Best Practices for Glass Primary Containers; 12-Apr-2023; Mainz, Germany

Strength and reliability of glass containers used in the pharmaceutical industry

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PDA Parenteral Drug Association

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Outline

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

Glass Breakage – Fundamentals

“Crackademy“

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
  - "Fracture toughness"
    - Material parameter

"strength"

↑

Glass breakage: *Surface flaw × tensile load ≥ fracture toughness*

stress intensity

Interpretation: Different cases

1) No breakage if no or only one factor is present
2) Flaw and mechanical load occur simultaneously
   - Impact
   - Misaligned crimping
3) Flaw is created prior mechanical load
   - Depyrogenation/heat sterilization
   - Lyophilization/freeze drying
   - Cryogenic storage
   - Auto-injector
4) Flaw is introduced while mechanical load is already present
   - Residual stresses
   - Constant internal pressure

one-step failure mechanism (cases 2)

two-step failure mechanism (cases 3–4)

Definition of "flaw"

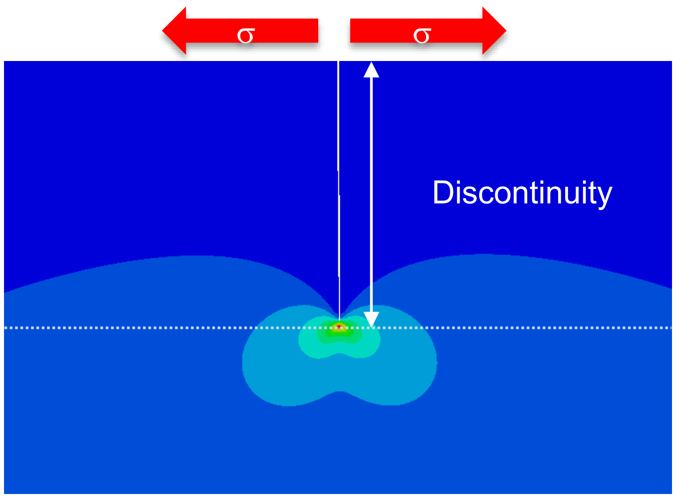
- Any type of "sharp" discontinuity within the isotropic, monolithic structure of the glass (including the surface) can act as flaw
  - "Sharp" geometry: radii → nanometers
  - Melting
    - Stones, refractory material, unmelted batch material
    - Variations in glass composition
    - Voids (pores, bubbles, airlines)
    - Crystals
  - Hot forming/shaping
    - Variations in glass composition
    - Voids (pores, bubbles, airlines)
    - Crystals
    - Tooling marks
  - Processing and handling
    - Contact damages (checks and cracks)

Intensification of stresses

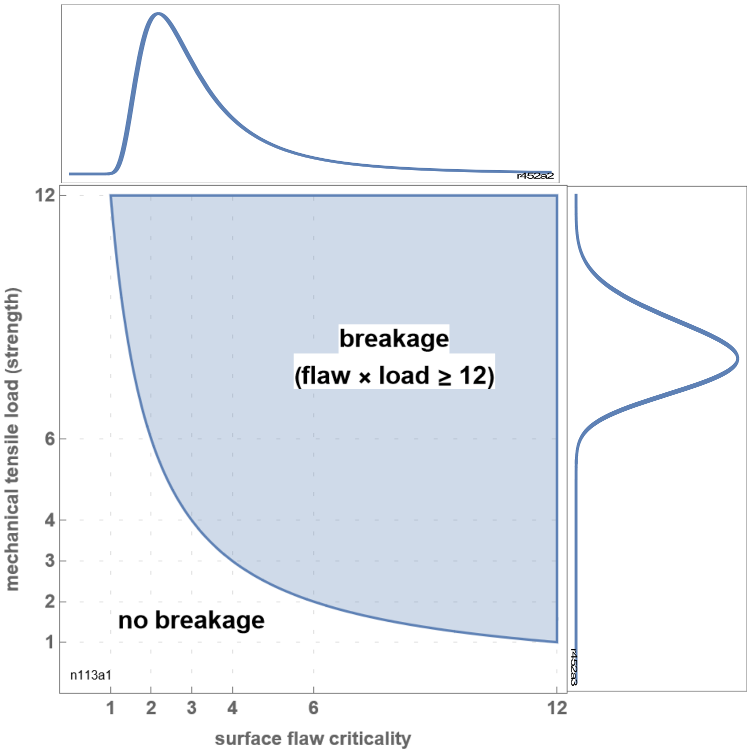
- Discontinuities act as concentrators for mechanical stresses (stress intensity)
- Size (dimension) and shape (geometry) of discontinuity affect criticality
  - Large flaws can exhibit low criticality
  - Small flaws can exhibit high criticality

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



Determination of failure criteria



Exercise

- Population with different flaw criticalities (between 1 and 12)
  - Statistical distribution
- Breakage occurs due to exceeding critical stress intensity value
  - Fracture toughness → material constant

The strength of glass is not a material constant

The strength of glass depends on flaw criticality

The flaw criticality is an expression for (surface) quality

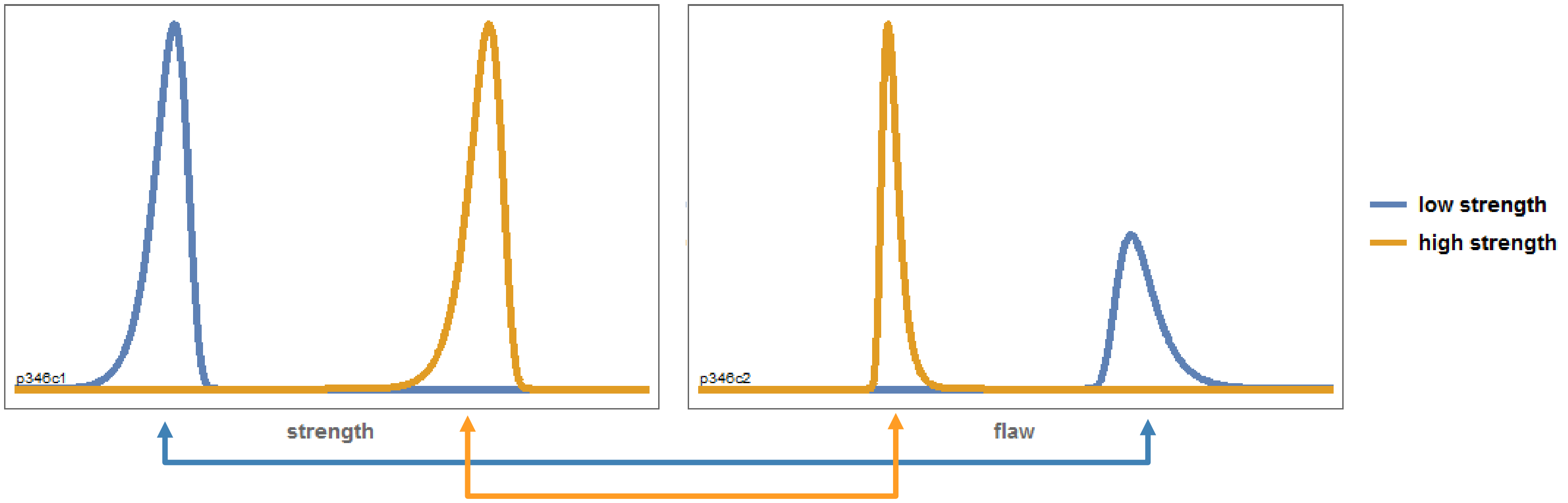
The strength of glass is a projection of its (surface) quality

The flaw criticality is described by statistical distribution(s)

The strength of glass is described by statistical distribution(s)

Determination of failure criteria

- Flaw criticality (size) distribution → strength distribution
  - Large flaws → low strength
  - Small flaws → high strength



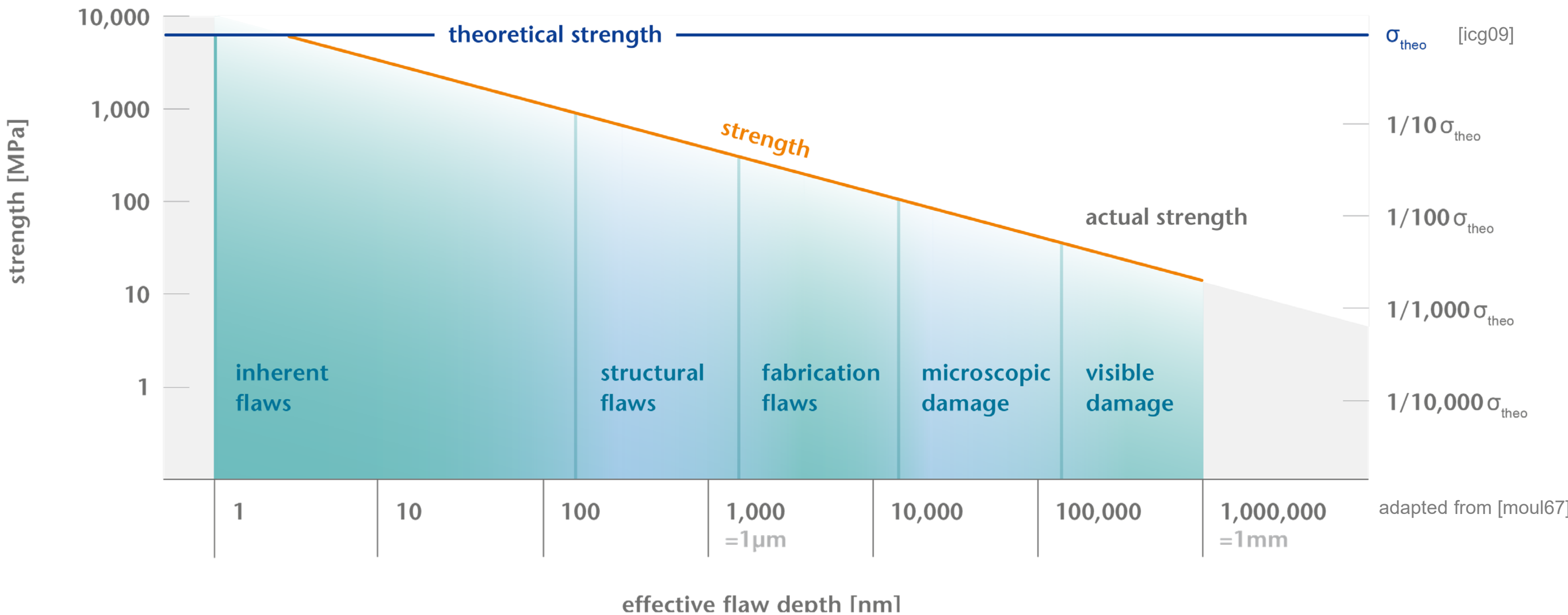
Determination of failure criteria

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

  of 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

Loss of strength

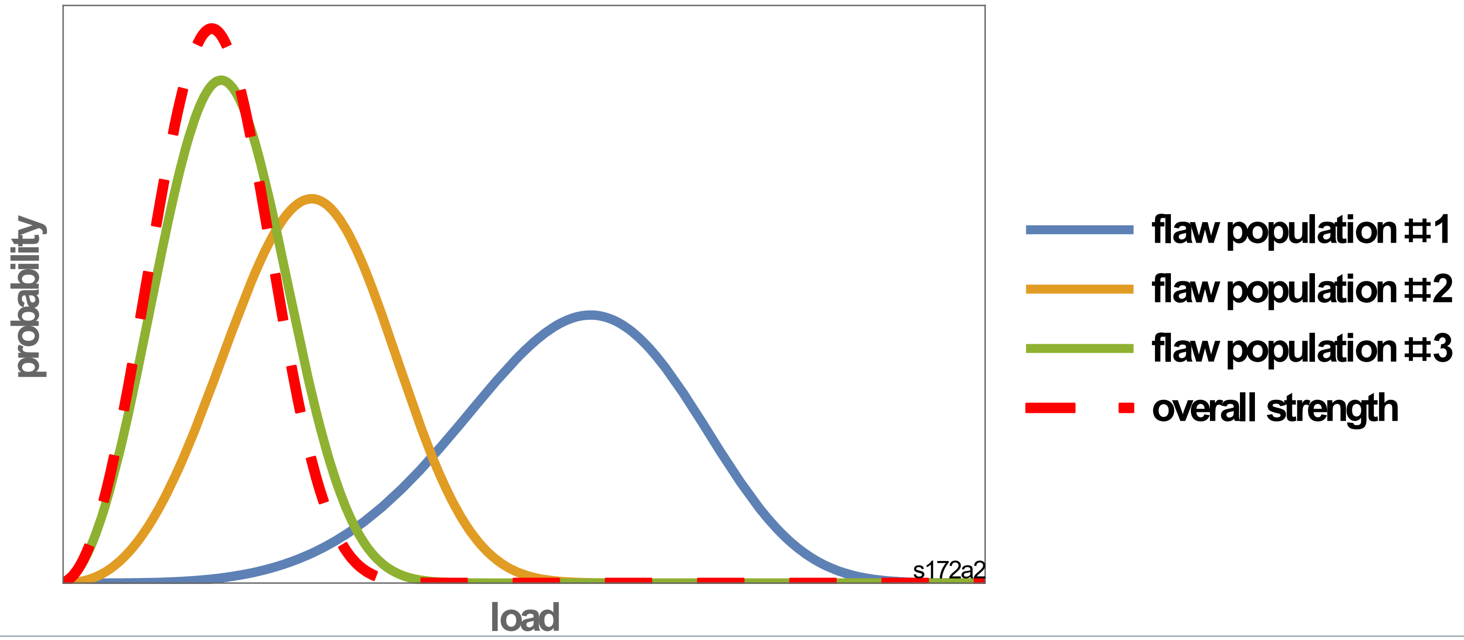


- Strength range: Several MPa to several GPa
- Theoretical strength: Weakest interatomic bond

Strength reduction due to flaws: Several orders of magnitude

Multiple flaw populations

- Coexistence of multiple strength distributions
  - Competition for failure ("weakest link")
- The distribution of the most critical defects dominate the overall strength

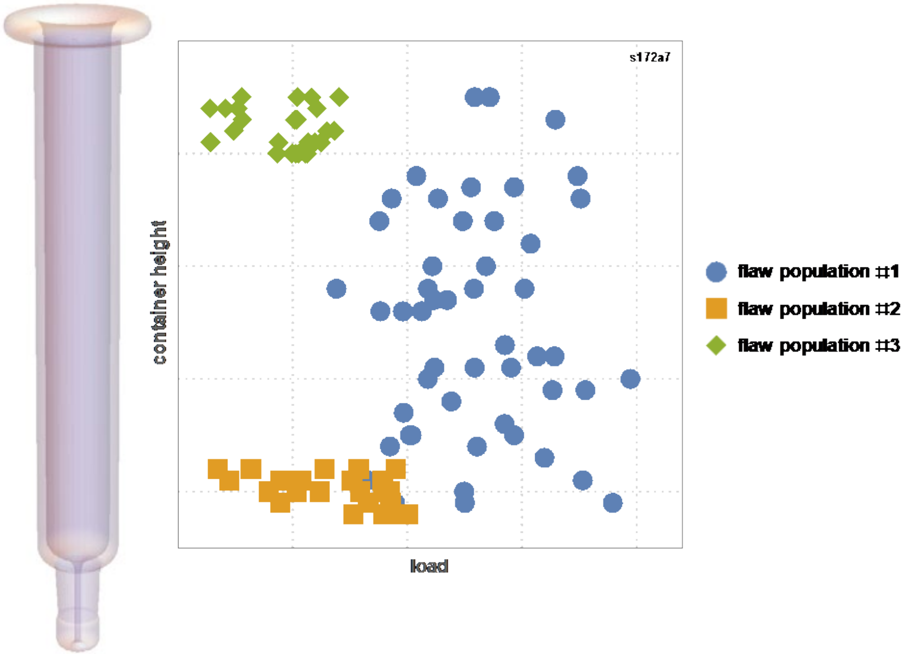


Multiple flaw populations (example)

- Damaging during process step
- Burst-pressure strength experiments
- Fractographic examinations
  - Location of fracture origin
- Before: High strength, no cluster (●)
- After: Two low-strength clusters (■◆)
  - Systematic damages

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

[hain16,maur21]

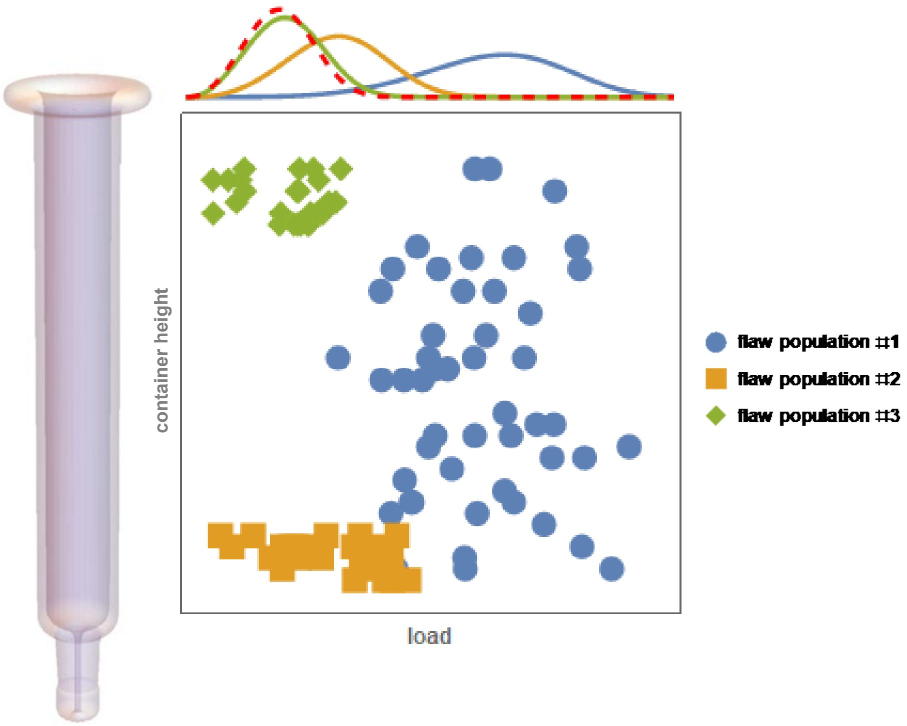


Multiple flaw populations (example)

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

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

[hain16,maur21]

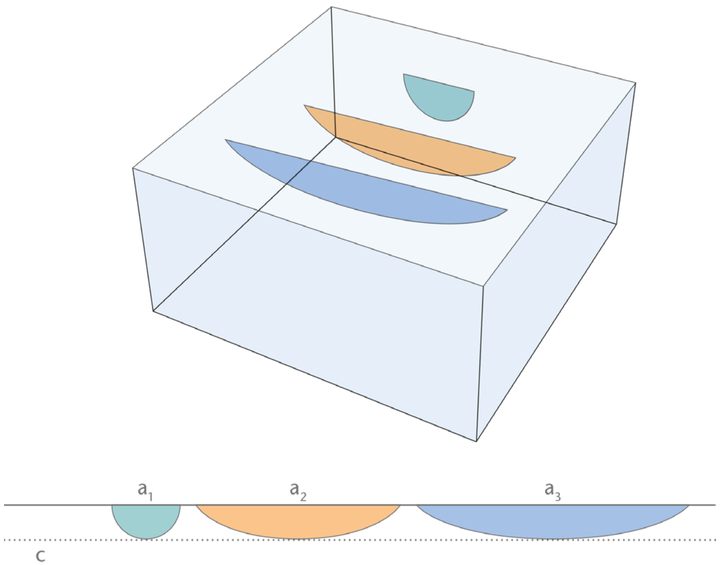


Assessment of flaws

Assessment of flaws (in terms of breakage criticality)

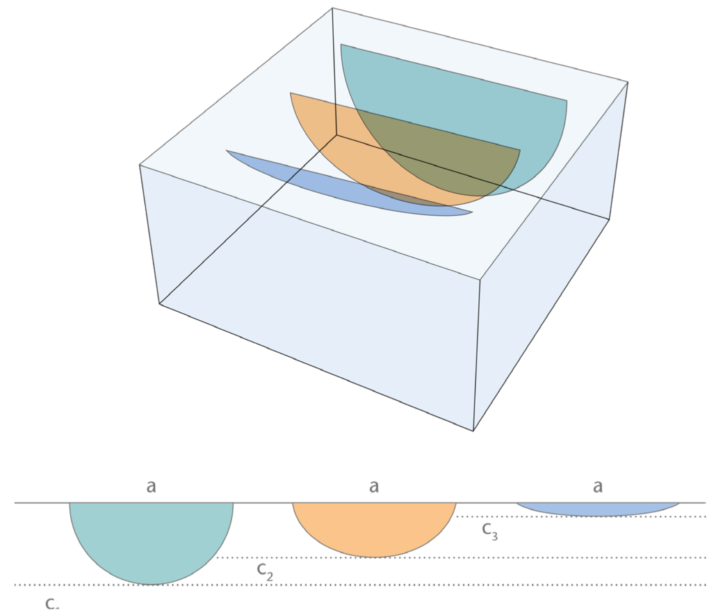
- Different publishers
  - PDA Technical Report #43 [pda43]
  - Editio Cantor Verlag [harl16]
  - Container vendors [pt07]
  - Independent entities [agr20]
  - Company-internal
- Defect catalogues
  - In general: No distinction between cosmetic and strength-affecting flaws
  - Characterization and assessment 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)



equal penetration depth

criticality: ■ > ■ > ■



equal lateral dimension

criticality: ■ > ■ > ■

Assessment of flaws (in terms of breakage criticality)

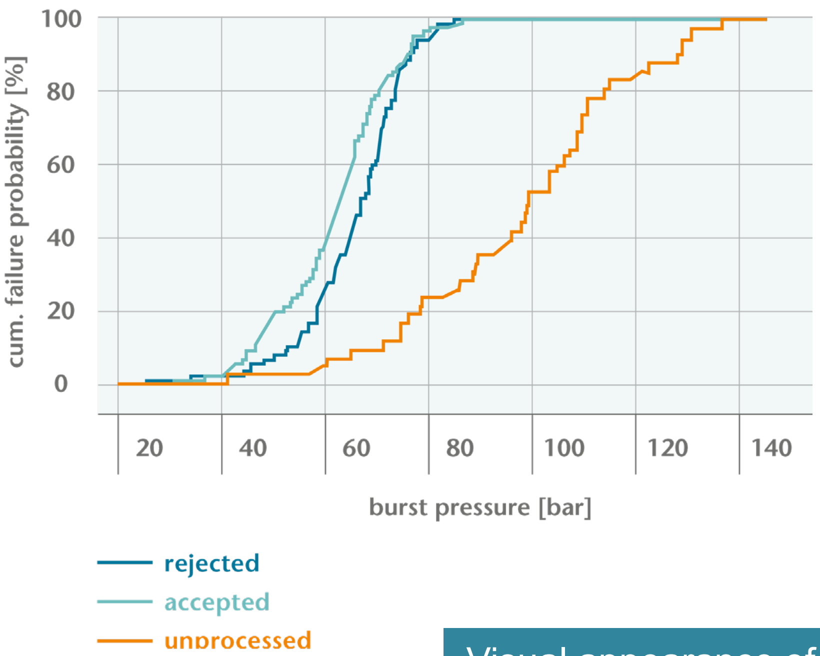
- Are optical techniques capable to acquire information about (three-dimensional) flaw geometry and depth?
  - Manual (human eye)?
  - Automated (camera/software)?

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)

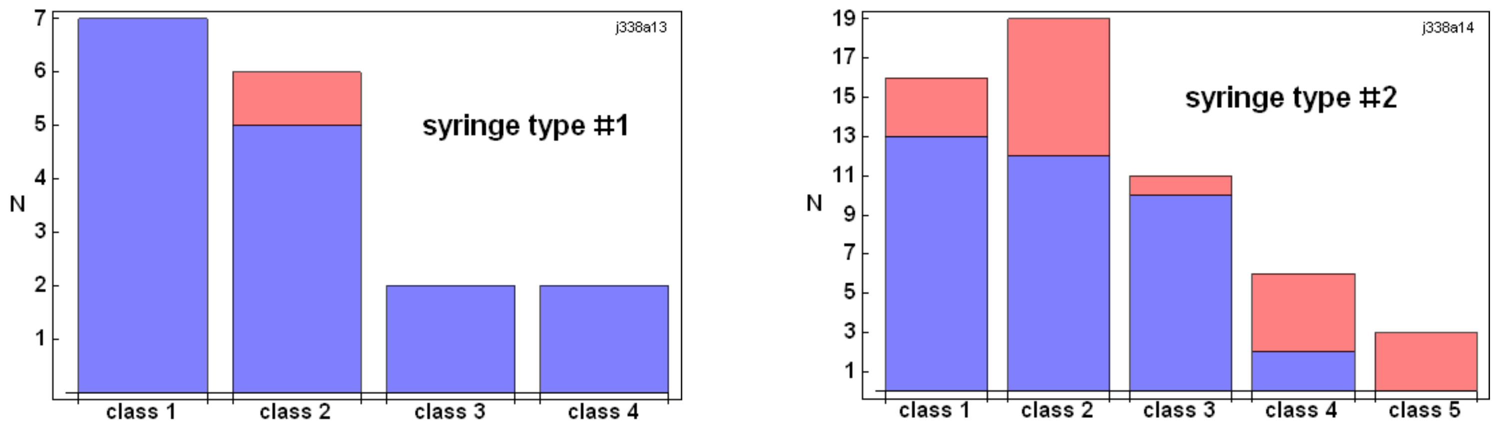


- Batch of glass vials rejected due to cosmetic flaws (■)
- Accepted reference batch (no cosmetic flaws) (■)
- Unprocessed batch (■)
- Burst-pressure strength experiments
- Fractographic examinations (location of fracture origin)

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

Size versus criticality of flaws (example)

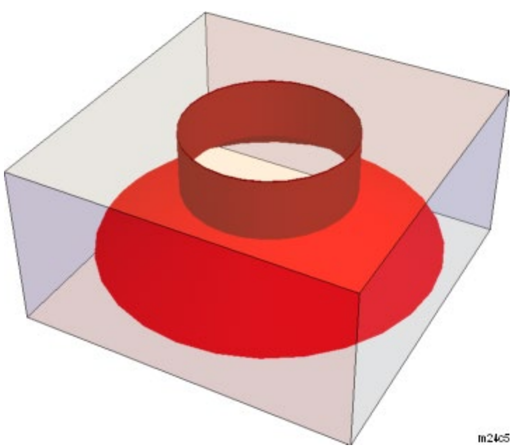
- Two types (formats) of glass syringes
- Classification of flaws by (lateral) size
- Burst-pressure strength experiments
- Fractographic examinations (location of fracture origin)
  - Failure at classified defect?

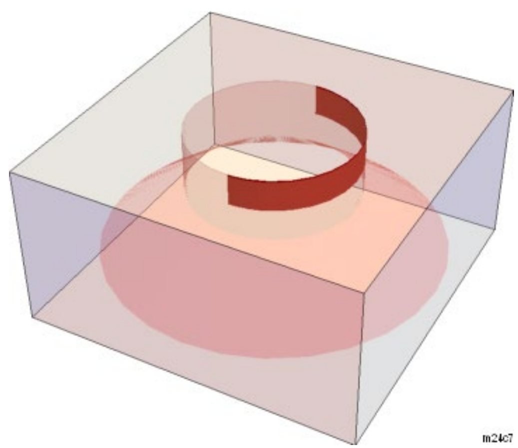


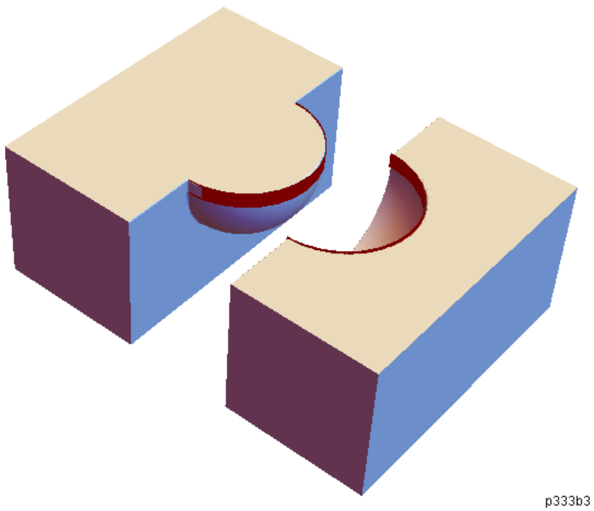
Optical assessment does not yield a reliable information about flaw criticality

Common fracture origins: Blunt contact damages

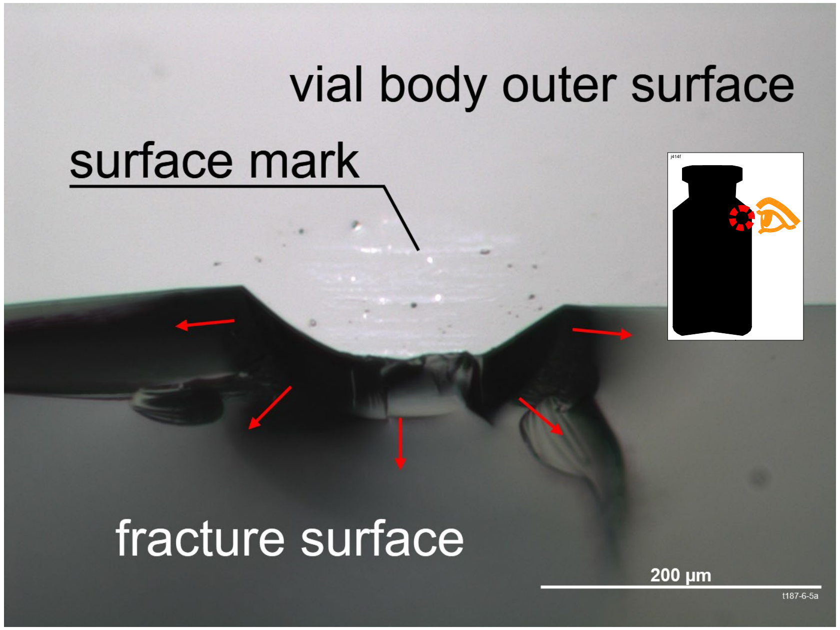
- “Bump check”, “scuff”, “percussion cone”
- Static or dynamic contact with blunt object
- Crack pattern: Hertzian cone crack [lawn93]
  - Not necessarily fully developed
  - After breakage, fracture origin forms a curved edge

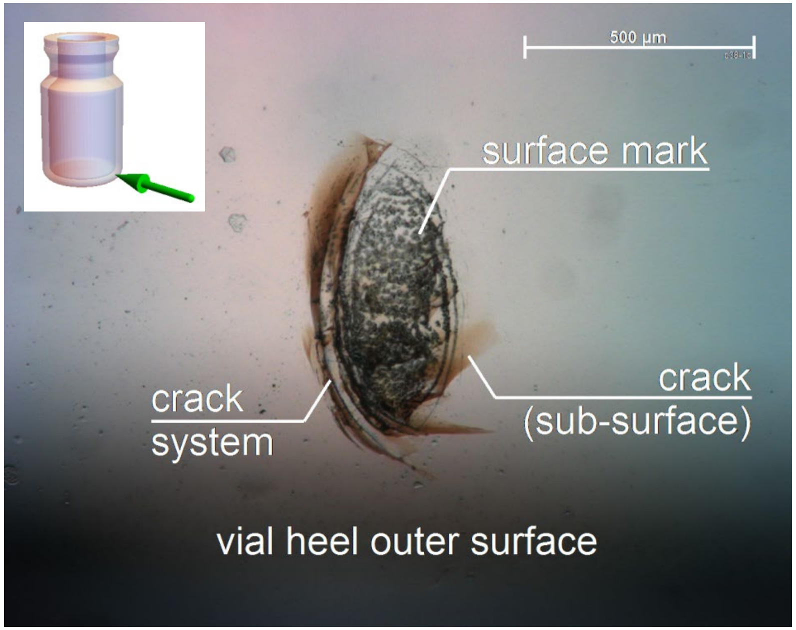






Blunt contact damages (examples)





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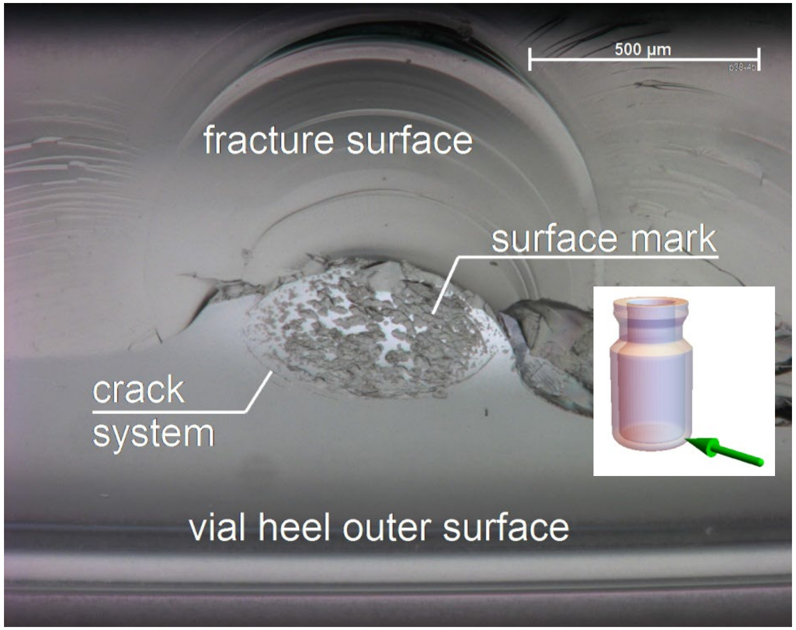
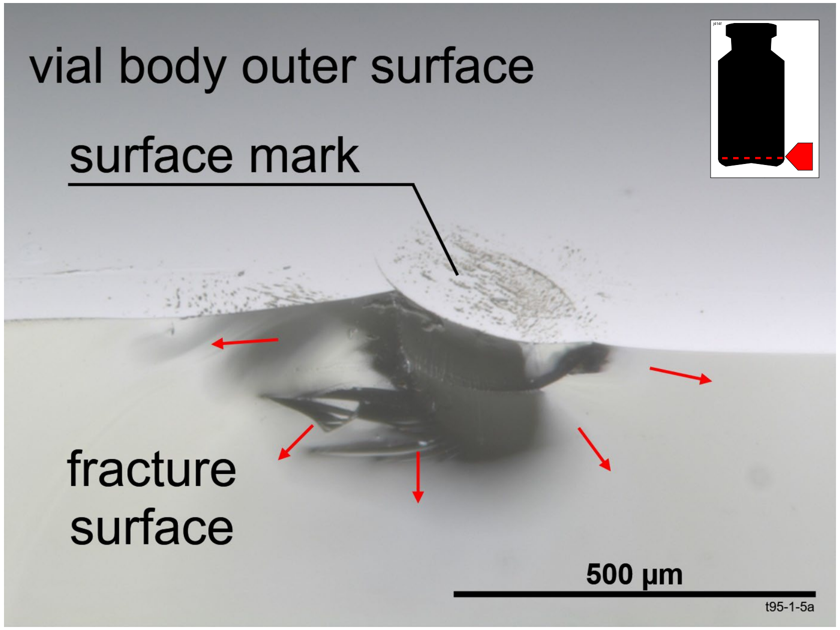
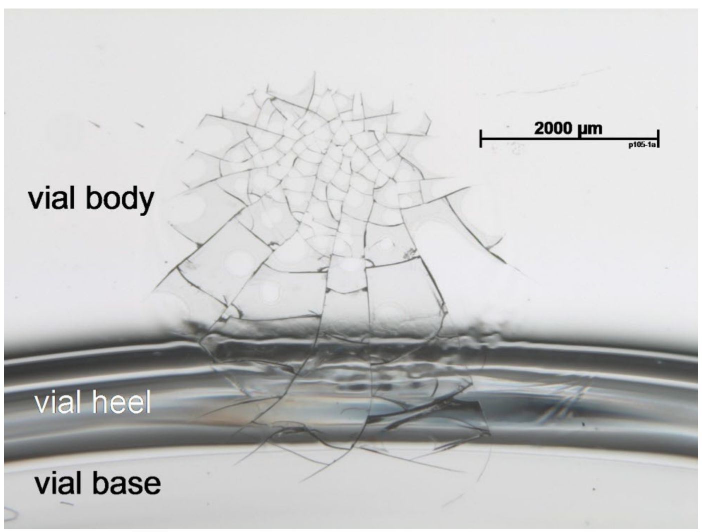
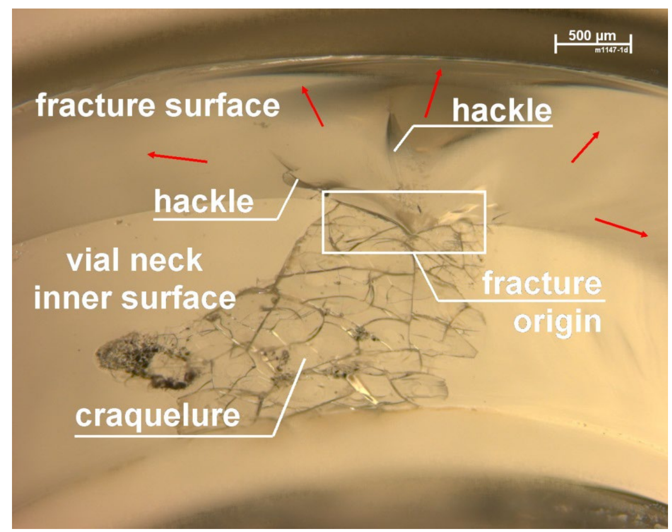




Common fracture origins: Craquelure (aka “crackles”)

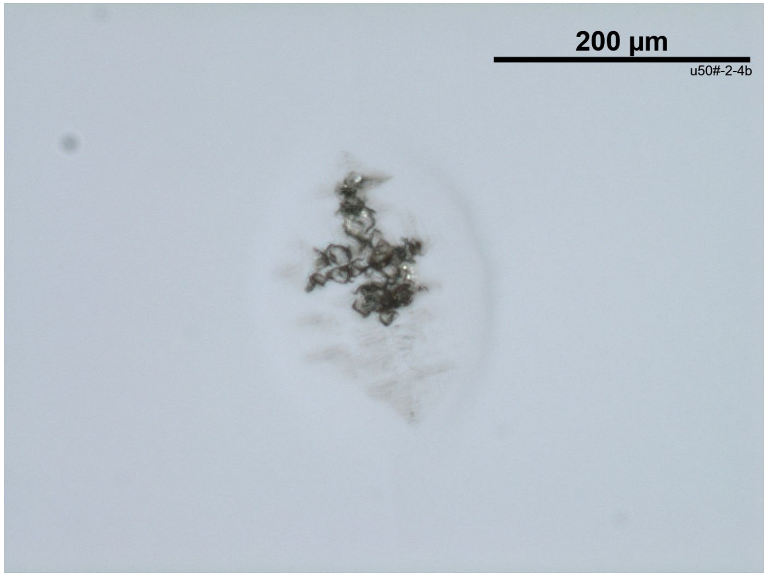
- Cracks induced due by thin, adhered layer of different coefficient of thermal expansion
  - Differences in chemical composition
  - Local condensation or evaporation of volatile components
- Development of filigree crack system (“spider web”)
- Cracks not penetrating deeply into bulk glass: Shallow,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

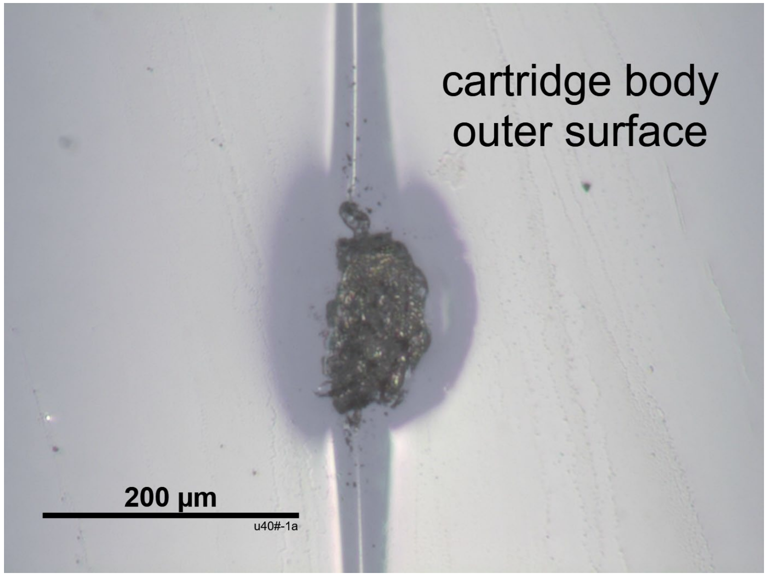




Common fracture origins: Crystals and stones

- Crystals: Local phase transition into thermodynamically-favored structure
  - Discontinuity
- Stones: Foreign inorganic material (refractory material) from melting tank and/or Danner mandrel





Fractography – Fundamentals

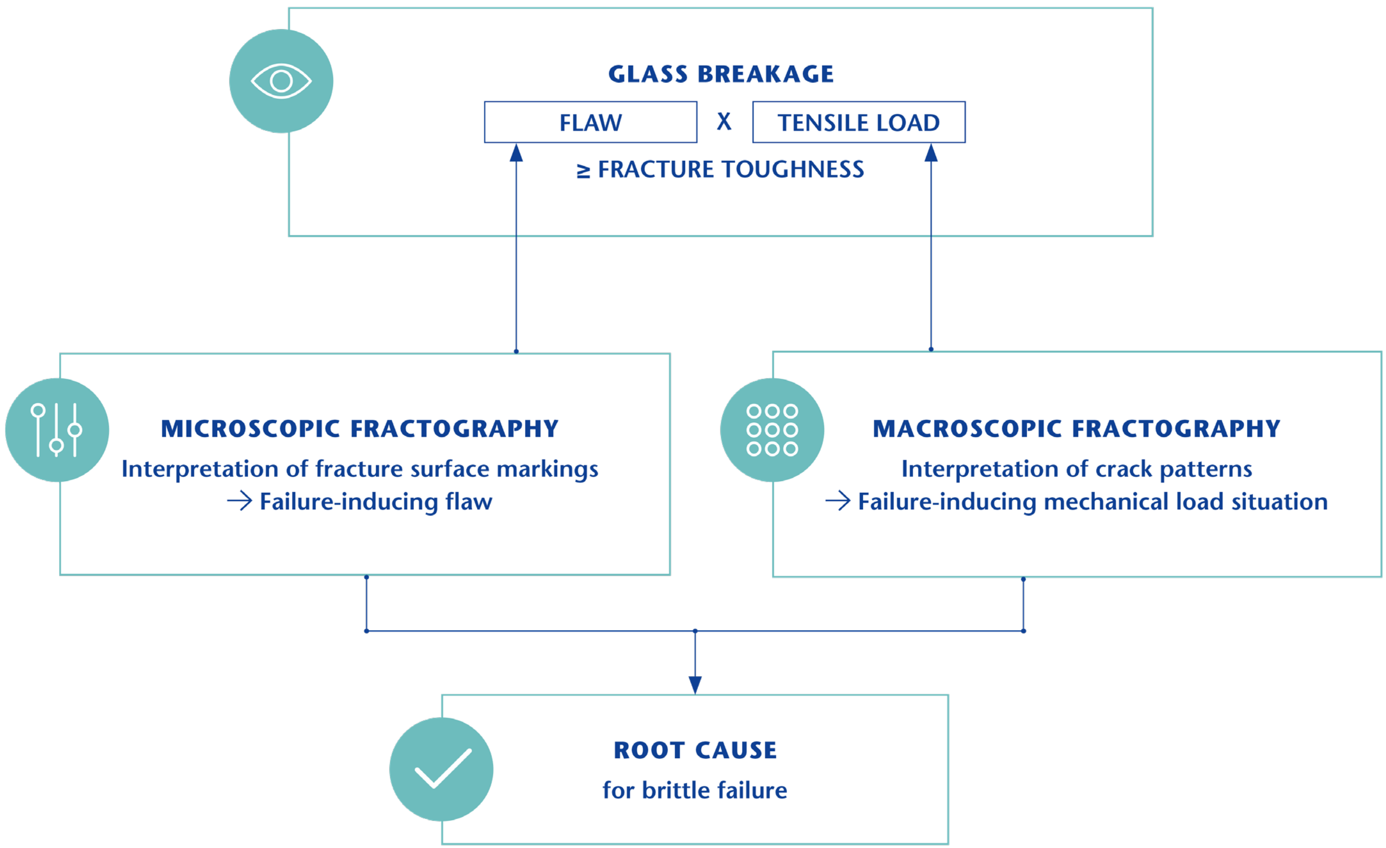
"Tracking The Cracking"

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



Fractography can answer many questions

Failure-inducing flaw

- Position
- Type

Failure-inducing mechanical load

- Direction
- Type (origin/circumstances)

Additional information

- Container integrity affected?
- Velocity of failure propagation?
- (Magnitude of failure-inducing mechanical load → strength)
- (Static or dynamic failure)
- (One/two-step failure)
- (Presence of corrosive medium)

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

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) principal 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

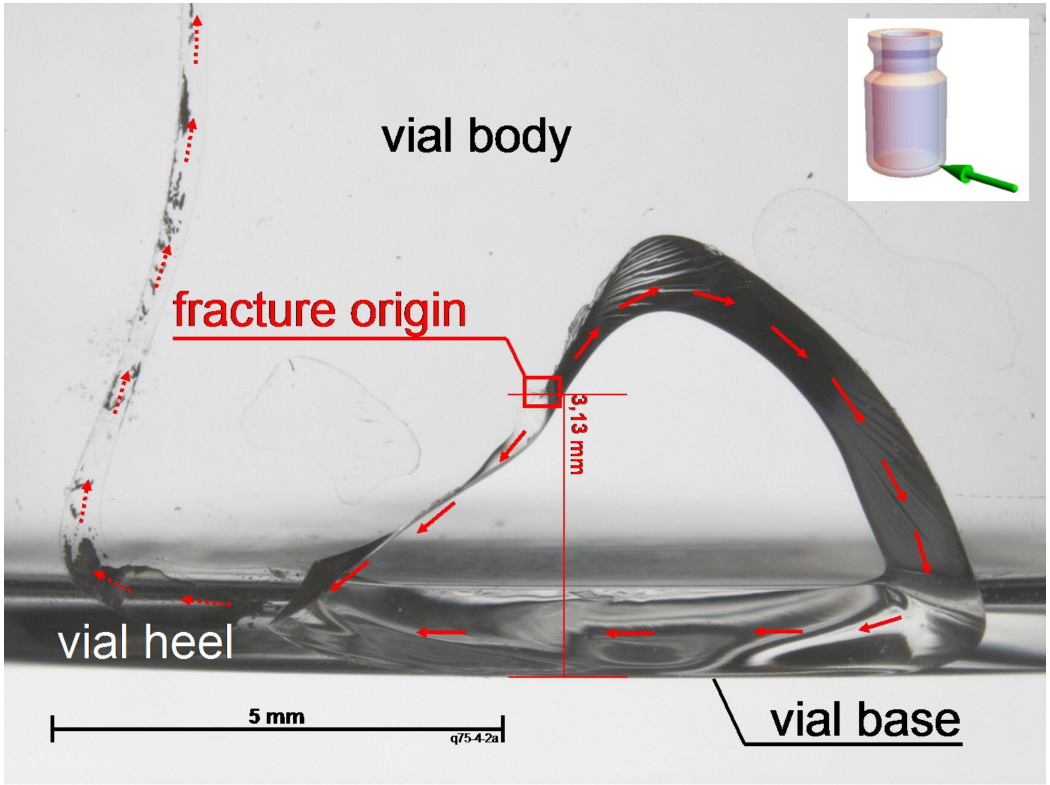
Crack branching starts at maximum propagation velocity

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)

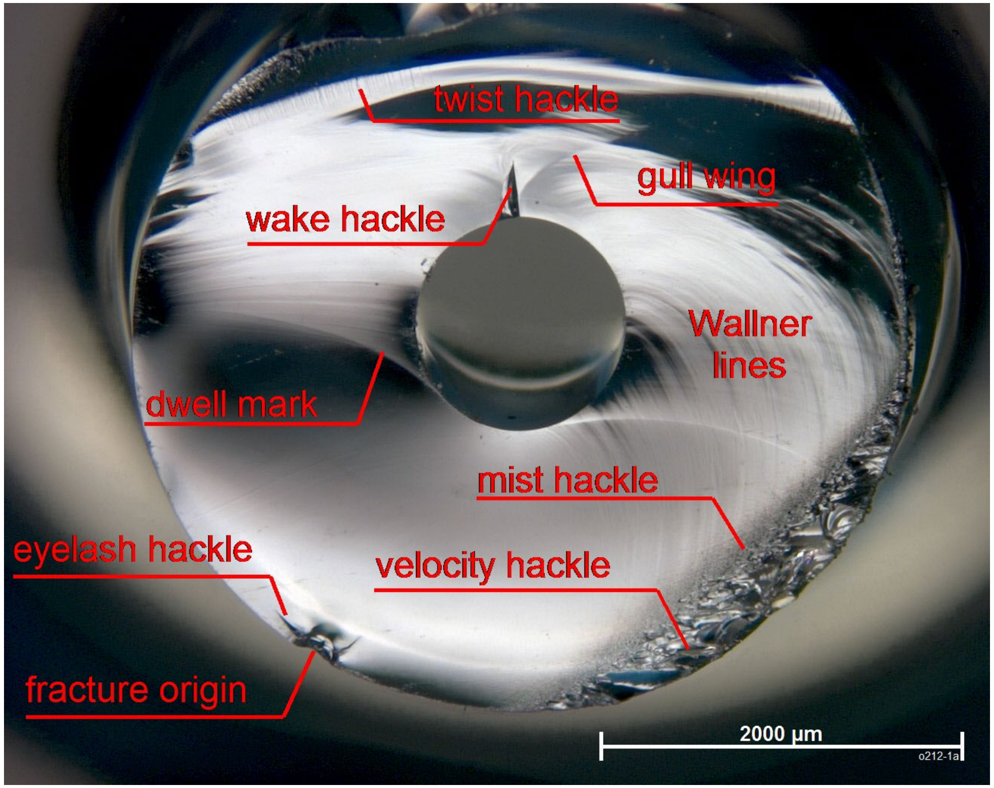


Fracture surface markings (microscopic fractography)

- 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)

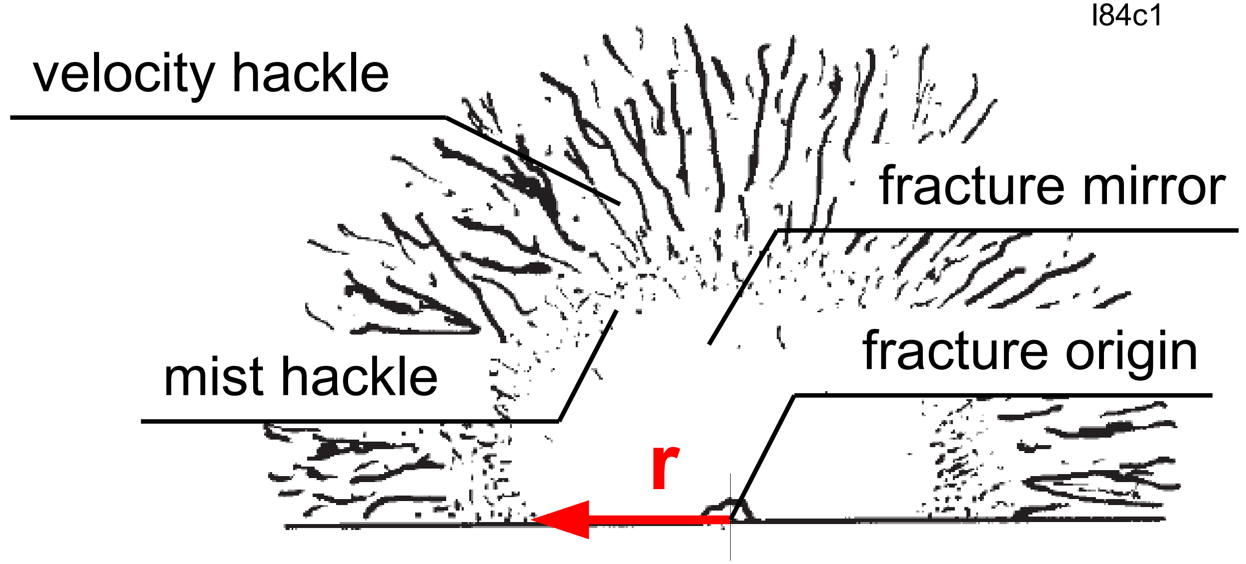


Quantitative fractography

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

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

[quin20]



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

References (1)

[agr20] American Glass Research; "Spotlight On: Pharmaceutical Glass Flaws" (2020).

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

[hain16] Haines, D. et al.: "Why do Pharmaceutical Glass Containers Break: The Underestimated Power of Strength Testing and Fractography"; International Pharmaceutical Industry 8/1 (2016) 88.

[hain16a] Haines, D. et al.: "Die Anwendung von Festigkeitsprüfungen und Fraktografie auf pharmazeutische Glasbehälter"; Pharm. Ind. 78/8 (2016) 1208.

[harl16] Harl, M.; Horst, S.; „Fehlerbewertungsliste für Behältnisse aus Röhrenglas"; Editio Cantor Verlag (2016).

[icg09] International Commission on Glass; "Strength of Glass – Basics and Test Procedures"; ICG Advanced Course (2009).

[lawn93] Lawn, B.; „Fracture of Brittle Solids – Second Edition"; Cambridge University Press (1993).

[maur21] Maurer, F.; "Tracking the Cracking"; in eBook: Primary Packaging for Optimized Fill & Finish; American Pharmaceutical Review (2021).

References (2)

[moul67] Mould, R.E.; „The Strength of Inorganic Glasses“; Fundamental Phenomena in the Materials Sciences (1967) 119.

[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).

[pt07] SCHOTT Rohrglas GmbH; „Aus Fehlern lernen – Glasfehler sichtbar gemacht“ (2007).

[quin20] Quinn, G.D.: „Fractography of Ceramics and Glasses”; NIST Special Publication 960-16e3 (2020).

Thank you for your attention!