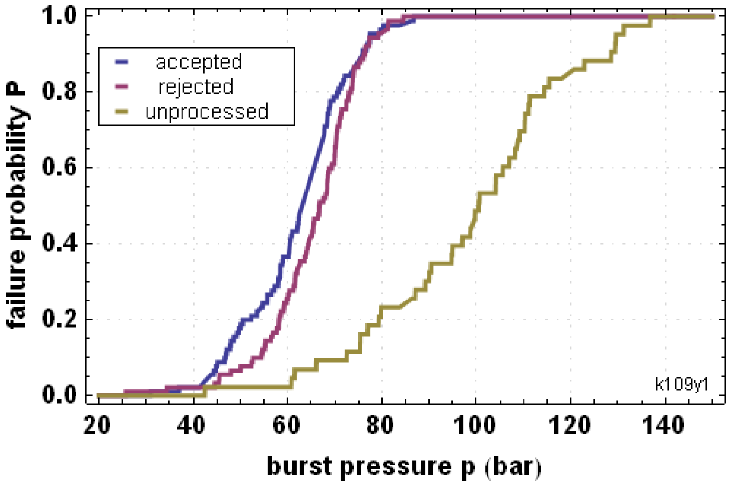
Optical inspection systems are inappropriate for an assessment of criticality

- Reliable assessment of strength-related flaws only possible via appropriate strength experiments

Only strength experiments are capable to acquire reliable information about criticality of flaws

Cosmetic versus critical flaws (example)

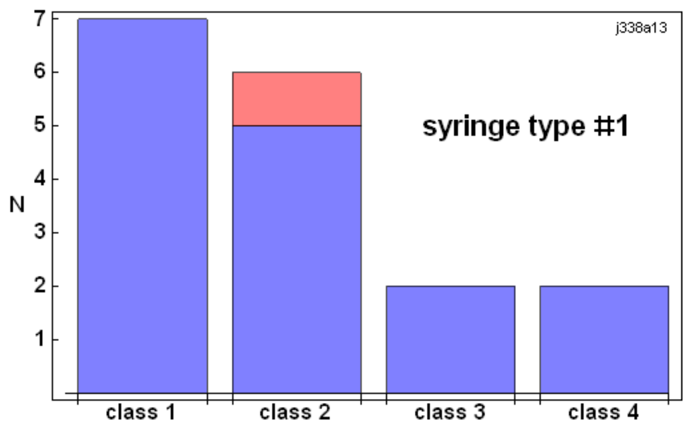
- Batch of glass vials rejected due to cosmetic flaws
- Accepted reference batch (no cosmetic flaws)
- Burst-pressure strength experiments
- Fractographic examinations (location of fracture origin)

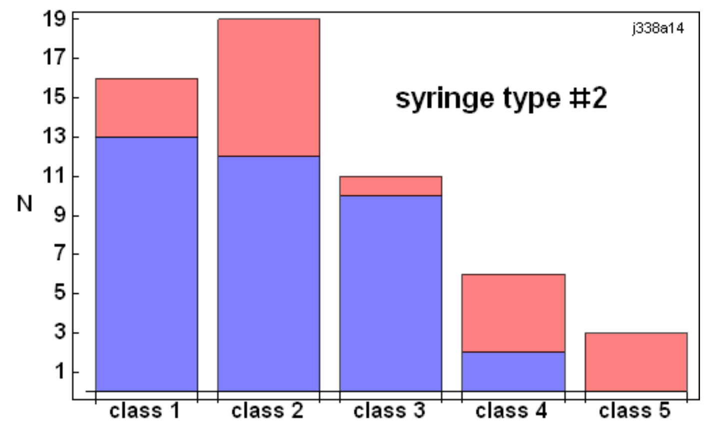


Visual appearance of flaws does not necessarily give a hint about the criticality

Size versus criticality of flaws (example)

- Two types (formats) of glass syringes
- Classification of flaws by (lateral) size
- Burst-pressure strength experiments
- Fractographic examinations (location of fracture origin)
  - Failure at classified defect?

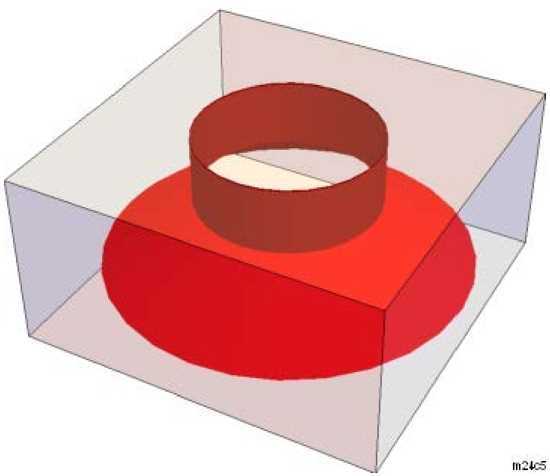


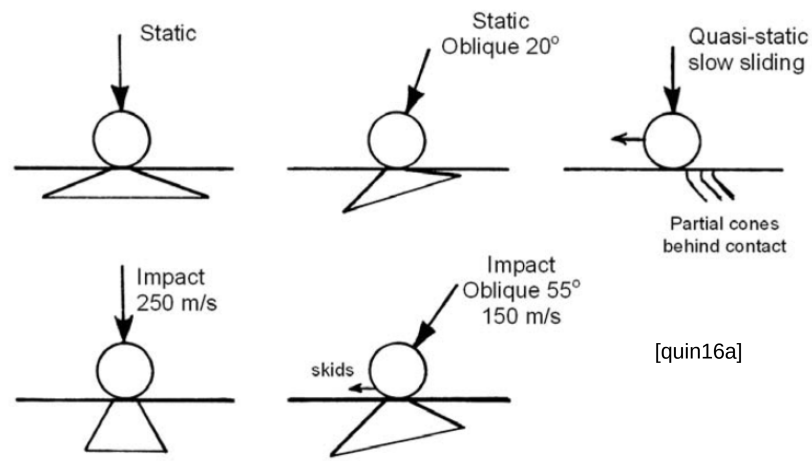


Optical assessment does not yield a reliable information about flaw criticality

Common fracture origins: Blunt contact damages

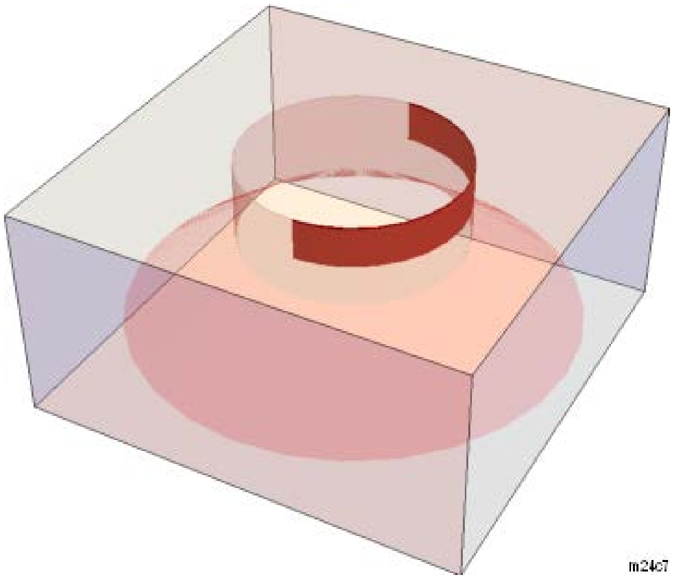
- "Bump check", "scuff", "percussion cone"
- Static or dynamic contact with blunt object
- Crack pattern: Hertzian cone crack [lawn93]
  - Not necessarily fully developed
  - After breakage, fracture origin often forms a curved edge

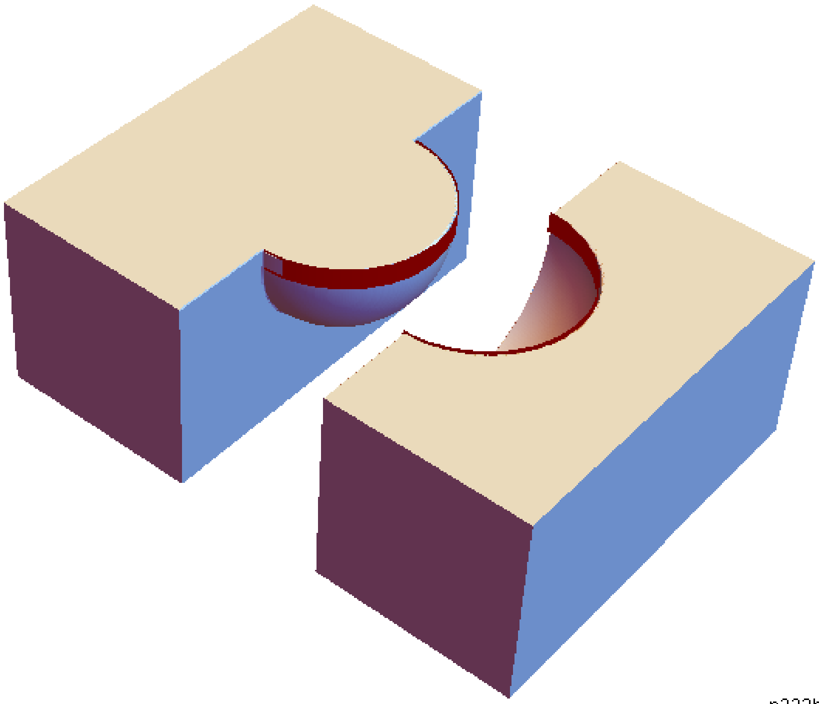




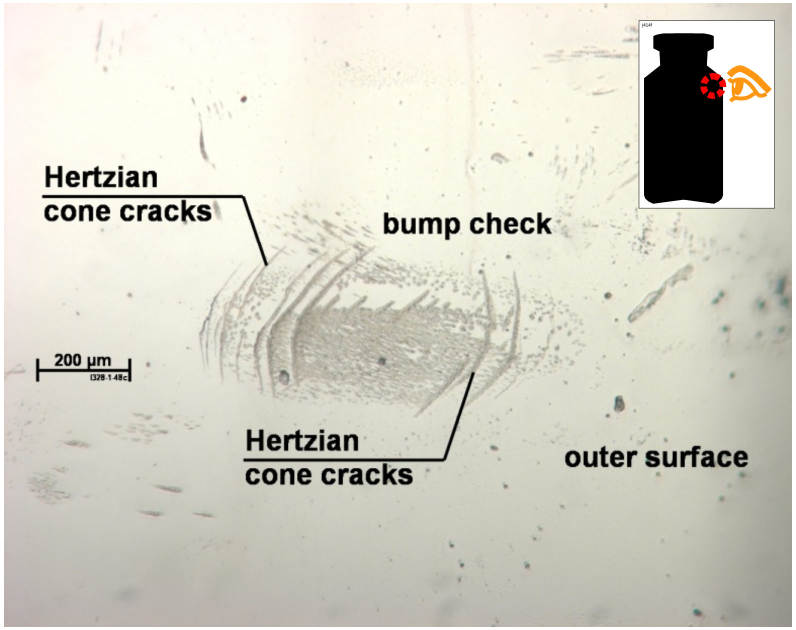
[quin16a]

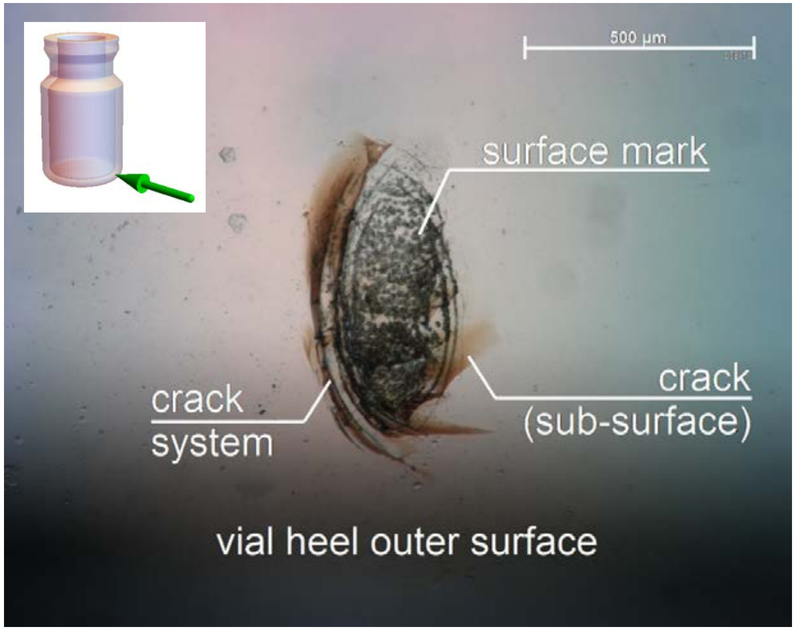
Common fracture origins: Blunt contact damages



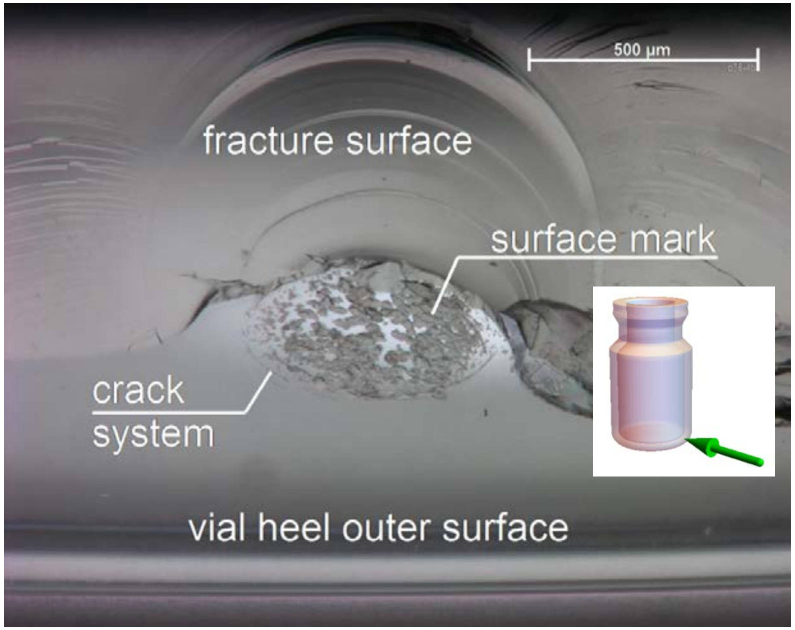


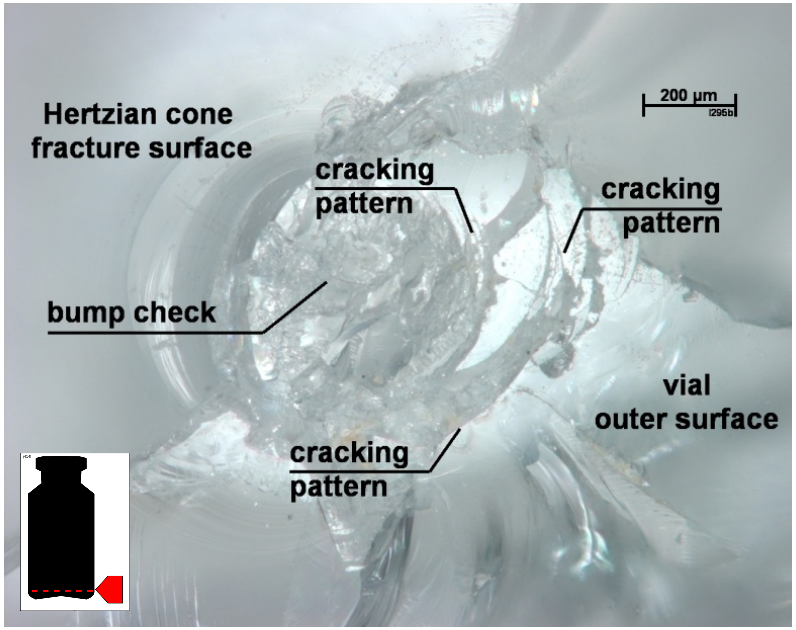
Blunt contact damages (examples)



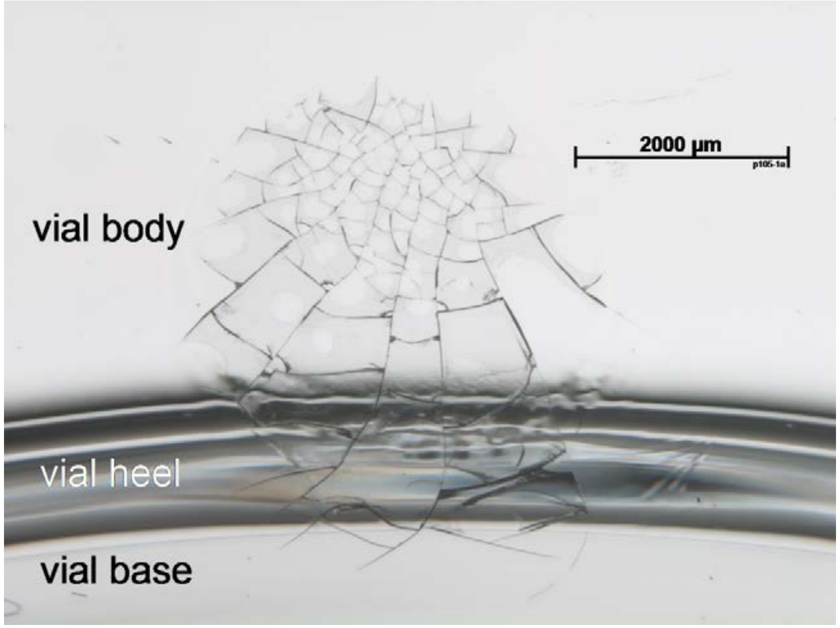


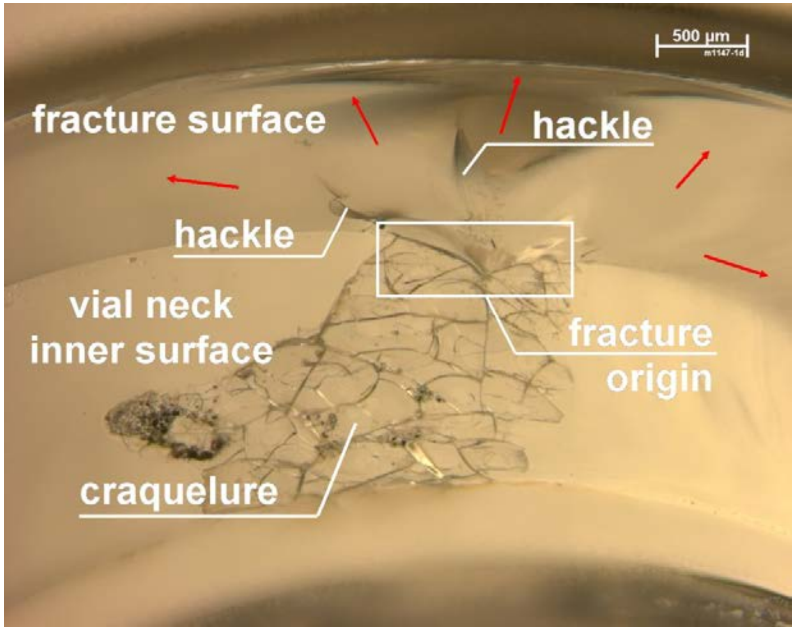
Blunt contact damages (examples)





Common fracture origins: Craquelure





Common fracture origins: Craquelure

- Cracks induced due by layer of different coefficient of thermal expansion
  - Differences in chemical composition
  - Local condensation or evaporation of volatile components
- Development of filigree crack system (“spider web”)
- Cracks not penetrating deeply into bulk glass: Shallow, cloddy fragments

Fractography – Fundamentals

"Tracking The Cracking"

Definition of fractography

- ASTM C 1145: “Means and methods for characterizing a fractured specimen or component” [astm1145]
- Macroscopic fractography: Examination and interpretation of crack patterns
- Failure-inducing mechanical tensile load
- Microscopic fractography: Examination of fracture-exposed surfaces and the interpretation of the fracture markings
- Failure-inducing flaw
- Art or science to conclude the failure of brittle materials from fracture surfaces and patterns

Fractography enables an objective assessment of the circumstances of failure of a solid

Definition of fractography

Glass breakage: *Surface flaw × tensile load ≥ breakage resistance*

Microscopic fractography

- Interpretation of fracture surface markings

↓

- Failure-inducing flaw

Macroscopic fractography

- Interpretation of crack patterns

↓

- Failure-inducing mechanical tensile load

Root cause for brittle failure

Fractography can answer many questions

- Position of failure-inducing flaw?
- Type of failure-inducing flaw?
- Direction of failure-inducing mechanical load?
- Type of failure-inducing mechanical load?
- Container closure-integrity affected?
- Velocity of failure propagation?
- (Magnitude of failure-inducing mechanical load?)
- (Static or dynamic failure?)
- (One-step or multiple step failure?)
- (Presence of corrosive medium?)

Initiation of failure (fracture)

- Application of mechanical load causes deformation (elastic strain)
- Elastic strain stores volume energy
- Impetus for failure: Release of stored volume energy
  - Release of energy by creation of surfaces (→ fracture surfaces)

Impetus for brittle failure: Release of stored elastic energy (creation of surfaces)

- Propagation perpendicular to (local) principle tension

Crack propagation direction *always* perpendicular to local principle tension

- Acceleration from v = 0 m/s up to maximum velocity (≈ km/s)
- Further release of energy by creation of additional surfaces → branching

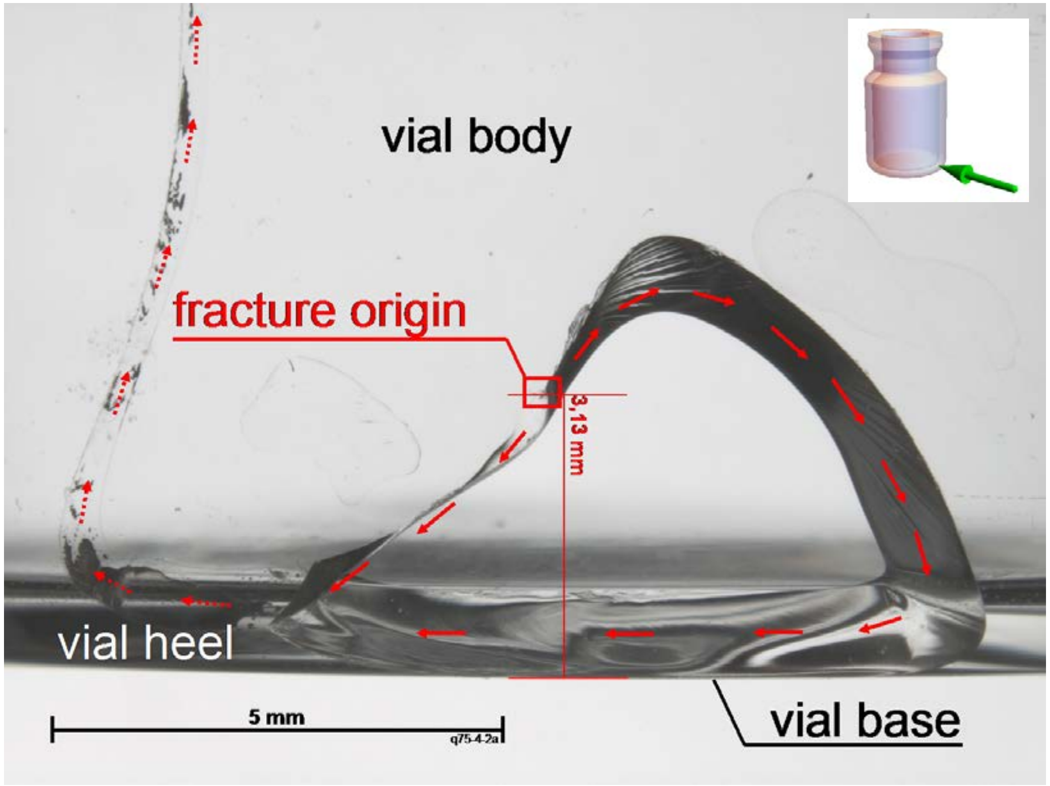
Crack branching starts at maximum propagation velocity

Fracture patterns (macroscopic fractography)

- Shape/orientation of cracks gives hints about direction of mechanical load
- Deduction of load situation
  - Constant or inhomogeneous
  - Bending
  - Side compression
  - Thermal gradients
  - Inner pressure
- Branching
  - Backtracking to first branching → vicinity of fracture origin
  - Maximum crack propagation velocity reached

Macroscopic fractography is capable to characterize the failure-inducing mechanical load

Fracture patterns (macroscopic fractography)

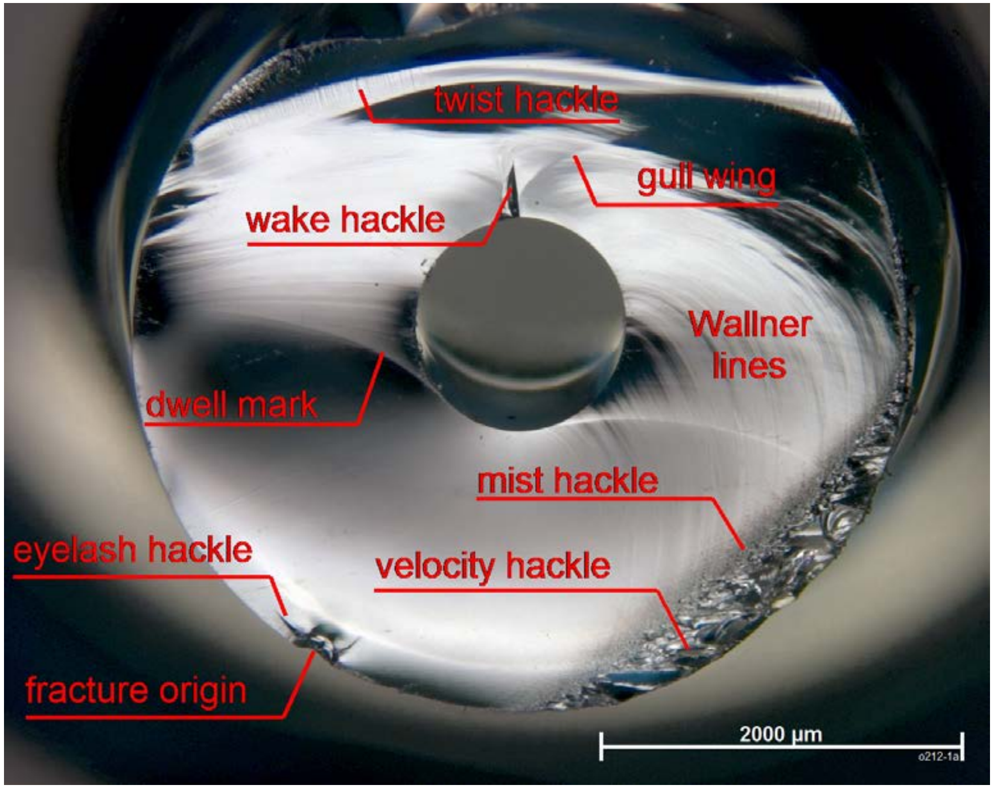


Fracture surface markings (microscopic fractography)

- Topographic features generated during crack propagation
  - Fracture mirror
  - Mist/velocity/twist/wake/eyelash hackle
  - Wallner lines, gull wings
  - Tilt/arrest line, dwell mark
  - Chipping
  - Scarps
- Observation gives hints about propagation conditions
  - Failure propagation velocity
  - Failure propagation direction
  - Change of direction and/or magnitude of mechanical load
  - Split crack front
  - …

Microscopic fractography is capable to determine the fracture origin position

Fracture surface markings (microscopic fractography)

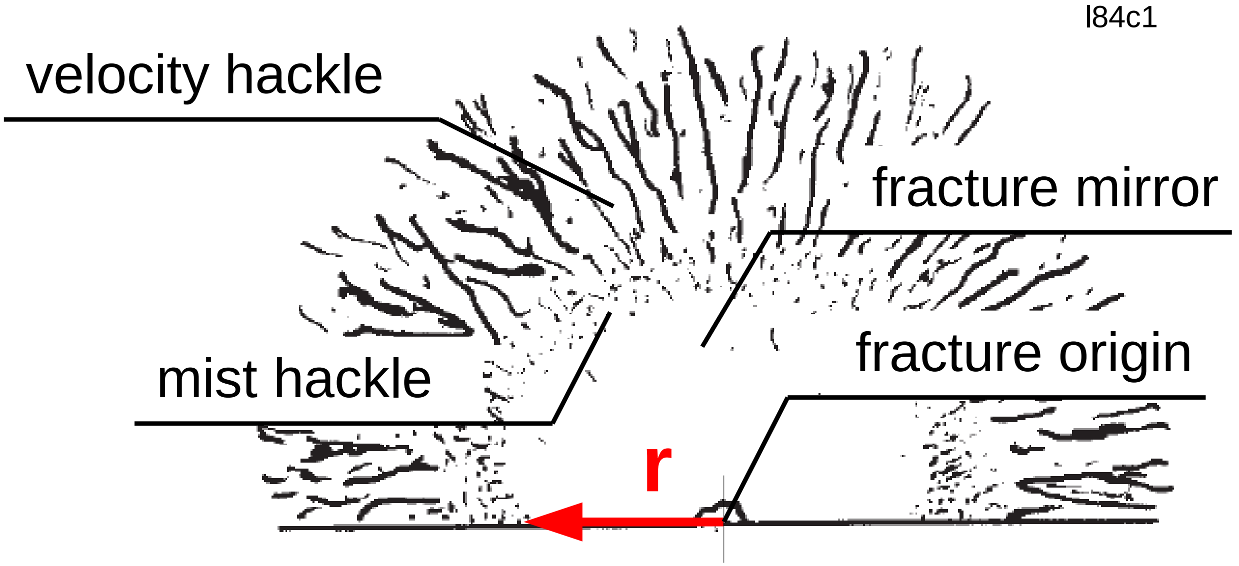


Quantitative fractography

- Determination/estimation of strength σ from fracture surface markings
- (Semi-)empirical law: $A=\sigma\sqrt{r}$
- A: Material constant
- σ: Strength
- r: Radius

$$\sigma = \frac{A}{\sqrt{r}}$$

[quin16a]



Summary

- The strength of glass is not a material constant
- The strength of glass is a projection of the surface quality
- Defined by flaw type and size distribution(s)
- The strength of glass can be described by statistical distributions
- The creation of new, more critical flaws during processing will reduce the overall strength
- Critical, strength-affecting flaws may differ from cosmetic flaws
- Visual inspection systems do not identify strength-affecting flaws
- Risk of wrong decisions (acceptance/rejection)
- Reliable assessment only possible from appropriate strength experiments
- The most critical flaw (fracture origin) can be determined by fractography
- Application: Process optimization (reduction of damage mechanisms) [hain16,hain16a]
- Quantitative fractography enables an estimation of the strength

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[astm1145] ASTM C 1145-06; „Standard Terminology of Advanced Ceramics“.

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[pda43] Parenteral Drug Association; „Identification and Classification of Nonconformities in Molded and Tubular Glass Containers for Pharmaceutical Manufacturing: Covering Ampoules, Bottles, Cartridges, Syringes and Vials “; Technical Report #43 (2013).

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[quin16a] Quinn, G.D.: „Fractography of Ceramics and Glasses”; NIST Special Publication 960-16e2 (2016).

Thank you for your attention!