

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

Cannabidiol (CBD)



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

Δ9-Tetrahydrocannabinol (THC)



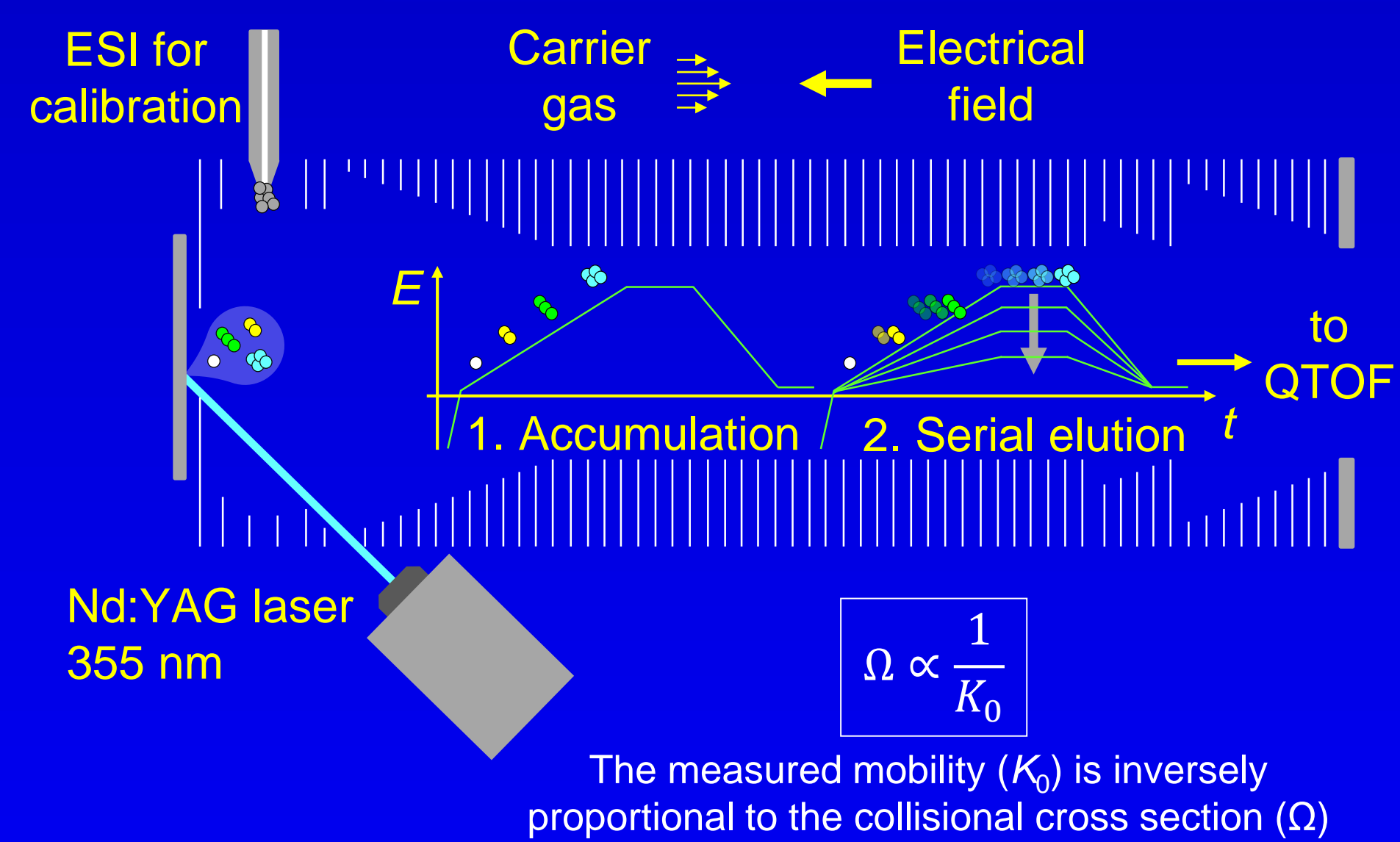
- Main psychoactive cannabinoid
- Inconsistent global regulation



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!

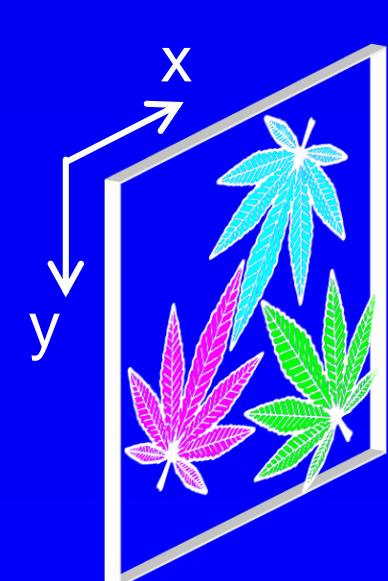
Instrumentation and workflow



timsTOF fleX (Bruker Daltonik)

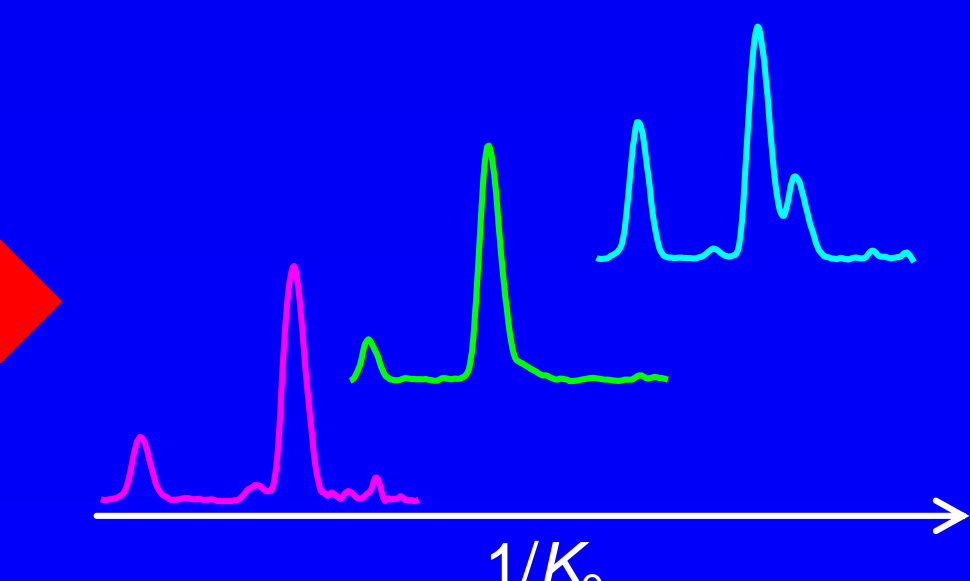
- Dual ESI/MALDI source
- TIMS: Carrier gas vs. electrical field: ions are trapped, pre-separated and serially eluted
- Detection via QTOF-MS enables MS² and high resolution of 50,000 (FWHM @ m/z 1222)

Desorption and ionization



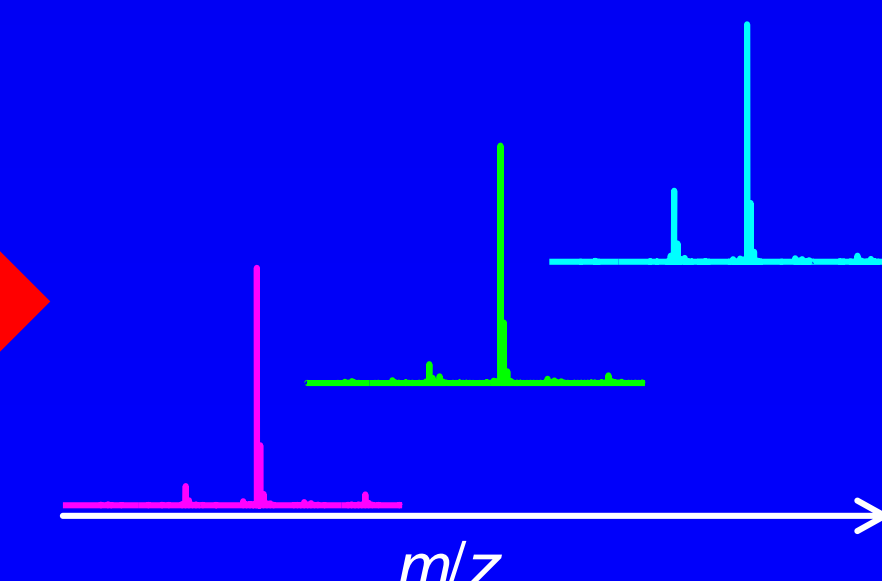
- Fixation by double sided conductive tape
- 9AA matrix sublimation

Ion mobility separation



- 1/K₀ range: 0.15 Vs/cm²
- Cycle time: 300 ms
- Mobility Resolution: R~100

m/z analysis



- Mobility resolved MS¹ and MS² experiments

a) Mobility separation of isomers

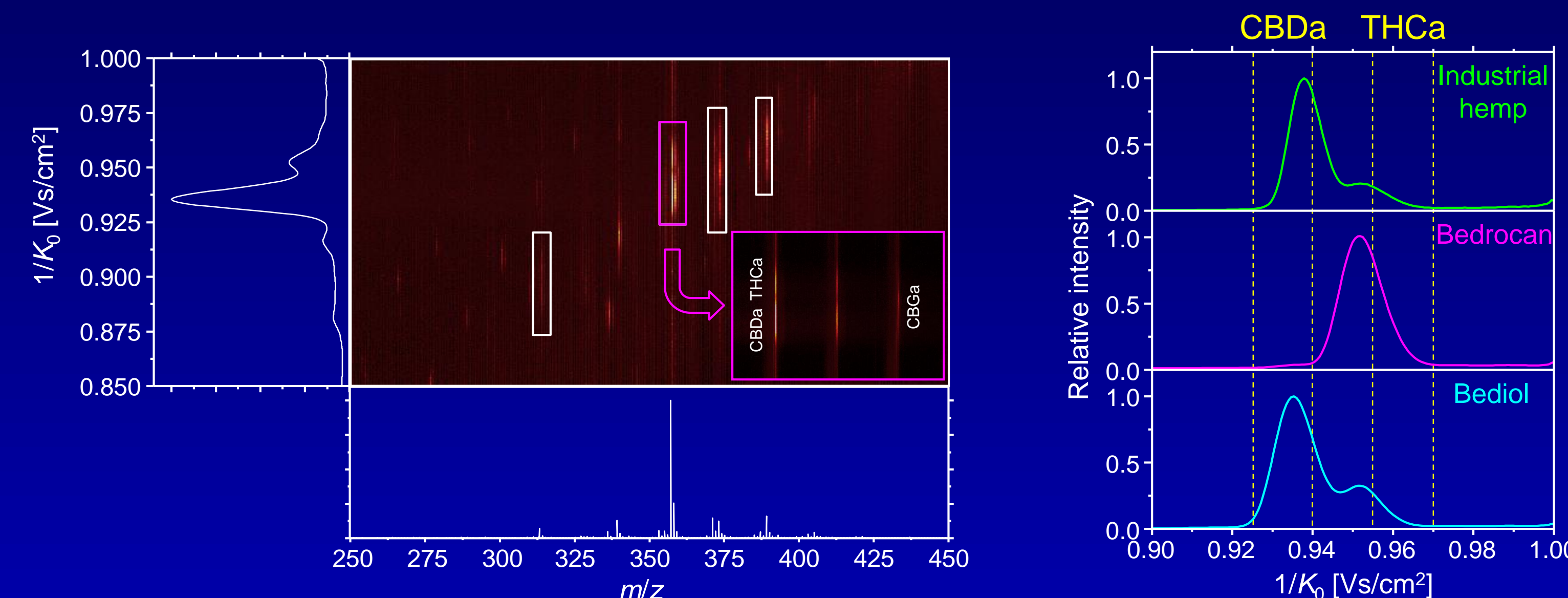


Fig. 1: Heatmap plot of a bediol TIMS-MS scan.

- 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

c) Imaging of isomer distribution

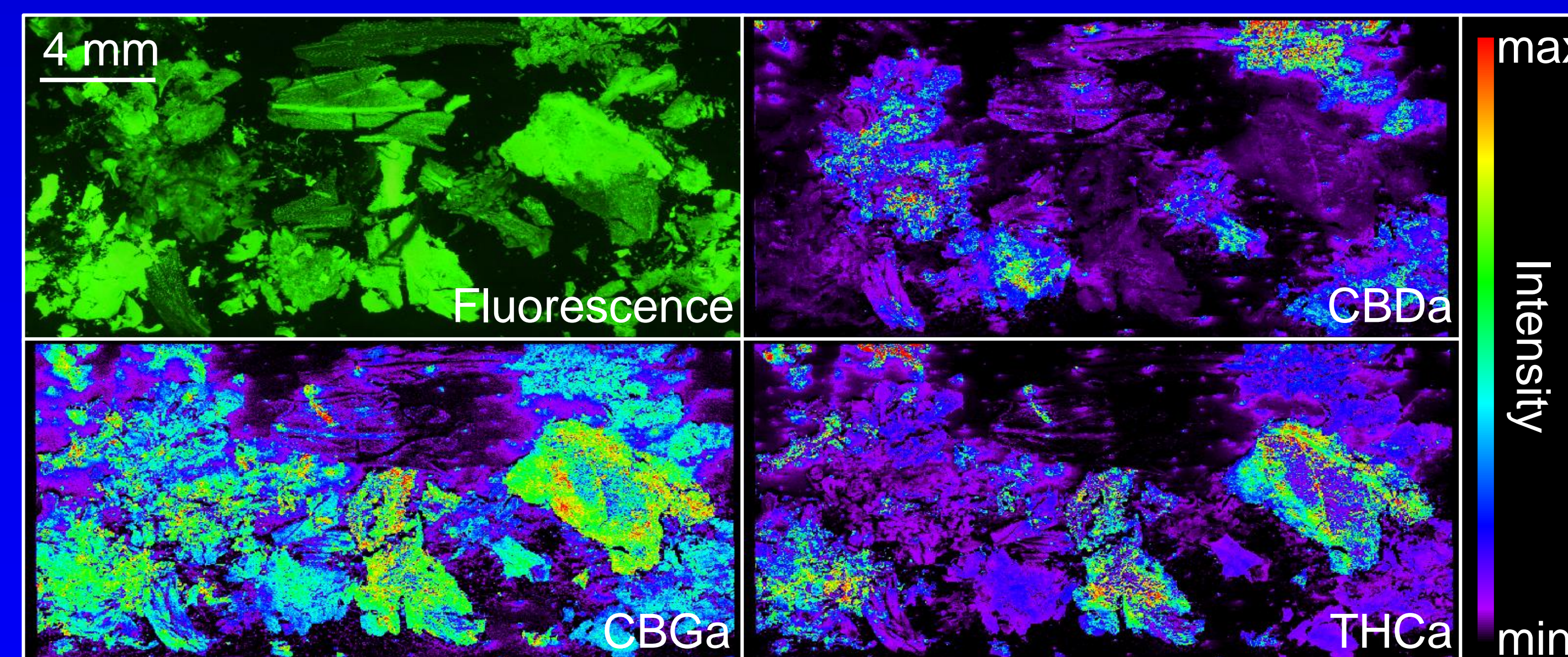


Fig. 4: Auto fluorescence image and molecular distributions of the cannabinoids CBDa, THCa and CBGa of a random mixture of bedrocan, bediol and industrial hemp.

- 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

Results

b) Isomer identification via mobility resolved MS²

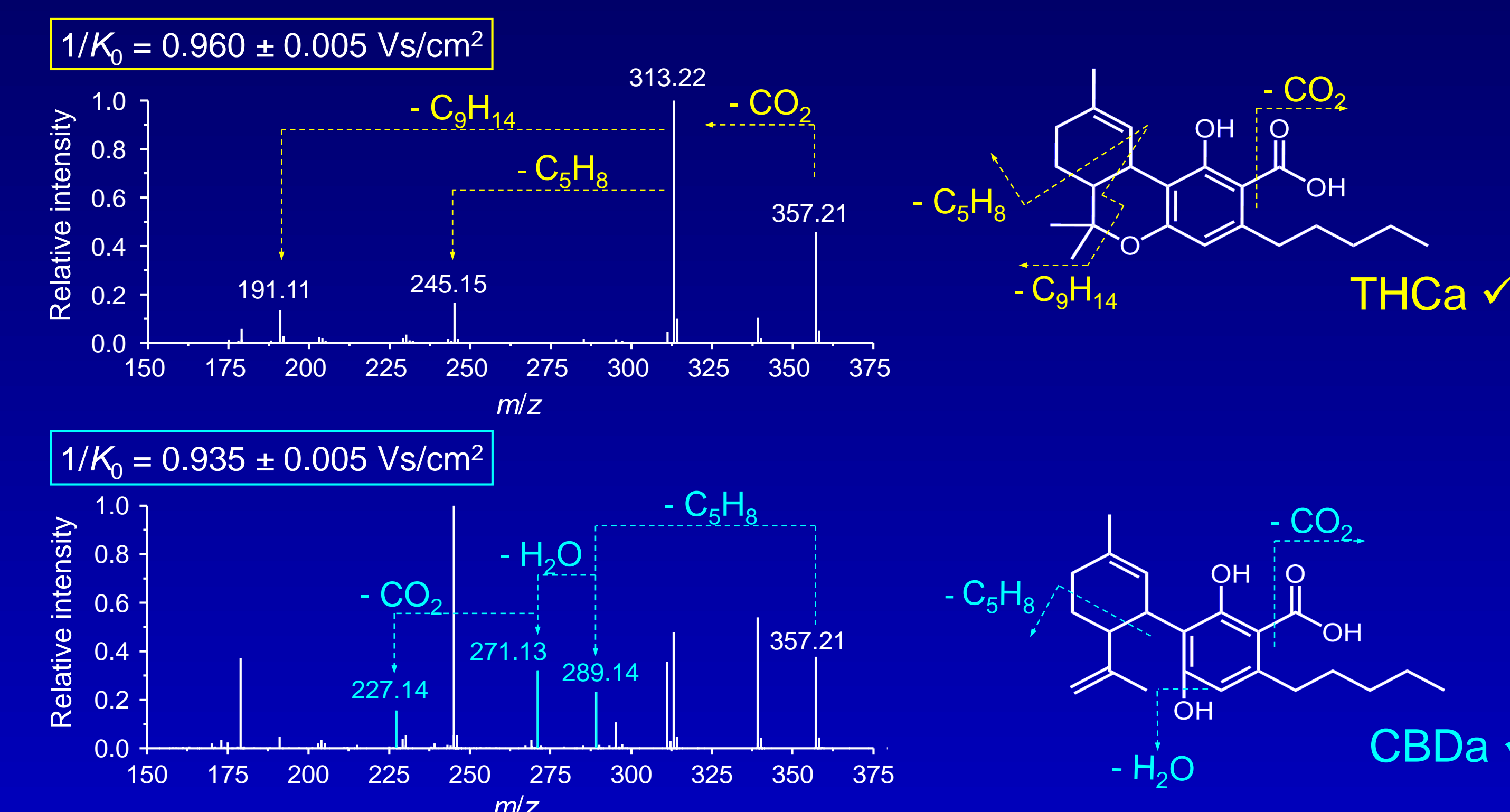


Fig. 3: Mobility resolved fragmentation patterns of the isomers CBDa and THCa.

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

d) Mobility based cannabis identification

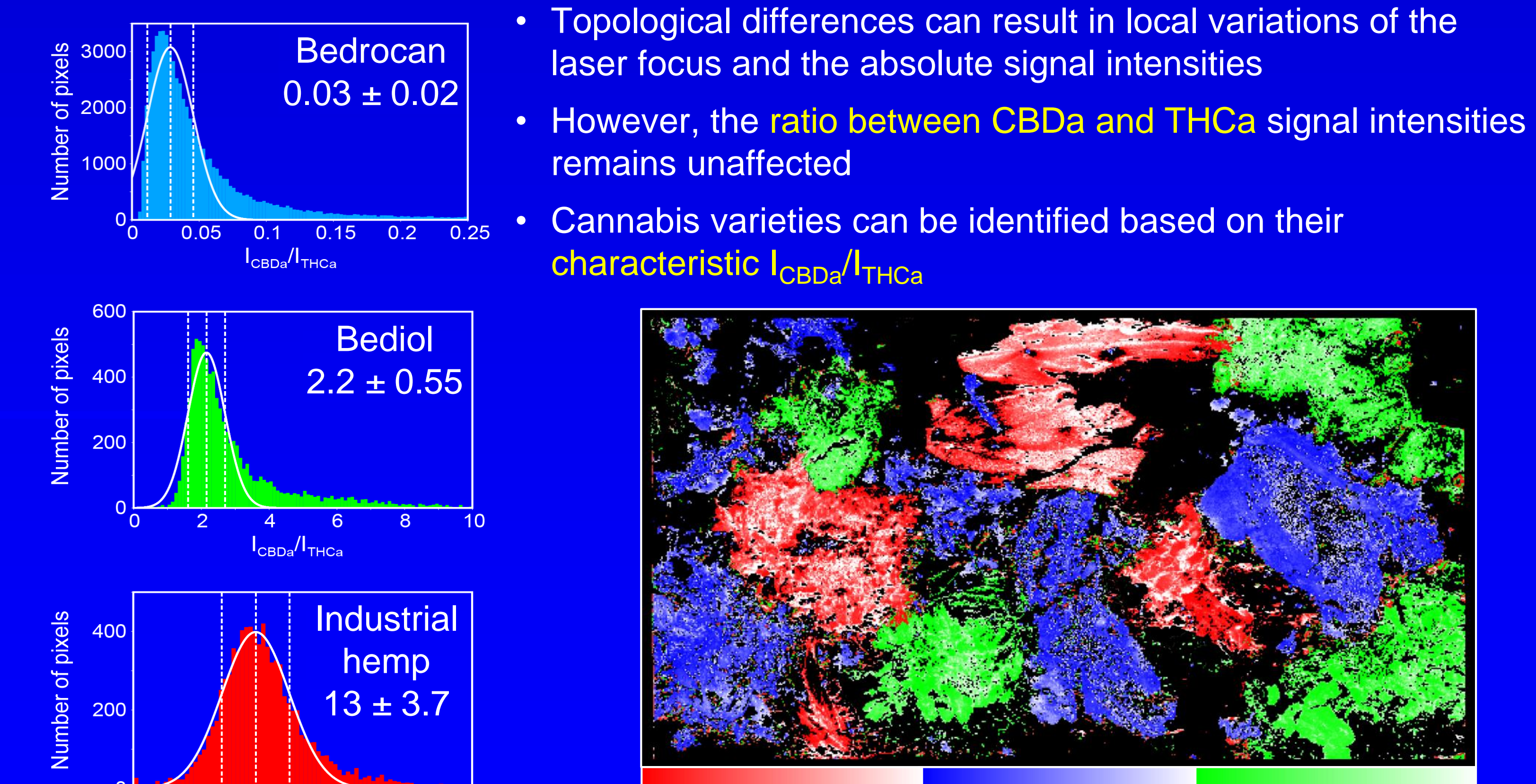


Fig. 5: Histograms of $I_{\text{CBDa}}/I_{\text{THCa}}$ for different cannabis varieties.

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

- 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 $I_{\text{CBDa}}/I_{\text{THCa}}$