Best Practices for Glass Primary Containers; 11-Jun-2024; Mainz, Germany

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Strength and reliability of glass containers used in the pharmaceutical industry

Dr. Florian Maurer, Principal Scientist, SCHOTT AG

PDA Parenteral Drug Association

PDA TRAINING

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)

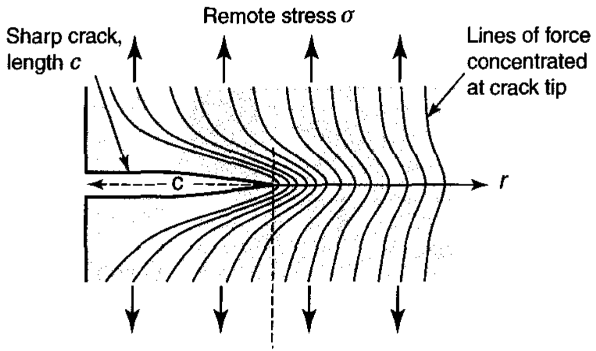
Definition of “flaw”

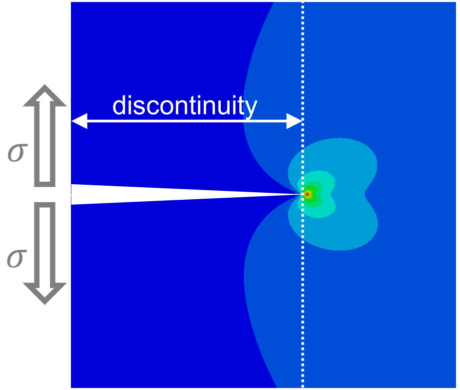
- Any type of “sharp” discontinuity within the isotropic, monolithic structure of the glass (including the surface), from which fracture surfaces (checks, cracks) can develop
    - “Sharp” geometry: radii < nanometers
    - Melting
        - Stones, refractory material, unmelted batch material
        - 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)

Likelihood for a critical flaw (in terms of strength) is different for different types of flaws

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 “sharp” 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

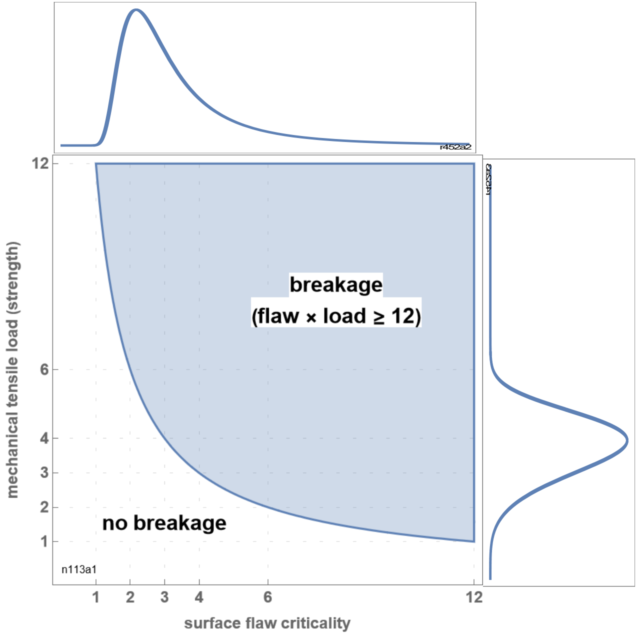
The strength of glass depends on flaw criticality

The flaw criticality is an expression for (surface) quality

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

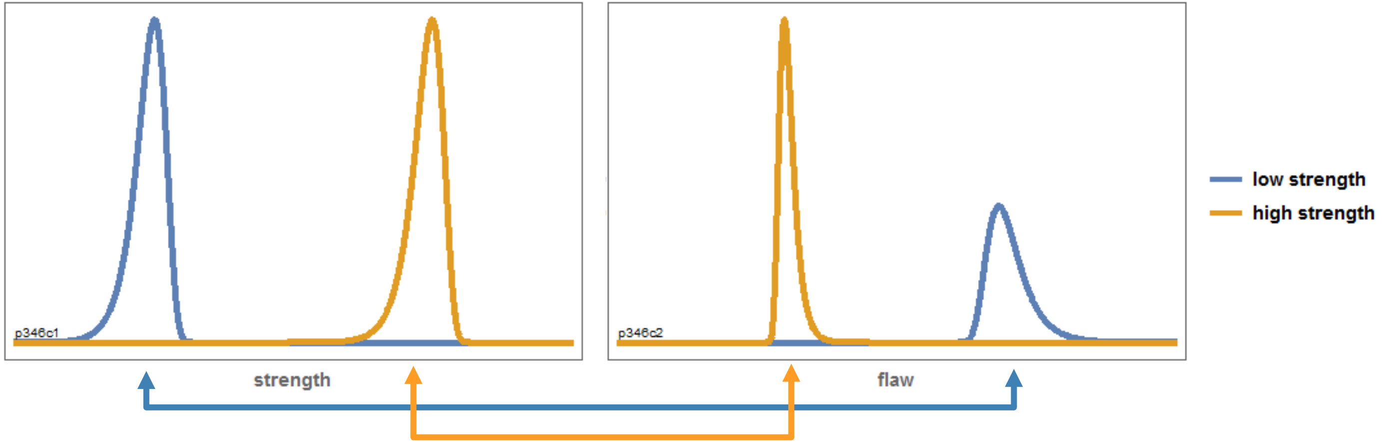
The flaw criticality is described by statistical distribution(s)

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



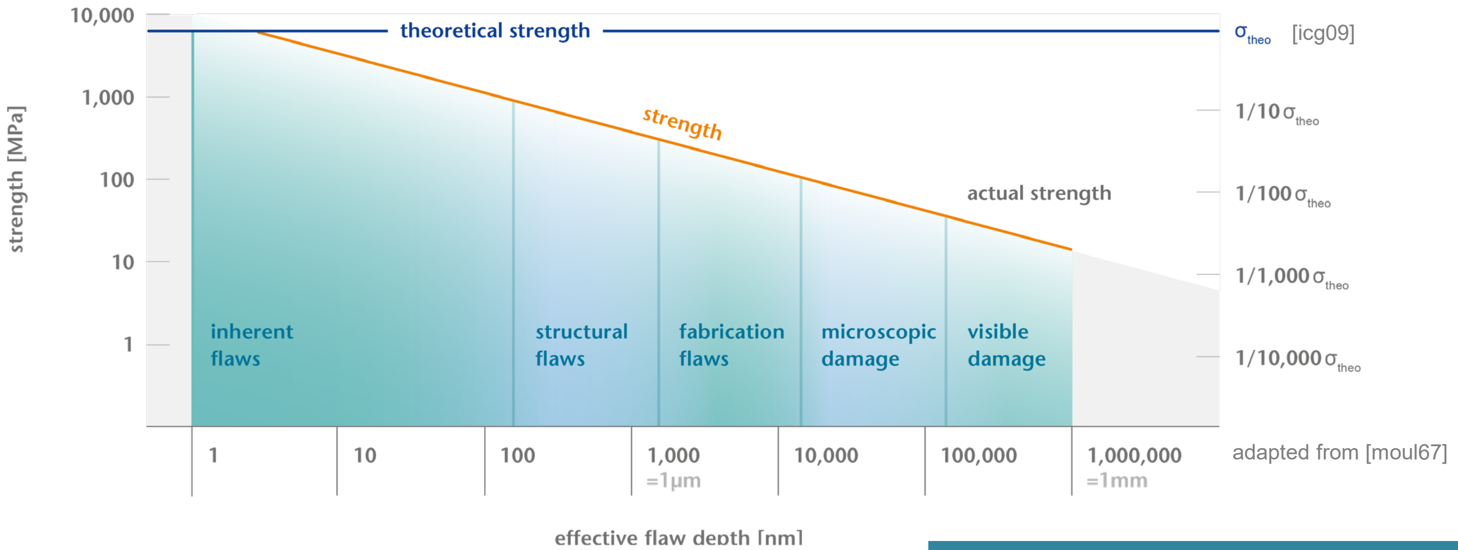
Determination of failure criteria

- 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

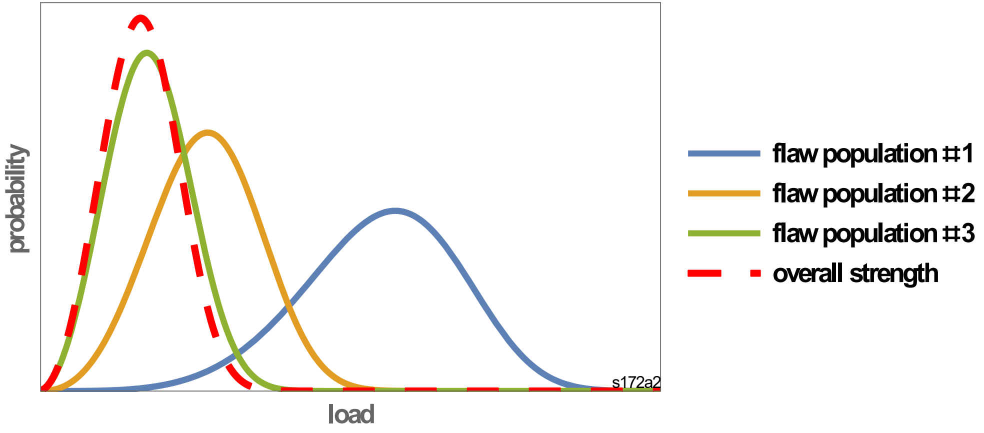


- Strength range: Several MPa to several GPa
- Theoretical strength: Weakest interatomic bond

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

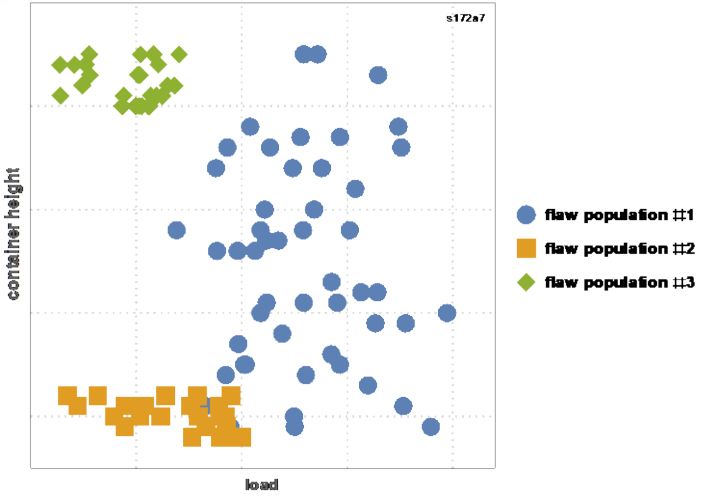


Multiple flaw populations (example)

- 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]



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Multiple flaw populations (example)

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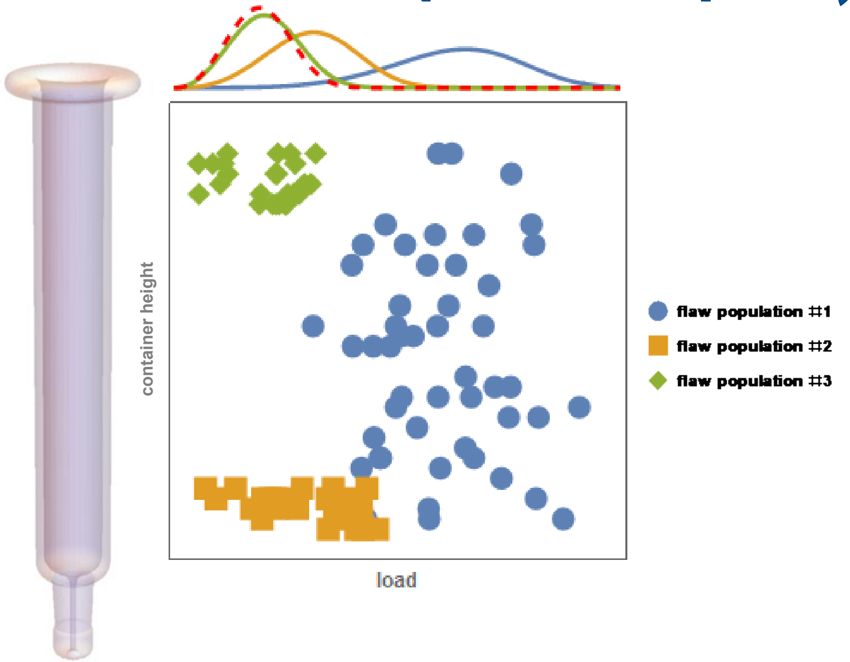
A systematic elimination of defect mechanisms approaches recovery of initial strength distribution

[hain16,maur21]

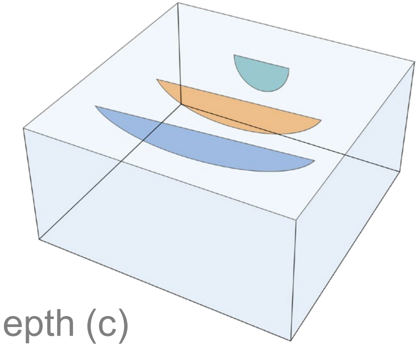


Assessment of flaws

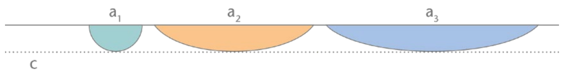
Assessment of flaws (in terms of breakage criticality)

- Different publishers
  - PDA Technical Report #43 [pda43]
  - “Defect Evaluation List”, 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”)

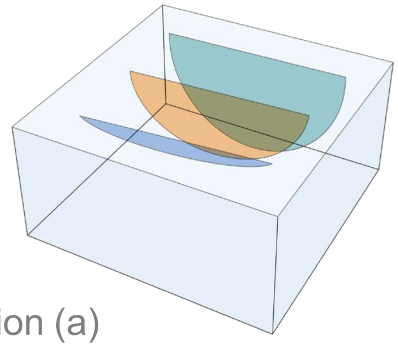
Assessment of flaws (in terms of breakage criticality)



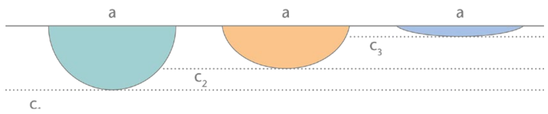
equal penetration depth (c)



criticality: ■ > ■ > ■



equal lateral dimension (a)



criticality: ■ > ■ > ■

Assessment of flaws (in terms of breakage criticality)

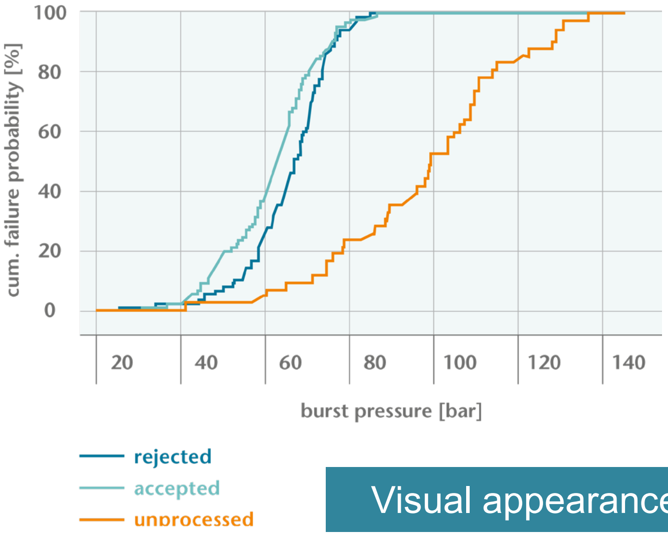
- Are optical techniques capable to acquire information about (three-dimensional) flaw geometry and depth?
  - Manual (human eye)?
  - Automated (camera/software)?

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)



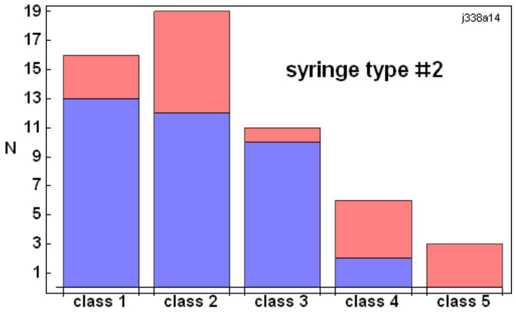
- Batch of glass vials rejected due to cosmetic flaws (■)
- Accepted reference batch (no cosmetic flaws) (■)
- Unprocessed batch (■)
- Burst-pressure strength experiments
- Fractographic examinations (location of fracture origin)

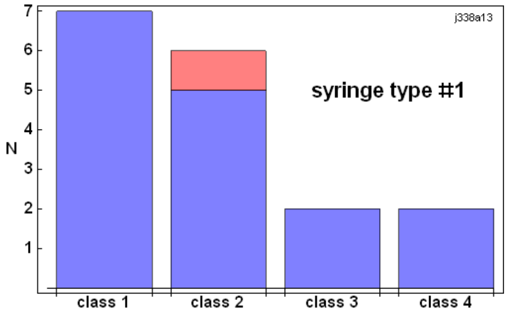
Visual appearance of flaws does not necessarily give a hint about the criticality

Cosmetic versus critical 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?

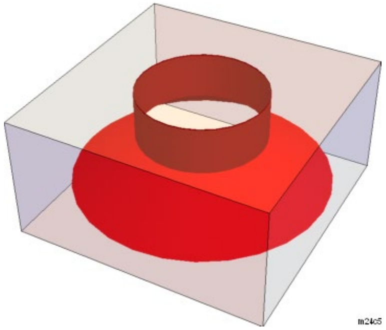
Optical assessment does not yield a reliable information about flaw criticality

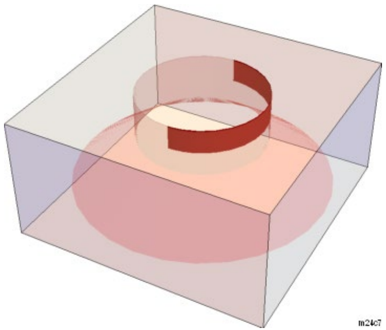


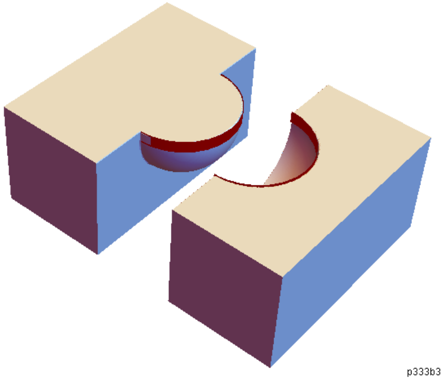


Common fracture origins: Blunt contact damages

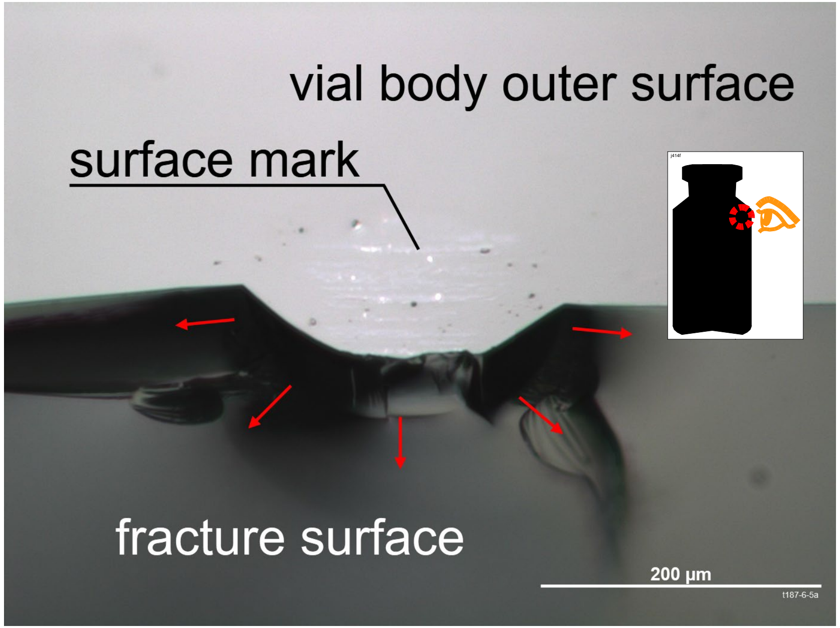
- “Bump check”, “bruise”, “percussion cone”
- Static or dynamic contact with blunt object
- Crack pattern: Hertzian cone crack [lawn93]
- Not necessarily fully developed
- After breakage, fracture origin forms a curved edge

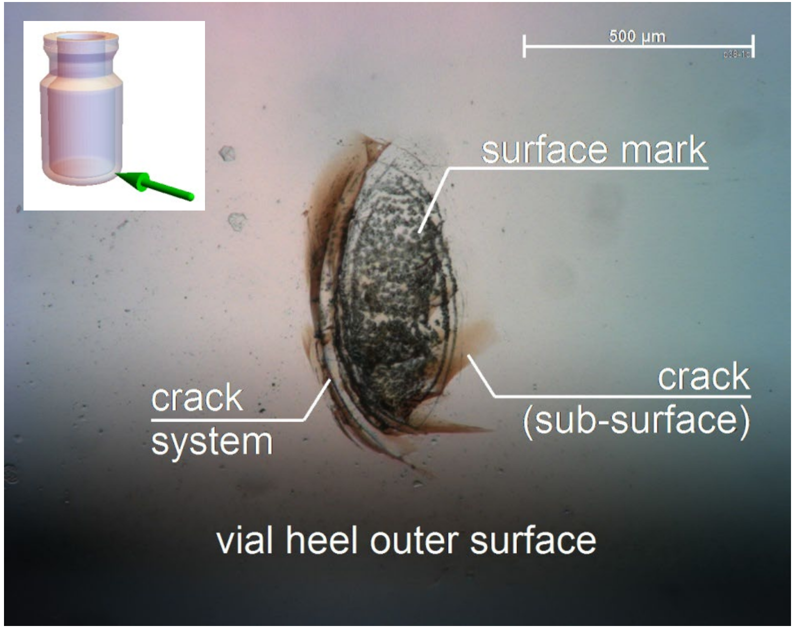




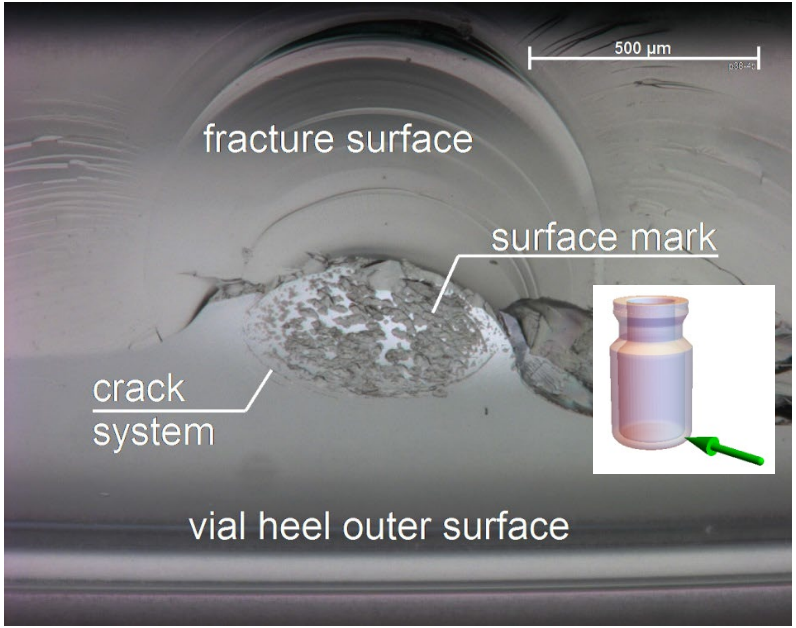


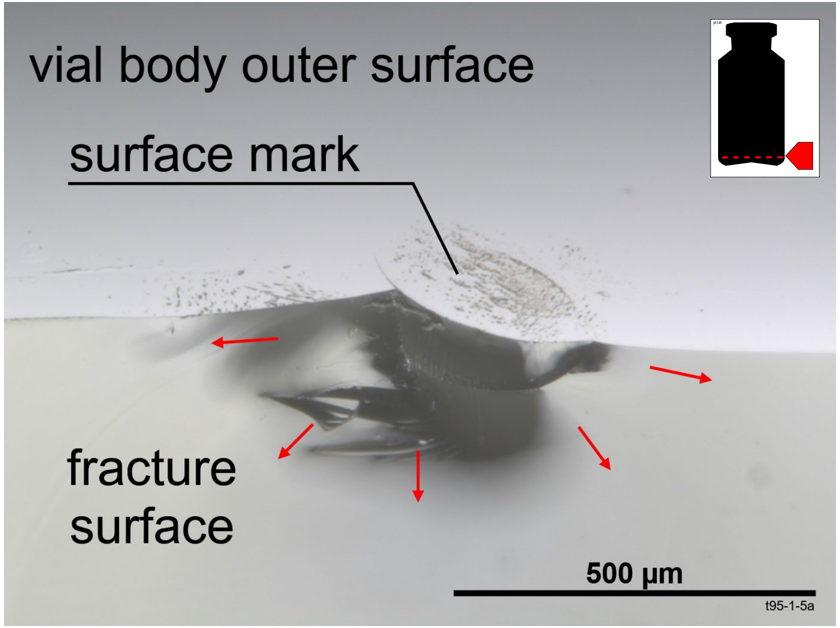
Blunt contact damages (examples)





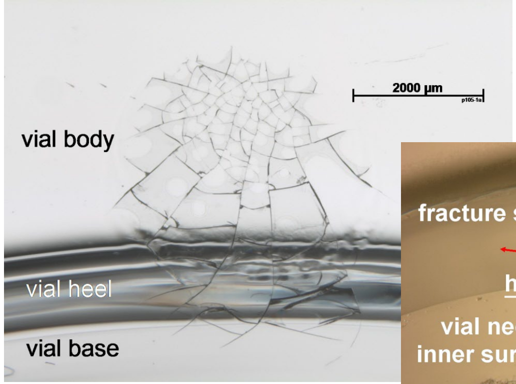
Blunt contact damages (examples)

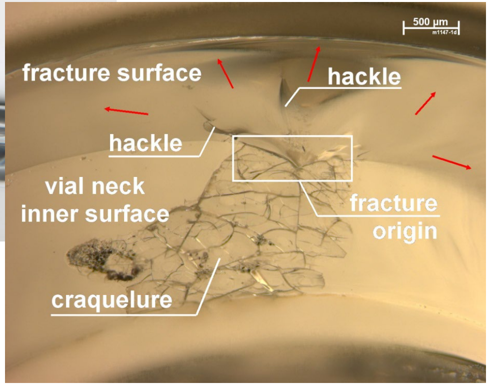




Common fracture origins: Craquelure (aka “crackles”)

- 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





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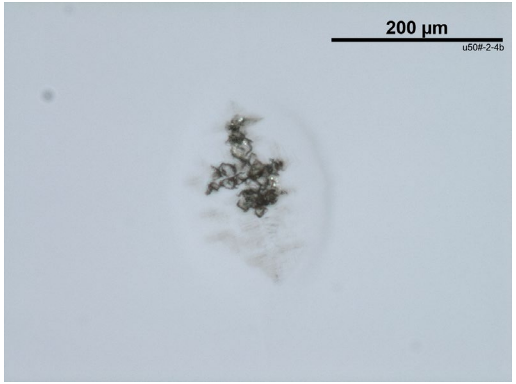
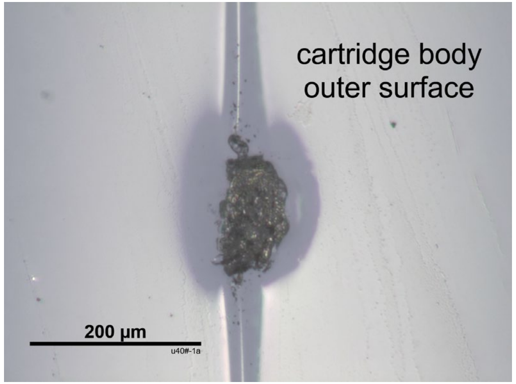
Common fracture origins: Crystals and stones

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





Fractography – Fundamentals

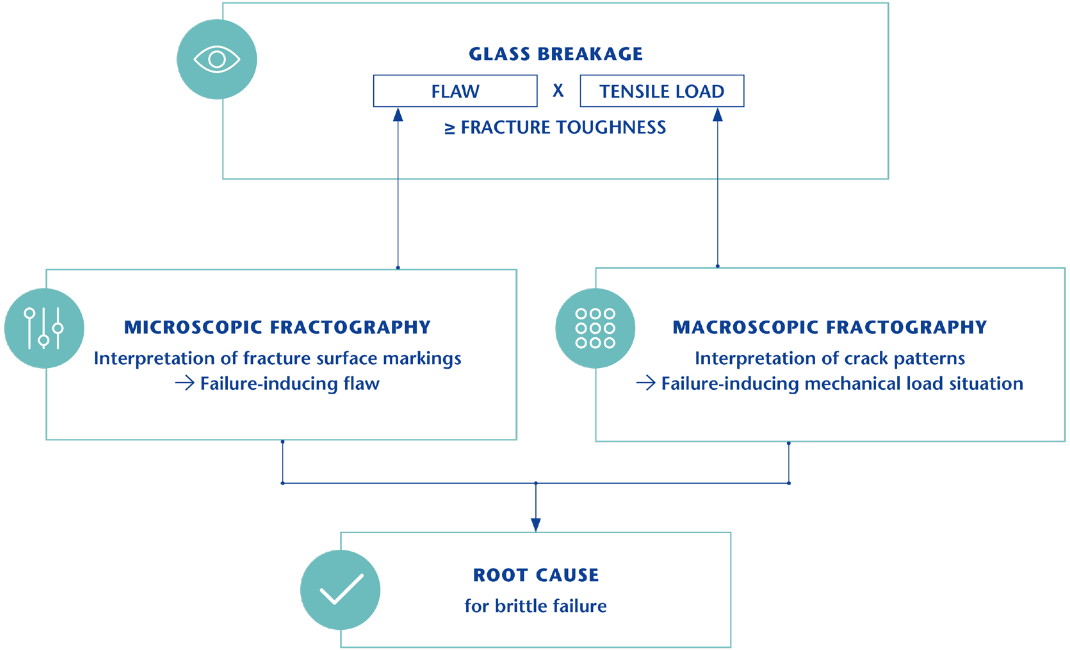
"Tracking The Cracking"

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)
- 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)

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 principal tension

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

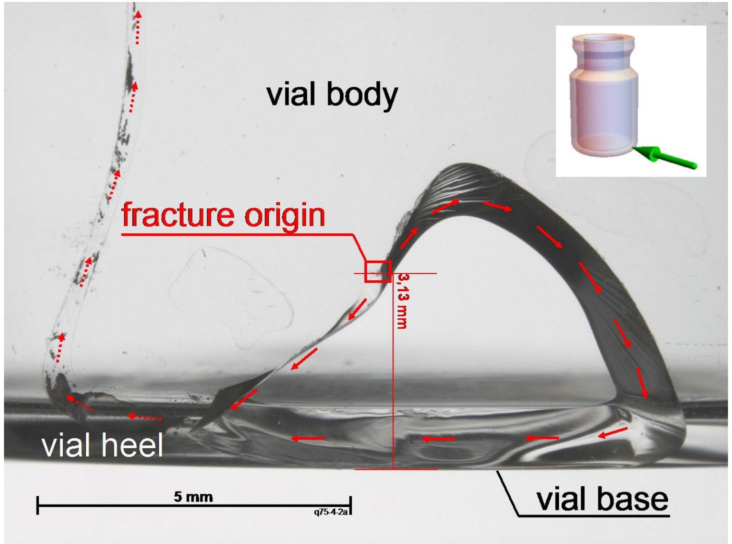
Crack branching starts at maximum propagation velocity

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)

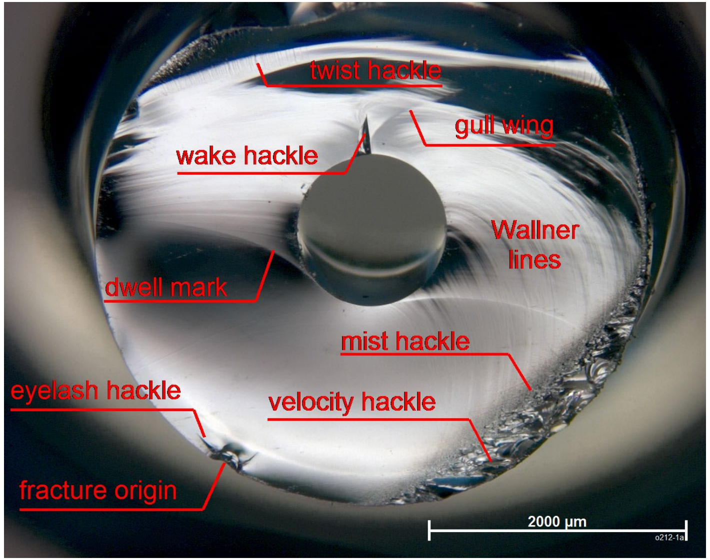


Fracture surface markings (microscopic fractography)

- Topographical 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

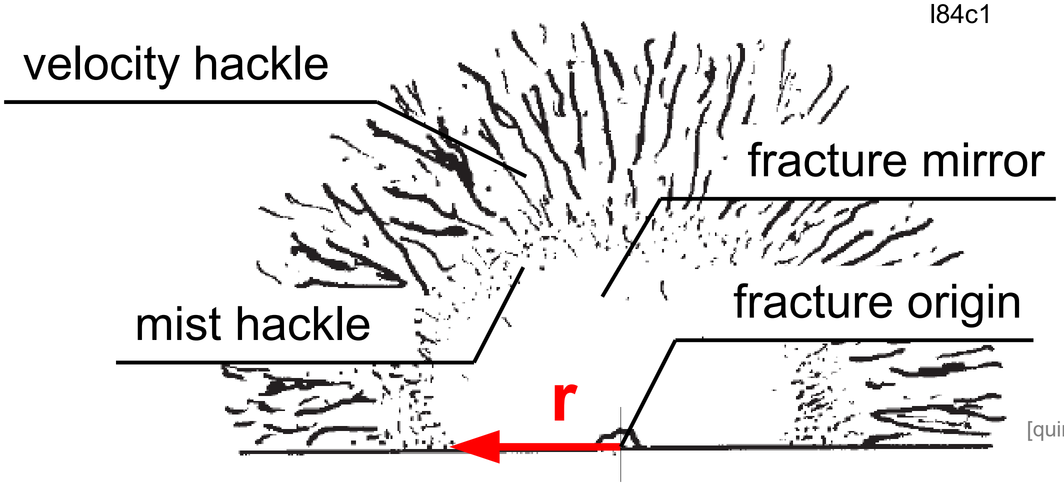
Fracture surface markings (microscopic fractography)



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

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