High-resolution bio-imaging with liquid-metal-jet x-ray sources

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Laboratory hard x-ray imaging

Image quality is source limited.
Electron-Impact X-Ray Sources

**X-Ray Brightness**

- **FELs**
- **ACCELERATORS**
- **TUBEs**

**History: Electron-impact sources**

- E-beam power density $\Leftrightarrow$ brightness
- Thermally limited

- Classic x-ray tube (1895) ~1 kW/mm²
- Rotating-anode source (1929) ~100 kW/mm²
- Liquid-metal-jet-target source (2003) >10 MW/mm²
- Regenerative, high speed

The liquid-metal-jet x-ray source:

Choice of anode material

E-Beam Power Density Capacity = \( v \rho (\Delta T_{c_p} + E_{vap}) \)

FOM = \( Z \sqrt[2]{\rho} (\Delta T_{c_p} + E_{vap}) \)

<table>
<thead>
<tr>
<th>Material</th>
<th>FOM ([\text{J/(kg}^{1/2}\text{m}^{3/2})])</th>
<th>Melting point ([\text{°C}])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plutonium</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>Bismuth</td>
<td>800</td>
<td>1600</td>
</tr>
<tr>
<td>Lead</td>
<td>600</td>
<td>1800</td>
</tr>
<tr>
<td>Mercury</td>
<td>400</td>
<td>2000</td>
</tr>
<tr>
<td>Tin</td>
<td>300</td>
<td>1800</td>
</tr>
<tr>
<td>Indium</td>
<td>200</td>
<td>1600</td>
</tr>
<tr>
<td>Silver</td>
<td>100</td>
<td>1400</td>
</tr>
<tr>
<td>Germanium</td>
<td>80</td>
<td>1200</td>
</tr>
<tr>
<td>Gallium</td>
<td>20</td>
<td>1000</td>
</tr>
</tbody>
</table>

Early results (<2008):

The liquid-(metal)-jet x-ray source

**Tin**

- **Kα**
- **Kβ**

**Gallium**

- **Kα**
- **Kβ**

**Methanol**

**Present data:**
- Jet diameter: 15-200 µm
- Jet speed: 10-100 m/s
- Source size: >5 µm
- Power: 50-300 W
- Power density: >2 MW/mm² (cf. ~10-100 kW/mm² existing sources)

**Future:**
- Power scalability: >100×
- Power dens. scal.: >10×

Present status:

**Liquid-Metal-Jet Microfocus Sources**

- GaInSn
- Room temp liquid metal alloy
- Metal circulation system
- 5-30 µm spot size
- 50-300 W power
- 2000 h
- Max: 15 MW/mm² short term

Commercialized by: eXcillum

![Graph](image)
Spot size

\[ \sigma_x = 0.07 \, \mu m \]
\[ \sigma_y = 0.09 \, \mu m \]

Spot stability 24 h

Comparison brightness

50 W/5 \( \mu m \): \( 1 \times 10^{11} \) ph/s \( \times \) mm\(^2\) \( \times \) mrad\(^2\) \( \times \) line

NEXT: 15 MW/mm\(^2\) @ 8 \( \mu m \) for 2000 h
Applications: XRD and SAXS

**S-SAD XRD**

*Theumatin*

Crystal: 0.18×0.20×0.22 mm  
Exp. time: 4 hours  
Resol: 1.7 Å  
Data cut off at 2.6Å

**SAXS**

*Rat tail tendon*  
(67 nm period)
**In/Ga anode**

for higher energy and thick-object imaging

- Higher In content (65%)
  → more 24 keV emission
  → better penetration through e.g., mouse

- Al filtering for reduced dose

- Elevated temp operation

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Larsson et al, RSI (2011)
X-ray in-line phase-contrast imaging with liquid-metal-jet sources

- Simple: no optics, no gratings
- Variations in density cause refraction
- Refraction cause edge enhancement
- Good at high spatial frequencies
- Requires:
  - small x-ray spot
  - a high-resolution detector

Test object

Tuohimaa et al, APL (2007)
Phase-contrast for enhanced CO$_2$ micro-angiography

Rat kidney vasculature

Phase retrieval

SNR$^2 = 25$ for 50 µm vessel in rat kidney

Tomography

Data: 360x14 sec
Power: 40 W
Dose: 160 mGy
Observe: 50 µm vessels

Lundström et al, PMB (2012b)
Quantitative detectability

How?

Ideal observer signal-to-noise ratio (SNR):

$$SNR^2 = \int \int \frac{|\Delta G(u)|^2}{W(u)} d^2u$$

- $u$: spatial frequency
- $\Delta G$: Fourier transform of the signal difference
- $W$: noise power spectrum.

$SNR^2 = 25$ is required to detect a vessel.

Adjust dose to give $SNR^2 = 25$

Lundström et al, PMB (2012a)
Tumours:
Natural-contrast tumour demarcation in mouse

**Natural contrast**
Absorption vs phase-contrast

Phase-contrast
19 mGy

Absorption CT
1.3 Gy

Phase-const    Abs contr
Same dose ≈19 mGy

Larsson et al, Med Phys (2013)
Phase-contrast CO₂ microangio:

Limitations

**Gas filling**
- Depends on gas pressure
- Required pressure is
  \[ P = 4\gamma/D, \]
  \( D = \) diameter of vessels
  \( \gamma = \) surface tension

**Photon noise**
- Depends on
  - Exposure time
  - Radiation dose
  - Imaging distances
  - X-ray source and detector

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**Graphs**

- **Gas pressure** vs. Vessel diameter [µm]
- **Radiation dose** vs. Vessel diameter [µm]

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Lundström et al, PMB (2012b)
Summary & Future

• Liquid-metal-jet sources promise 100× higher brightness
  – High-spatial resolution imaging
  – Spatial coherence for strong in-line phase contrast

• Phase-contrast imaging
  – Micro vasculature imaging with CO$_2$
  – Single-cell-size detail
  – Dose levels acceptable for small-animal studies.

• Next
  – Source:
    • Higher power, higher brightness, shorter exposure times
  – In-line CO$_2$ micro angiography:
    • Tumor angiogenesis studies
    • Plaque
  – Comparison between propagation-based and grating-based phase-contrast imaging
Biomedical & X-Ray Physics group

Thanks!

Soft x-rays:
Sources, optics, & microscopy

Hard x-rays:
Sources, optics & imaging

Ultrasonics & μ-fluidics:
Bio-analytics and cell biol.

Optics:
Peripheral vision

Teaching & technical