Post-ionization mobility separation for MALDI based analysis of isomeric cannabinoids in plant samples

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Isomeric cannabinoids in the focus

- More than 100 isolated cannabinoids in cannabis
- Biosynthesis based on cannabigerolic acid
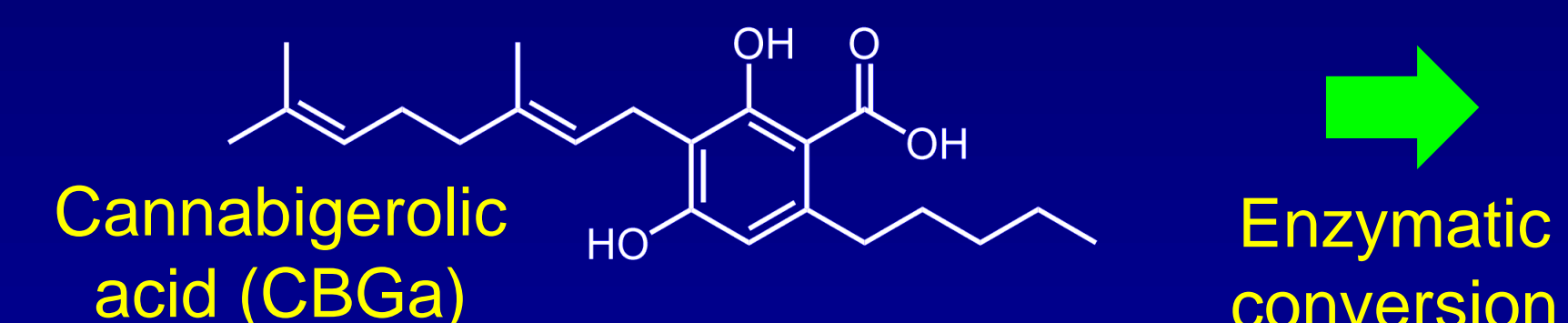- Content of the two most discussed cannabinoids, CBD and THC, differs between varieties

Cannabigerolic acid (CBGa)

Enzymatic conversion

Cannabidiol (CBD)

ΔT $-CO_2$

- Non-psychoactive
- Anti-epileptic, anxiolytic
- Wide distribution in consumables

$\Delta 9$-Tetrahydrocannabinol (THC)

ΔT $-CO_2$
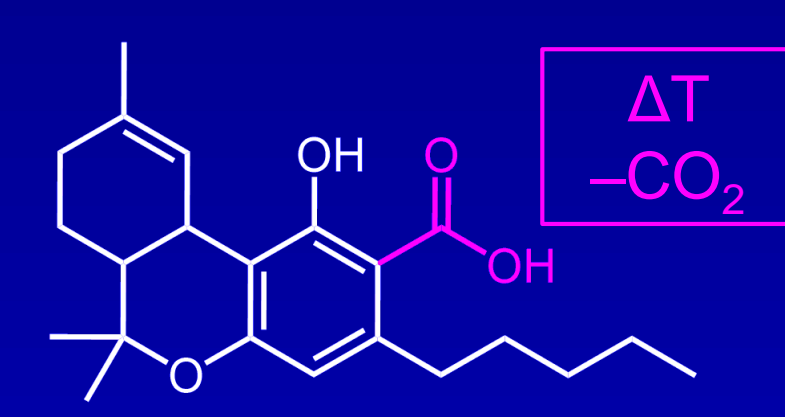
- Main psychoactive cannabinoid
- Inconsistent global regulation

Variety	CBD	THC
Industrial hemp	High	< 0.2 %
Bediol	8 %	6.3 %
Bedrocan	0.1 %	22 %

MALDI-TIMS-MS: Potential for fast and direct isomer analysis!

Instrumentation and workflow

ESI for calibration

Carrier gas
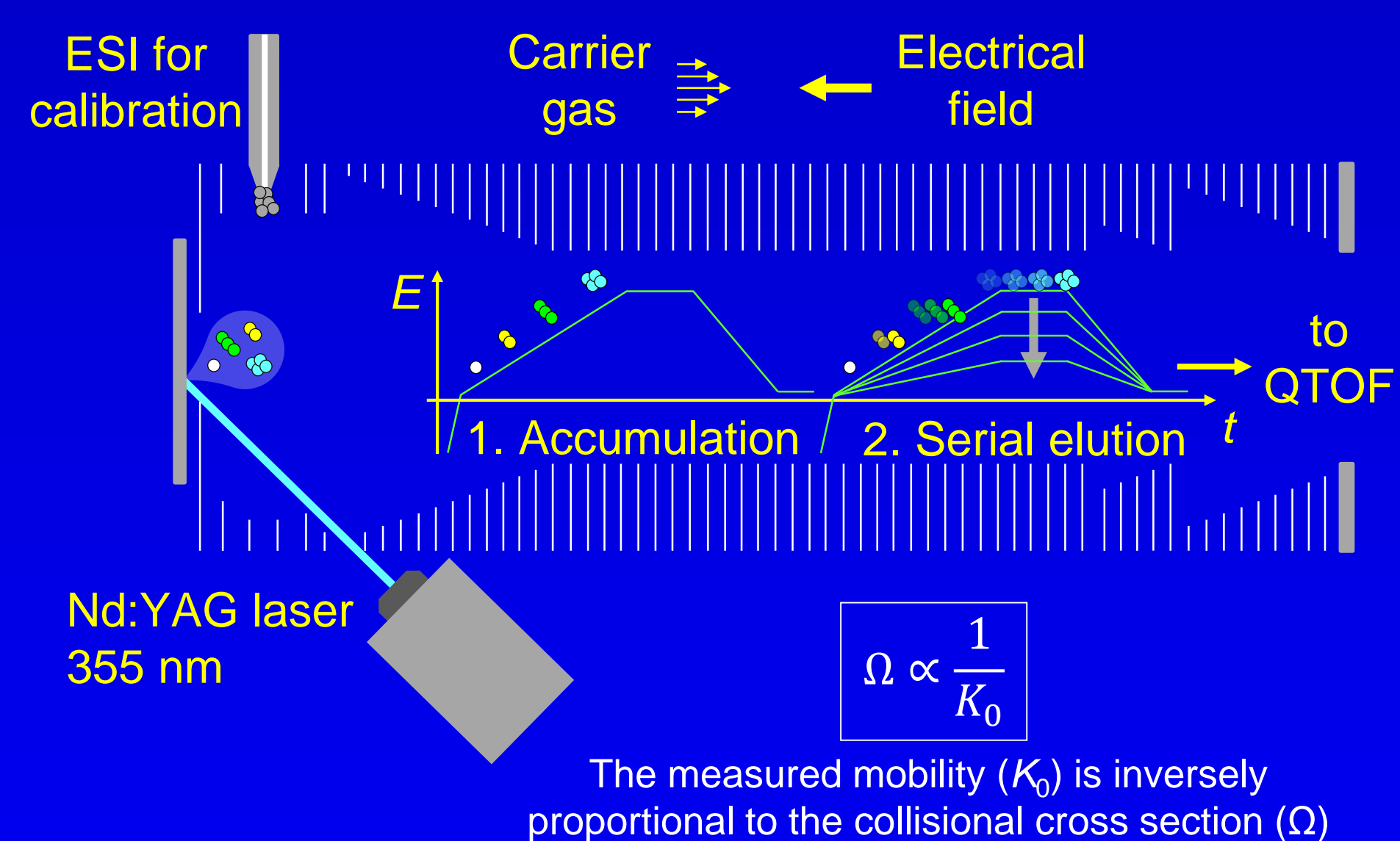
Electrical field
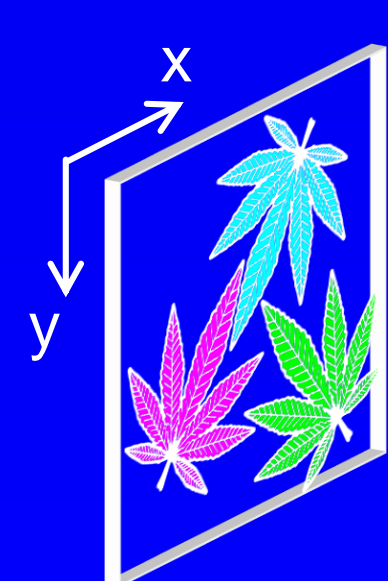
timsTOF fleX (Bruker Daltonik)

→ Dual ESI/MALDI source

→ TIMS:
Carrier gas vs. electrical field: ions are trapped, pre-separated and serially eluted

→ Detection via QTOF-MS enables MS[2] and high resolution of 50,000 (FWHM @ m/z 1222)

E
to QTOF
1. Accumulation   2. Serial elution t

Nd:YAG laser 355 nm

$$\Omega \propto \frac{1}{K_0}$$

The measured mobility (K_0) is inversely proportional to the collisional cross section (Ω)

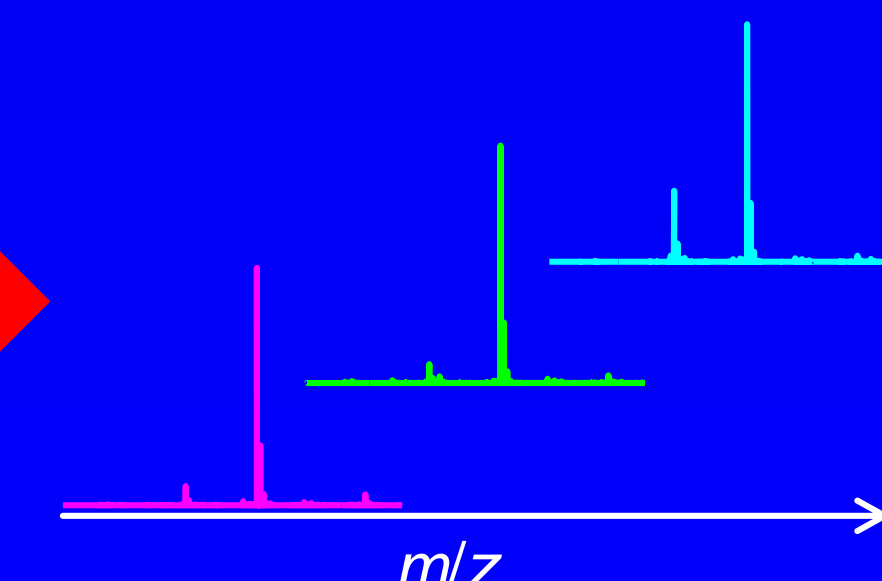Desorption and ionization

Ion mobility separation

m/z analysis

$1/K_0$

m/z

- Fixation by double sided conductive tape
- 9AA matrix sublimation
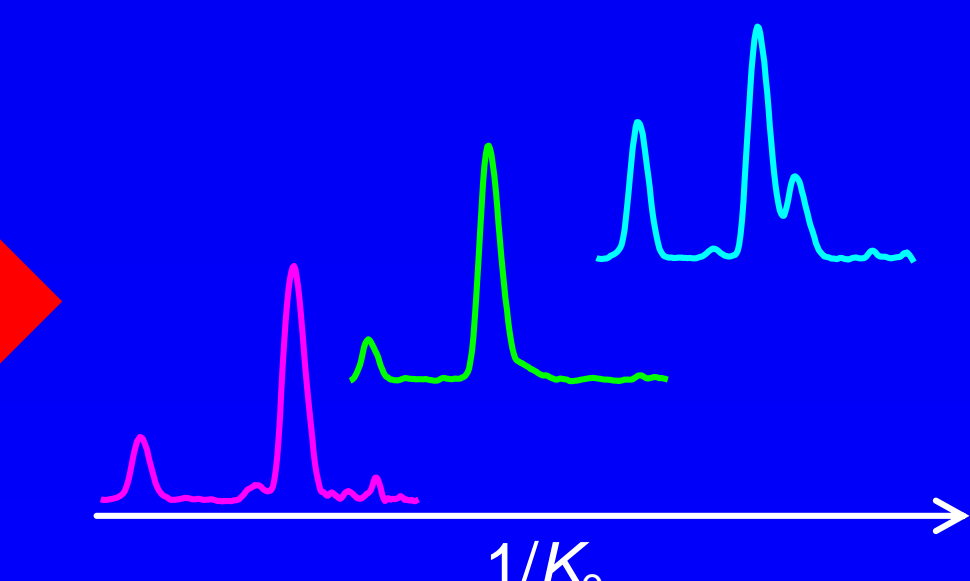
- $1/K_0$ range: 0.15 Vs/cm^2
- Cycle time: 300 ms
- Mobility Resolution: R~100

- Mobility resolved MS[1] and MS[2] experiments

Results

a) Mobility separation of isomers
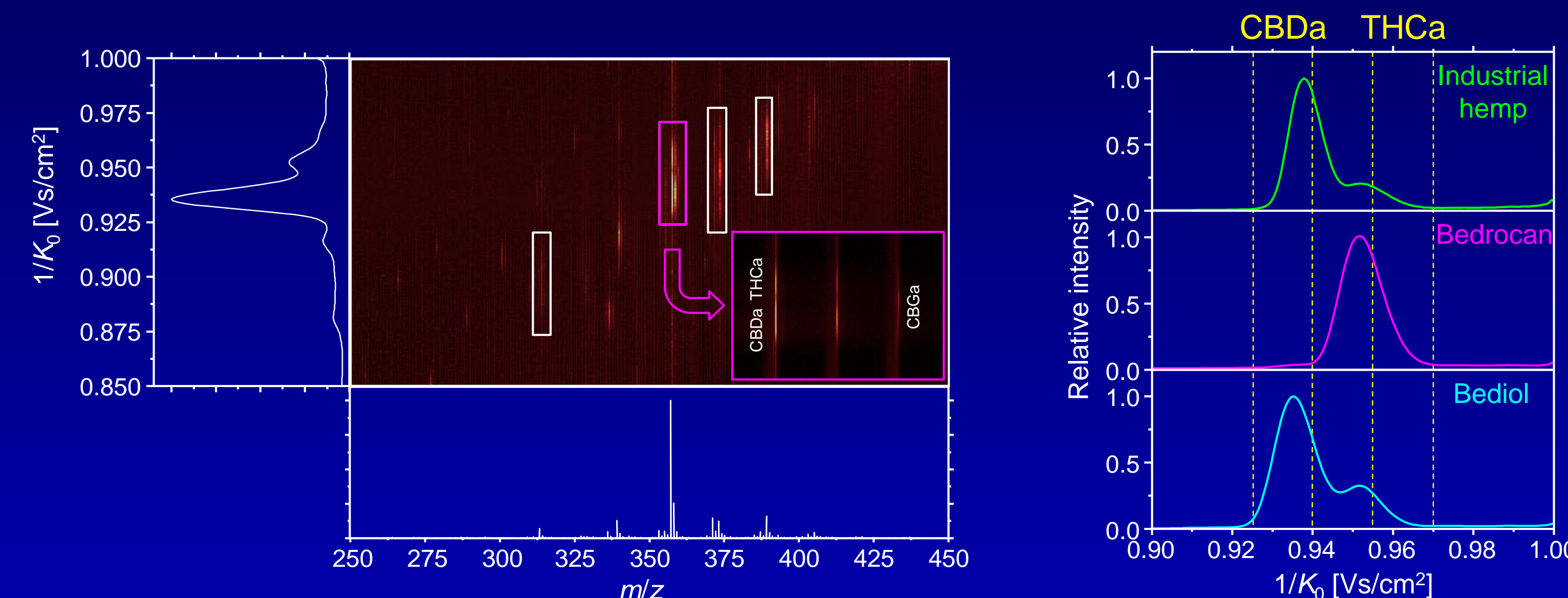
Fig. 1: Heatmap plot of a bediol TIMS-MS scan.

Fig. 2: Extracted ion mobilograms for m/z 357.21 ± 0.01 of different varieties.

- Detection of numerous cannabinoids by single MALDI-TIMS-MS scans within ms
- Main signals beyond m/z 350 → carboxylic acids are predominant in plants
- Multiple signals in the mobility dimension indicate the presence of isomers
- Isomers THCa and CBDa are almost baseline separated, signal maxima in line with sample declaration

b) Isomer identification via mobility resolved MS[2]

$1/K_0 = 0.960 \pm 0.005$ Vs/cm^2

$1/K_0 = 0.935 \pm 0.005$ Vs/cm^2

THCa ✓

CBDa ✓

Fig. 3: Mobility resolved fragmentation patterns of the isomers CBDa and THCa.

- After their separation in the TIMS funnel, isomers are serially fragmented in the qToF
- Distinct isomer identification based on characteristic fragmentation patterns

c) Imaging of isomer distribution

4 mm

Fluorescence   CBDa

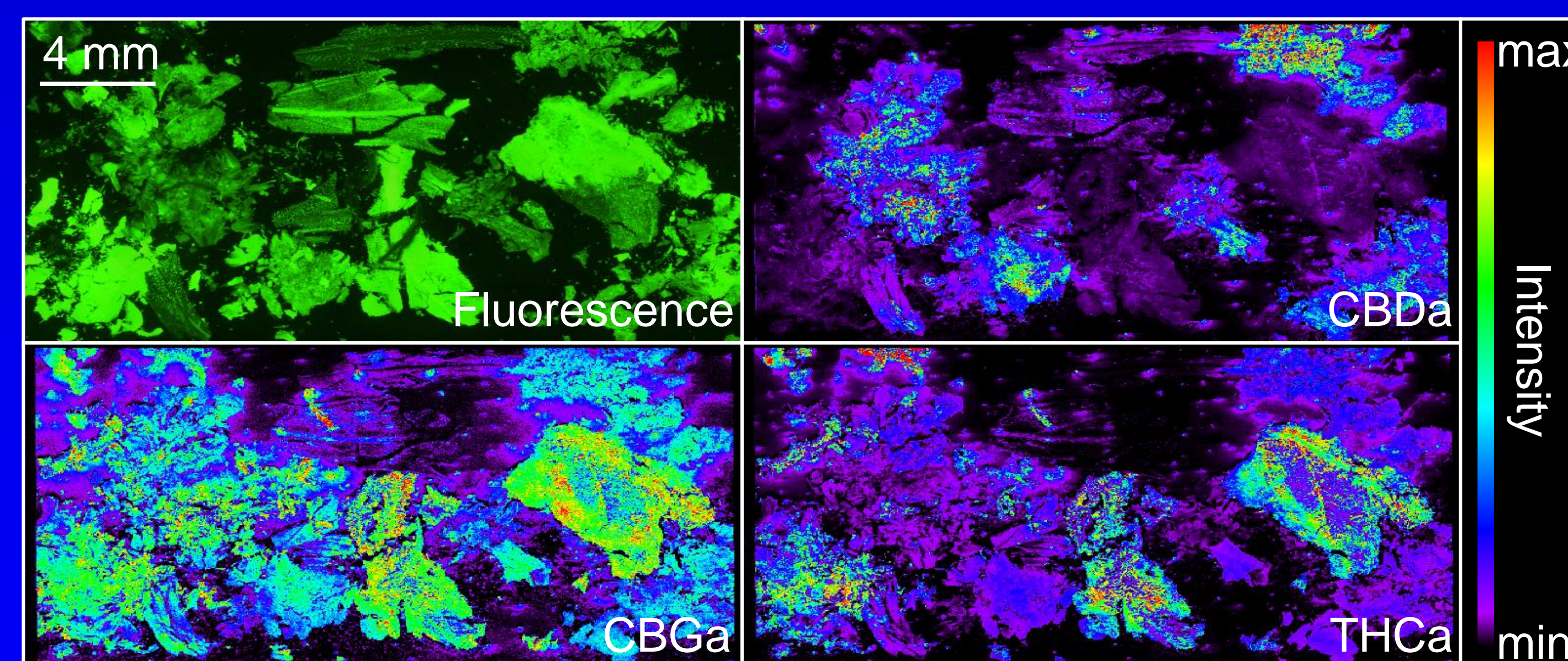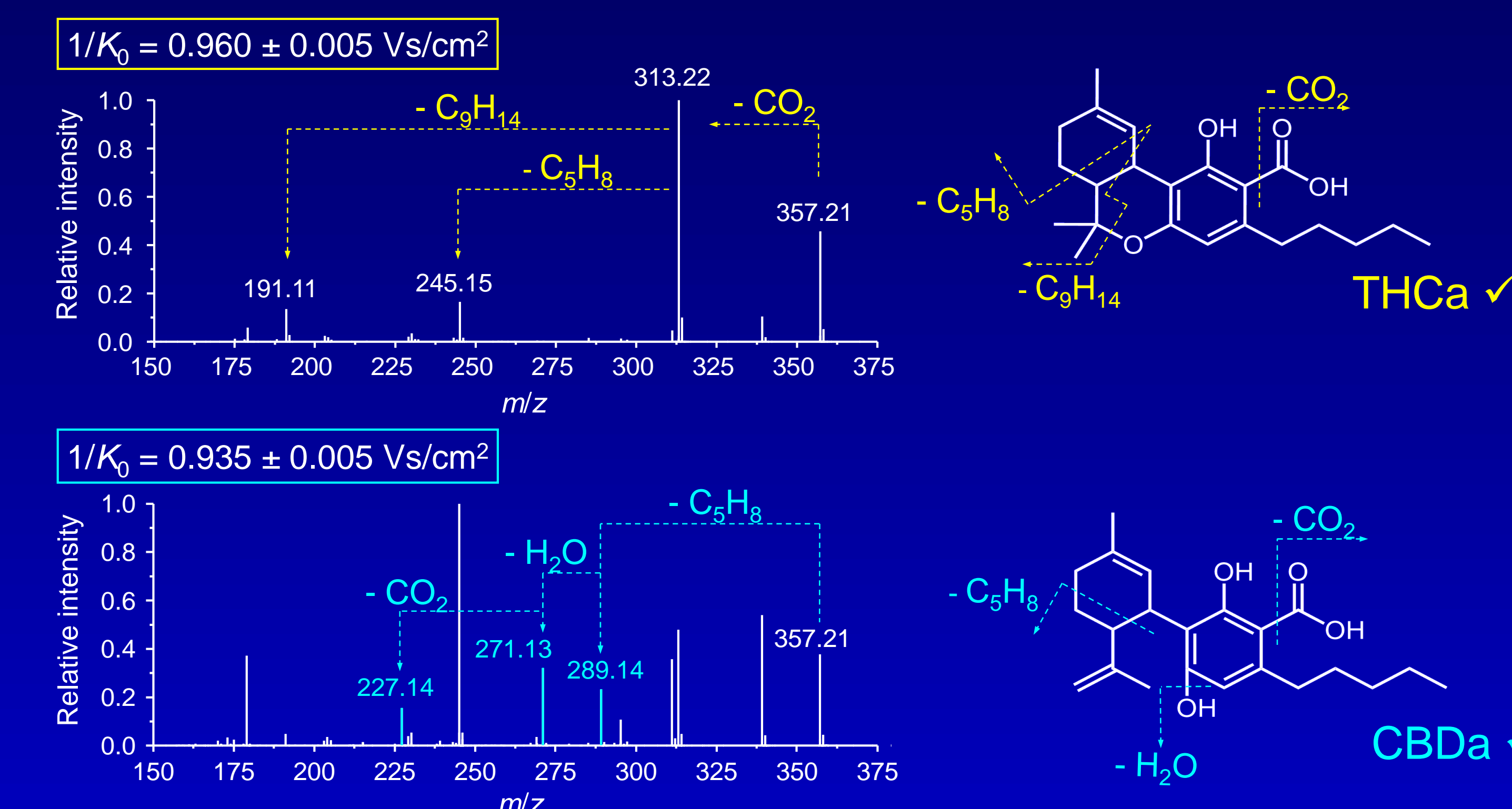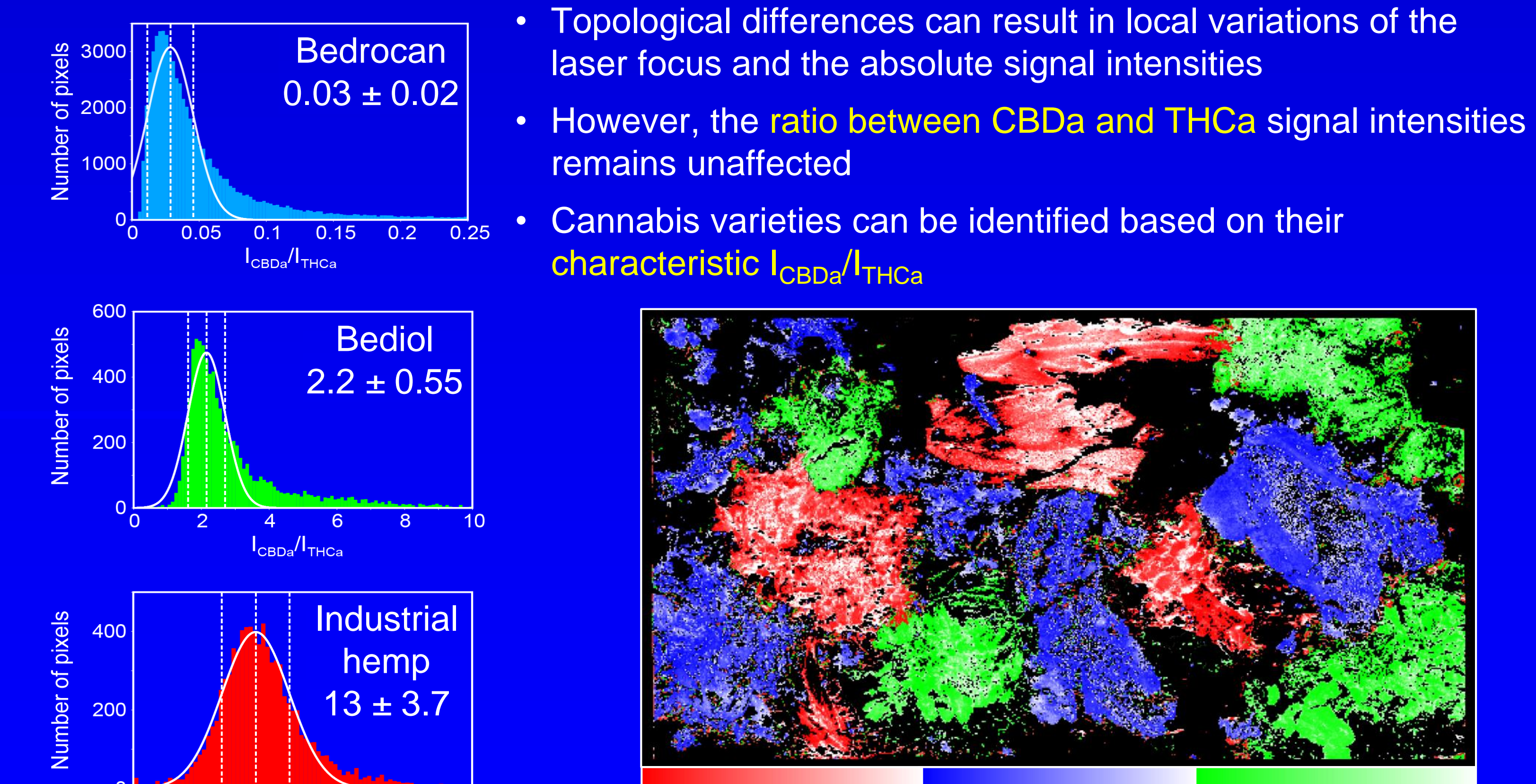CBGa   THCa

max   Intensity   min

Fig. 4: Auto fluorescence image and molecular distributions of the cannabinoids CBDa, THCa and CBGa of a random mixture of bedrocan, bediol and industrial hemp.

- A random mixture containing three different cannabis varieties was prepared on ITO slides
- Molecular images are extracted based on mass and mobility ranges
- The isomers THCa and CBDa show an inverse distribution, while their precursor CBGa is evenly distributed among different varieties

d) Mobility based cannabis identification

- Topological differences can result in local variations of the laser focus and the absolute signal intensities
- However, the ratio between CBDa and THCa signal intensities remains unaffected
- Cannabis varieties can be identified based on their characteristic I_{CBDa}/I_{THCa}

Bedrocan
0.03 ± 0.02
I_{CBDa}/I_{THCa}

Bediol
2.2 ± 0.55
I_{CBDa}/I_{THCa}

Industrial hemp
13 ± 3.7
I_{CBDa}/I_{THCa}

Fig. 5: Histograms of I_{CBDa}/I_{THCa} for different cannabis varieties.

Industrial hemp   Bedrocan   Bediol

Fig. 6: Colour coded distribution of different cannabis varieties based on their characteristic I_{CBDa}/I_{THCa}.