REAL-TIME CHEMICAL PUFF PROFILING OF VAPOR PRODUCT AEROSOL WITH PROTON TRANSFER REACTION – MASS SPECTROMETRY

TSRC 2019

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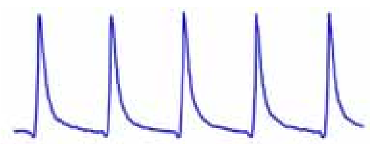
Outline

1. Introduction

2. Puff-by-puff analysis with Vocus PTR-MS

3. Experiments and results
   a) Constant delivery of nicotine and main components
   b) Puff-by-puff measurement of HPHCs
   c) End-of-liquid characterization



4. Conclusions

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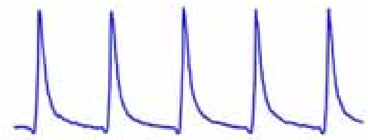

4. Conclusions

ENDS Technology

Significant variation in products and emissions

- Disposable or rechargeable
- Refillable or replaceable cartridges
- Adjustable power/voltage (Temperature, flow)

Variable HPHC emission per puff

Nicotine Salt Pod System (NSPS) v1.0

- Reusable device
- Disposable, non-refillable pods
- Temperature-controlled, designed not to be modifiable by user

Motivation for Change of Screening Methods

- Off-line collection (pad/impinger) of ~50 puffs, derivatization for several compound groups required → ageing, no time resolution
- European regulation (2014/40/UE) requires proof of **constant delivery of nicotine**
- ENDS: Majority of measurements returned below limit of quantitation
- 29 compounds - 10 different methods: GC-FID, IEC, ICP-MS, LC-MS/MS, GC-MS, HPLC-UV → work-intensive
- Turn-around time: 2-4 weeks at a high cost

Goal: Faster & direct analysis: quantification of aerosol components puff-by-puff

Source: PMTA Draft Guidance document by U.S. Department of Health and Human Services Food and Drug Administration Center for Tobacco Products (CTP), March 2012.

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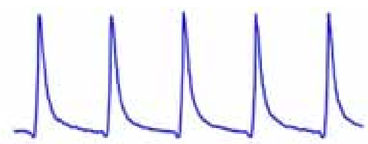

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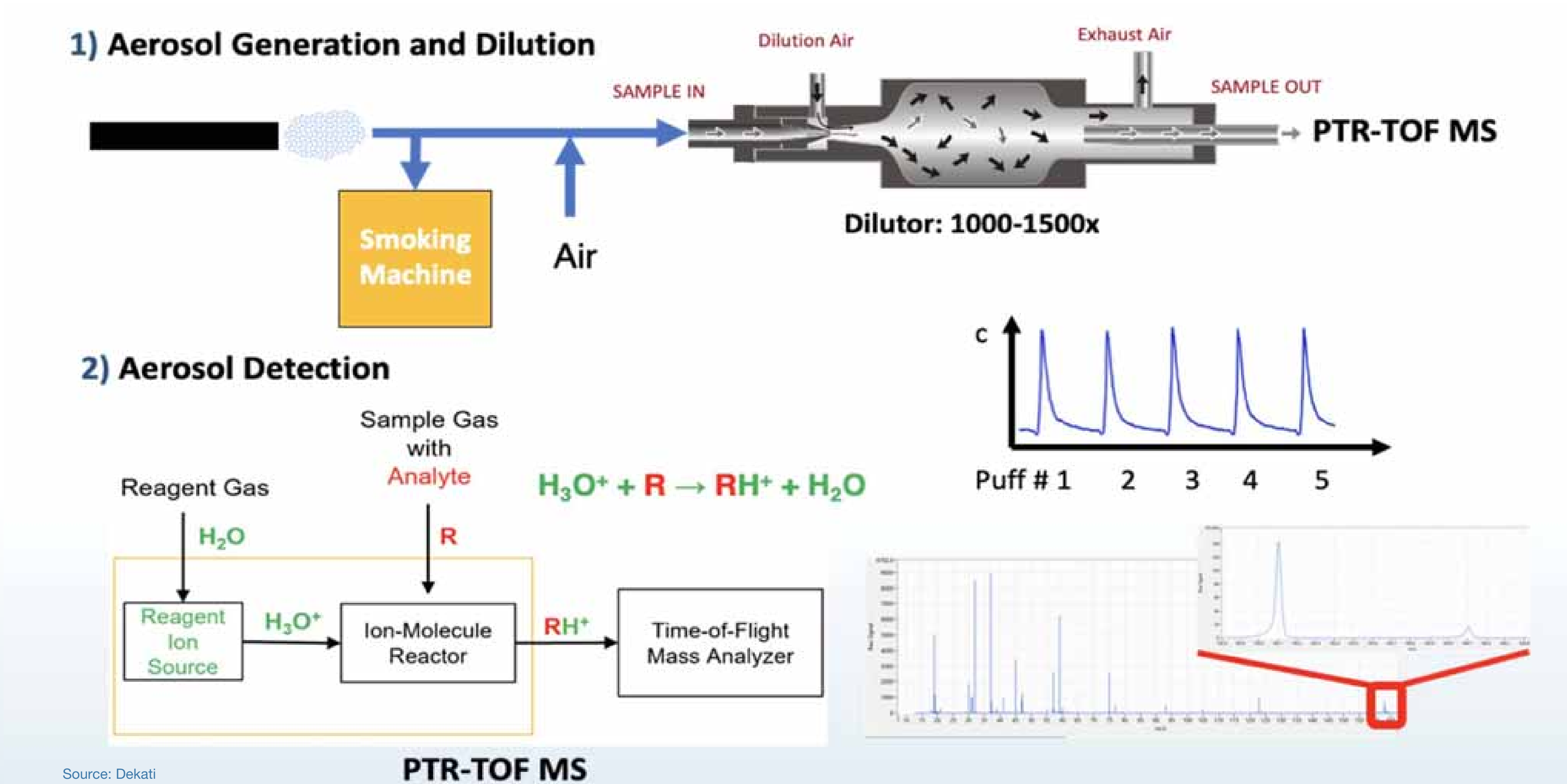
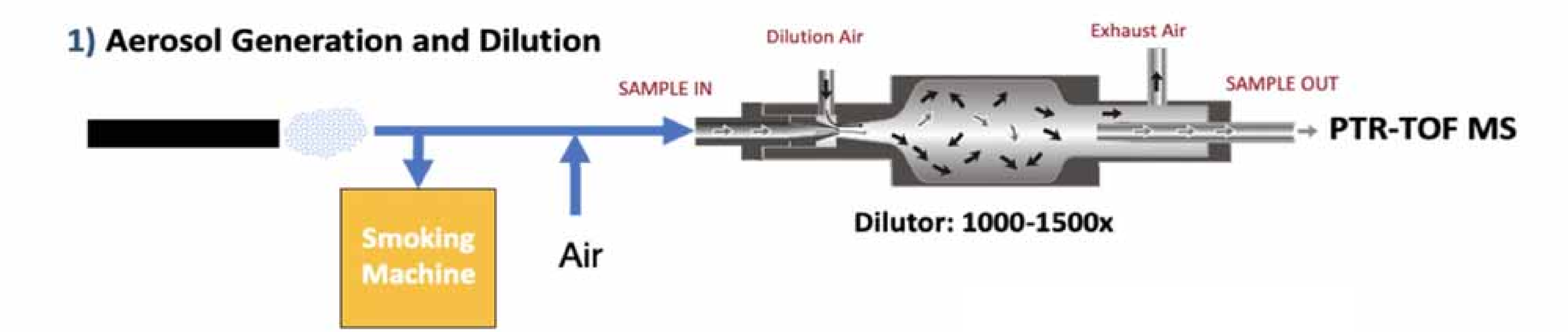
Concept of Online ENDS Aerosol Analysis



Source: Dekati

Concept of Online ENDS Aerosol Analysis



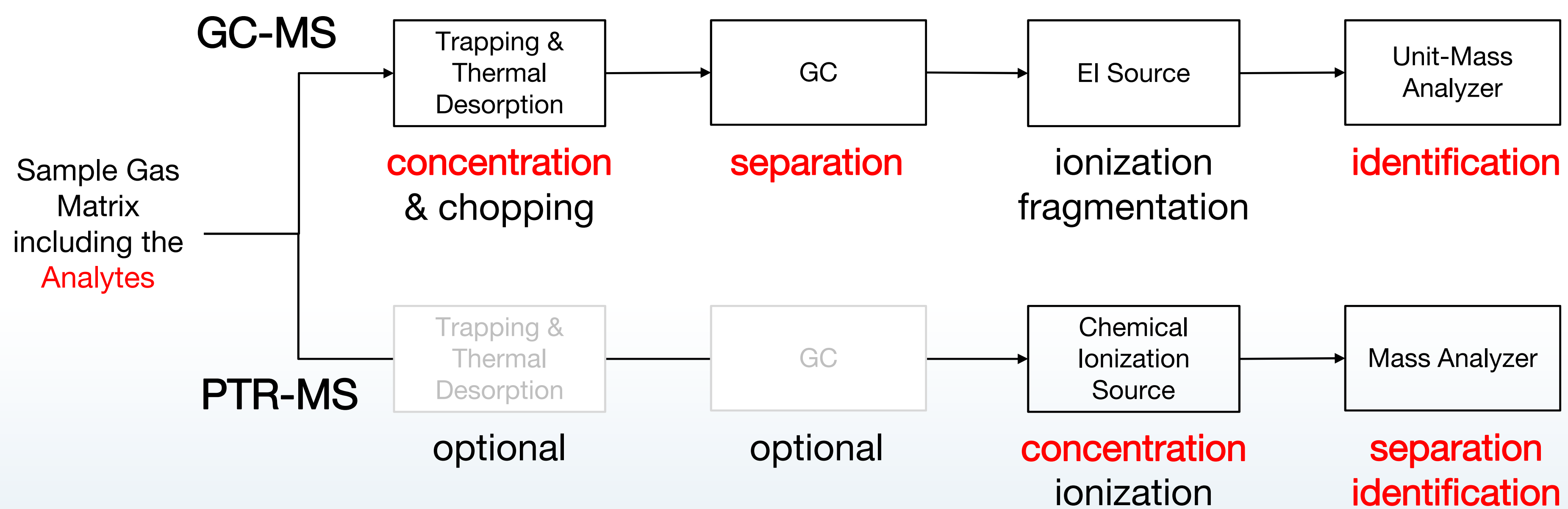
Vocus Proton Transfer Reaction Mass Spectrometry (Vocus PTR-TOF)

- Versatile and soft ionization method
- No sample preparation
- Real-time quantification without calibration
- High sensitivity (sub-ppt LODs)
- Dynamic range > 6 orders of magnitude

Source: Dekati

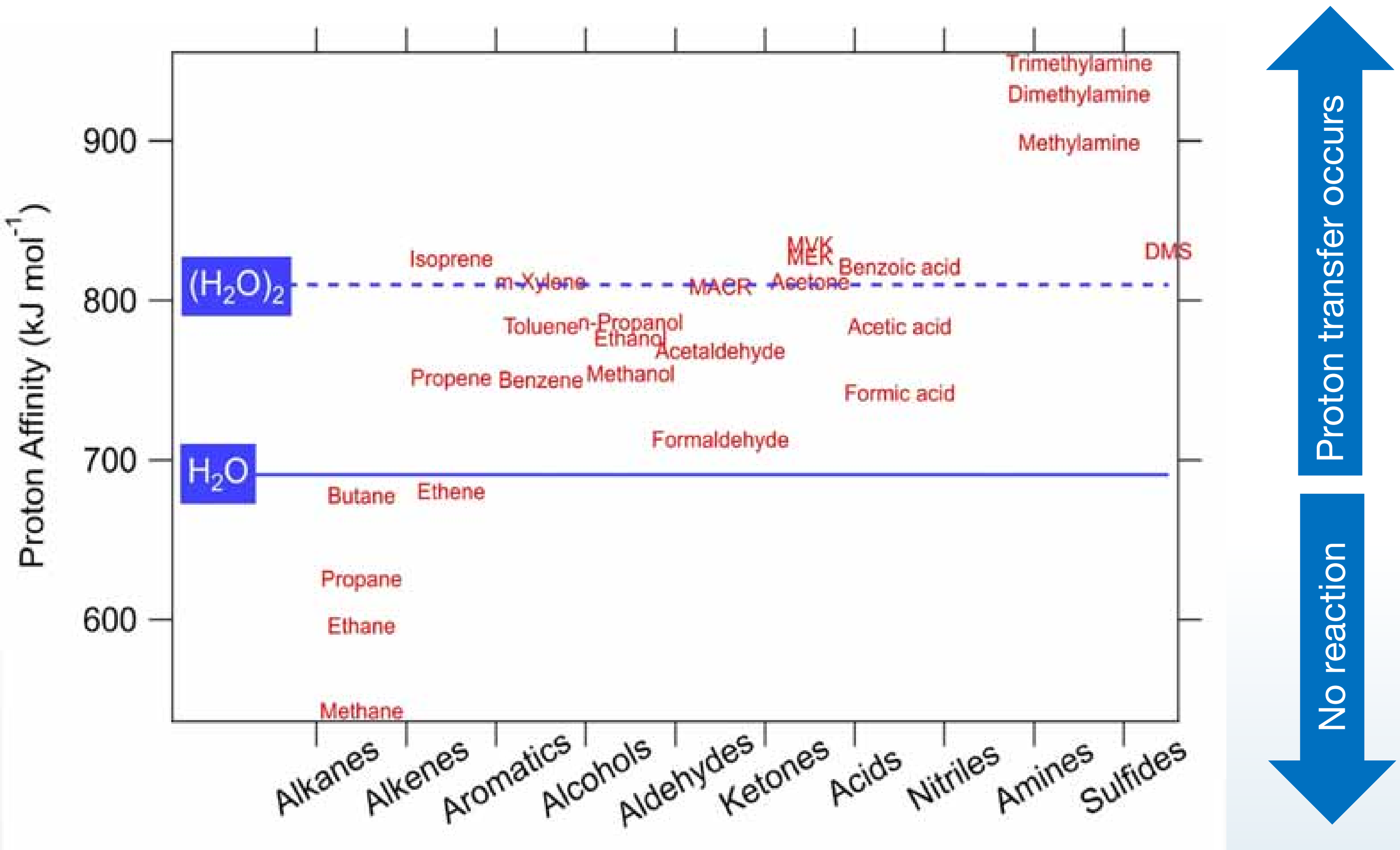
PTR-MS vs. GC-MS

- ❖ GC-MS and CI-MS are two methods for analyzing gas samples
- ❖ The essential steps are: concentration, separation, identification



Source: Tofwerk

Which HPHC can be measured?



Source: Tofwerk

Analytes

Classification	Analyte	Chemical Sum Formula
Primary Constituents	nicotine	C10H14N2
	water	H2O
	carbon monoxide	CO
	propylene glycol	C3H8O2
	menthol	C10H20O
	diethylene glycol	C4H10O3
	glycerol	C3H8O3
	ethylene glycol	C2H6O2
	glycidol	C3H6O2
Polynuclear Aromatic Hydrocarbons	benzo(a)pyrene	C20H12
Volatile Organic Compounds	1,3-butadiene	C4H6
	isoprene	C5H8
	acrylonitrile	C3H3N
	benzene	C6H6
	benzyl acetate	C9H10O2
	ethyl acetate	C4H8O2
	isoamyl acetate	C7H14O2
	isobutyl acetate	C6H12O2
	ethyl acetoacetate	C6H10O3
	methyl acetate	C3H6O2
	n-butanol	C4H10O
	furfural	C5H4O2
	propionic acid	C3H6O2
	propylene oxide	C3H6O
	toluene	C7H8
Poly Aromatic Amines	1-aminonaphthalene	C10H9N
	2-aminonaphthalene	C10H9N
	4-aminobiphenyl	C12H11N
Tobacco Specific Nitrosamines	NNN	C9H11N3O
	NNK	C10H13N3O2
Nicotine Degradants	nornicotine	C9H12N2
	anatabine	C10H12N2
	anabasine	C10H14N2
	myosmine	C9H10N2
	nicotine-N-oxide	C10H14N2O
	cotinine	C10H12N2O
	ß-Nicotyrine	C10H10N2
Carbonyls and Diketones	formaldehyde	CH2O
	acetaldehyde	C2H4O
	butyraldehyde	C4H8O
	acrolein	C3H4O
	crotonaldehyde	C4H6O
	2,3-butanedione	C4H6O2
	2,3-pentanedione	C5H8O2

- Metals cannot be analyzed
- Isomers: only different functional groups

Currently can be analyzed by PTR-MS

Isomer Separation with SRI

- SRI – Selective Reagent Ionization
- Different ionization mechanism:

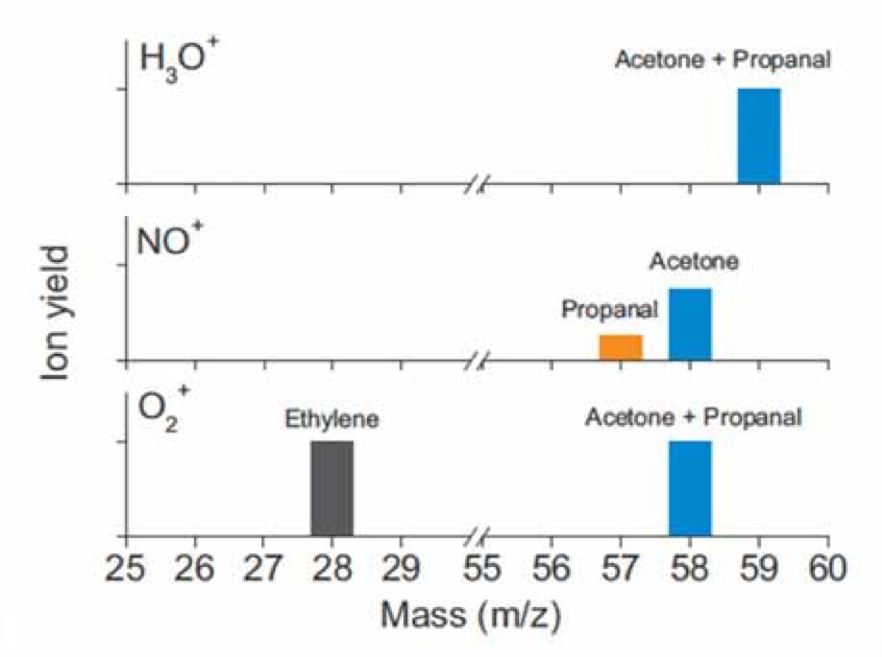
  NO^+, NH_4^+ (Kr^+, O_2^+, Xe^+ , I^-)

Aldehydes

$NO^+ + RH \rightarrow R^+ + HNO$

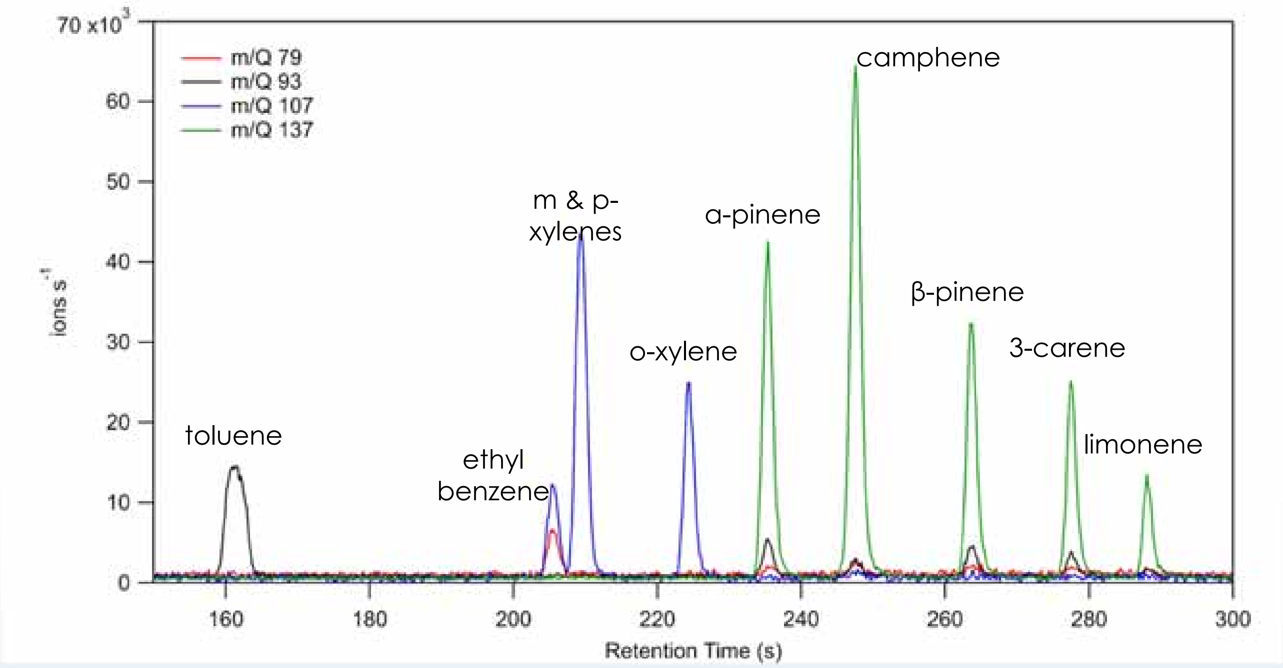
Ketones

$NO^+ + RH \rightarrow RH^+ + NO$



Source: Ionicon

Isomer Separation with Optional Fast GC
coupled to Vocus PTR-TOF



Source: Tofwerk

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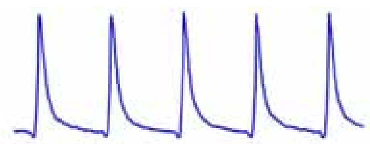

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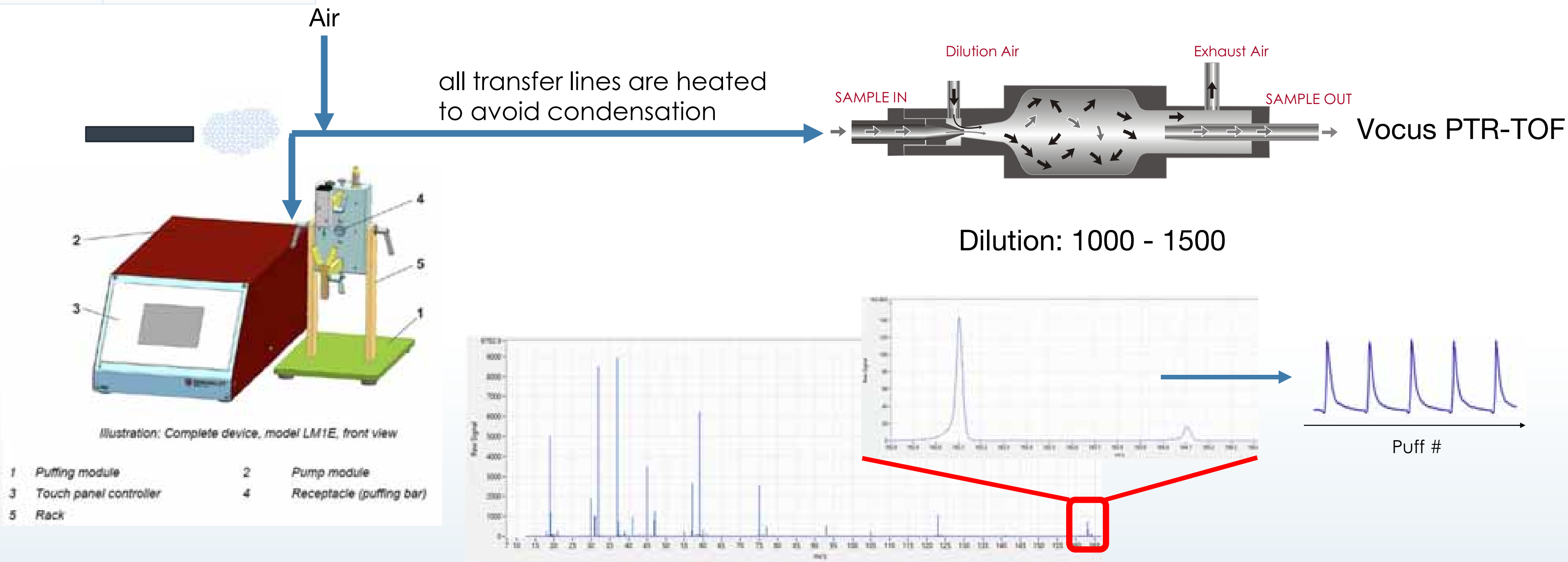
Experimental Setup

Puff Volume	70 ml
Puff Duration	3 s
Puff Interval	30 s
Puffing Profile	Square



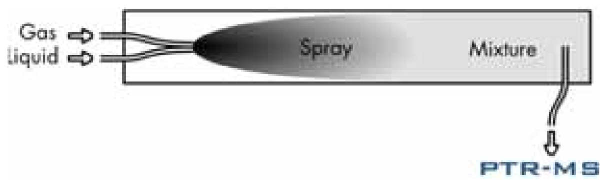
Source: Borgwaldt, Dekati

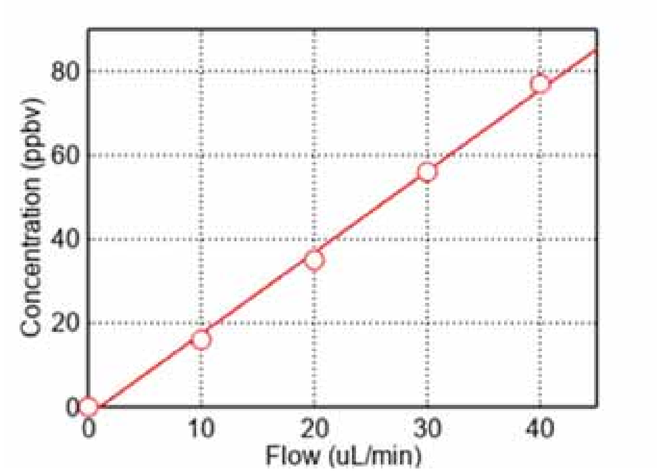
Calibration

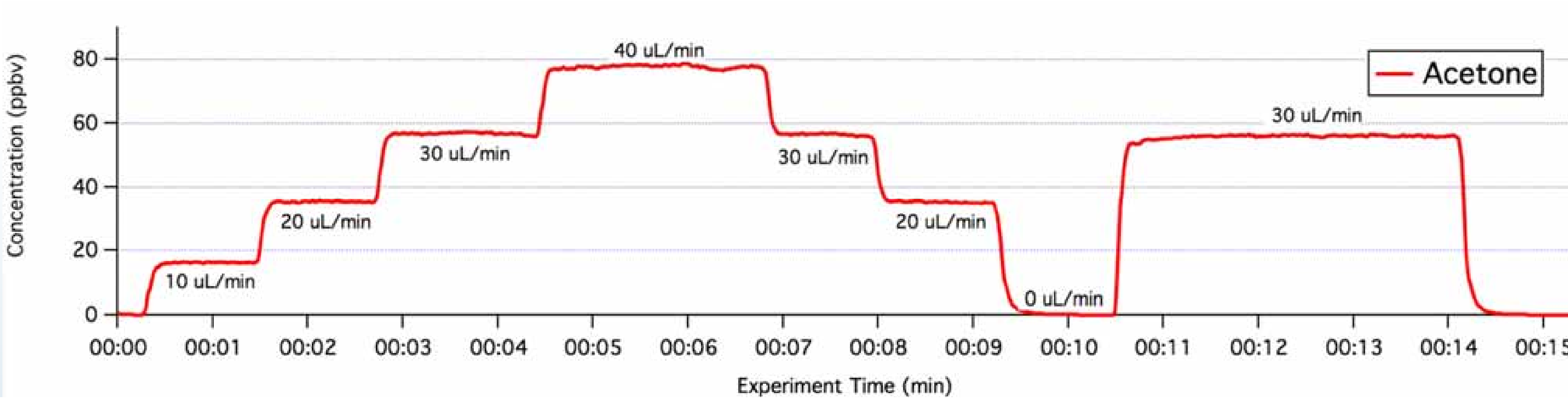
- Smoking Machine
- Dilution System
- Gas (VOC gas standard)
- Liquid (Liquid Calibration System)

➔Concentration (Transmission, *k*-rate)

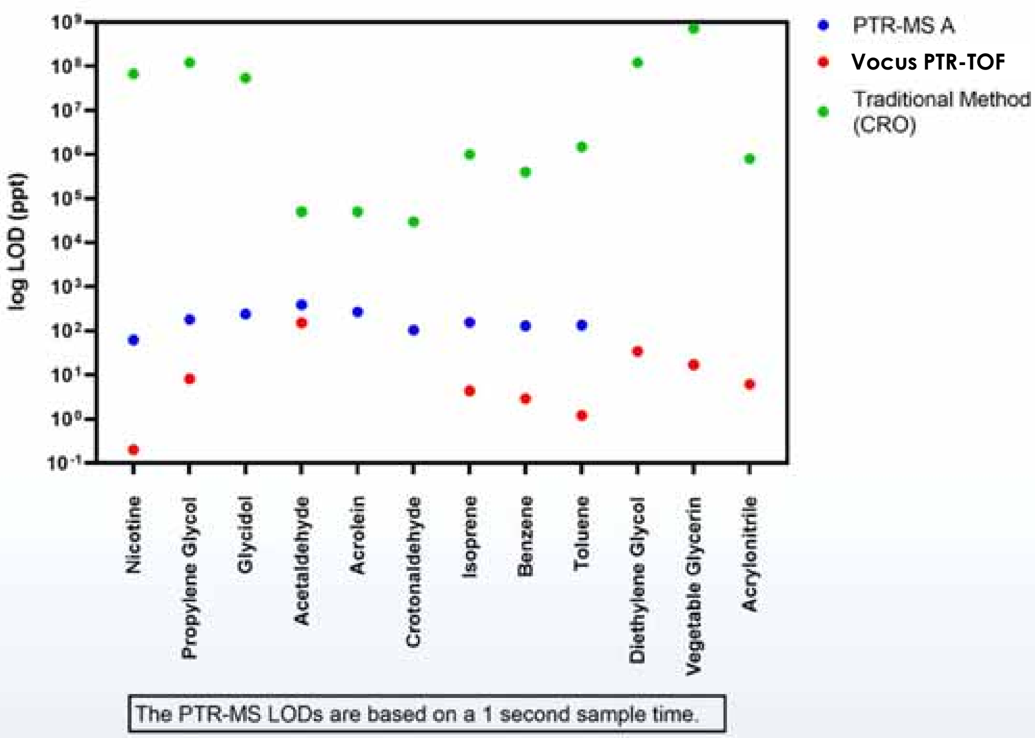
➔Fragmentation, cluster formation, back reactions







Improvement of LODs (H_3O^+-mode)



with x1000 dilution

Traditional methods

LOD µg/ml (1s)	HPHC Aerosol Classification	Analyte	Method	Units	LOD
0.062		Nicotine			6
0.179	Primary Constituents	Propylene Glycol	GC-FID	µg/collection	12
		Menthol			12
		Ethylene Glycol			2
		Diethylene Glycol			12
0.238		Glycidol			5
		Glycerin			72
	Ammonia	Ammonia	IEC	µg/collection	1
	Carbonyls	Formaldehyde	GC/MS	µg/collection	< 0.5
0.388		Acetaldehyde			
0.268		Acrolein			
0.103		Crotonaldehyde			
		Diacetyl			
		Acetyl Propionyl			
	Volatile Organic Compounds	1,3-Butadiene	GC/MS	µg/collection	< 0.6
0.155		Isoprene			
		Acrylonitrile			
0.129		Benzene			
0.134		Toluene			

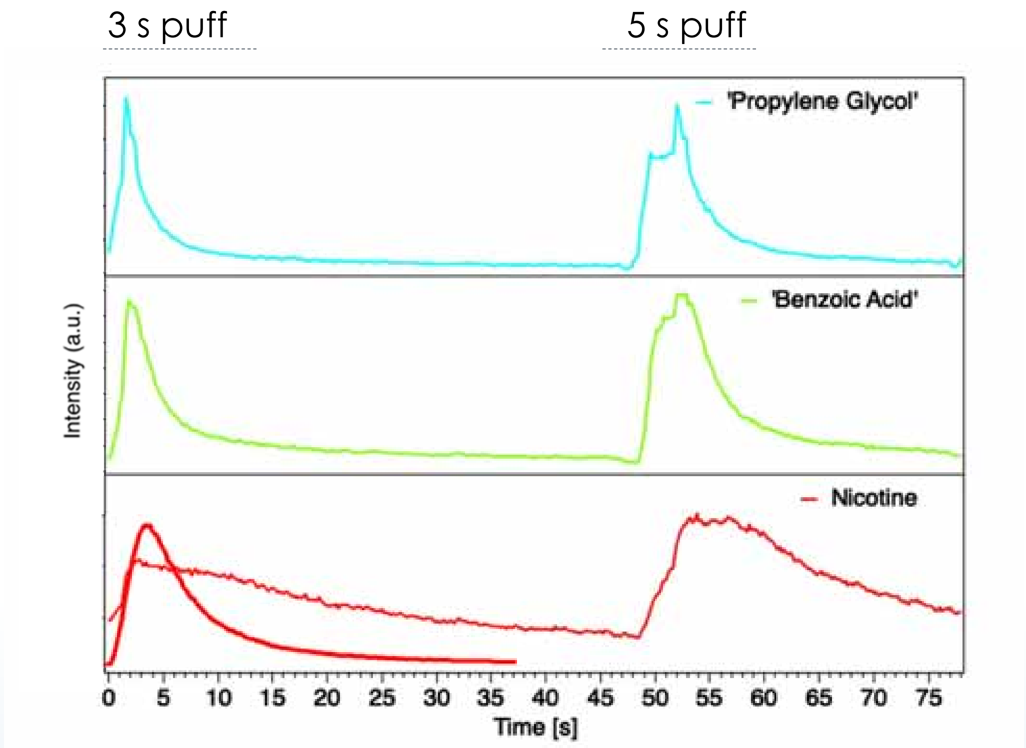
Vocus PTR-TOF

1 collection = 50 x 3 s (70 ml) puffs

Single Puff Profiles

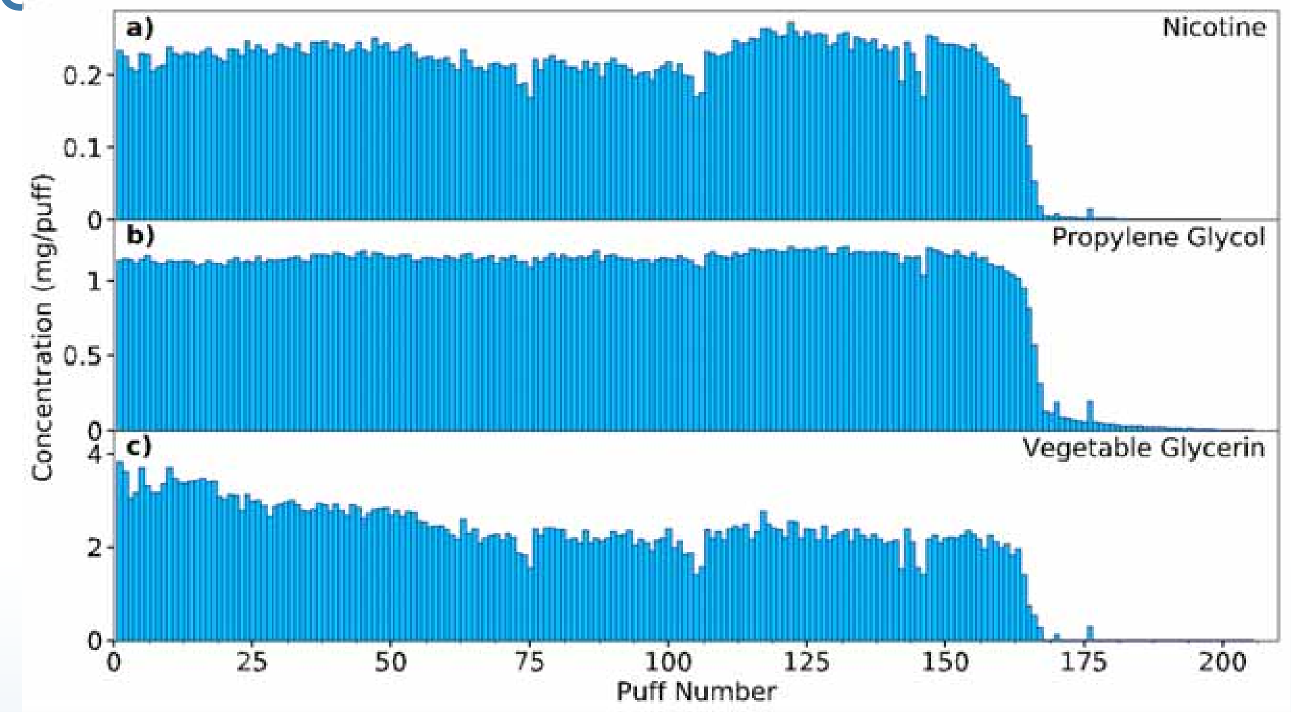
- 200 ms time resolution → 1 mass spectrum every 200 ms (with 1000x dilution)
- Instead of 50 puff average

➔ Different dilution system
➔ Reduced cold spots
➔ Improved materials



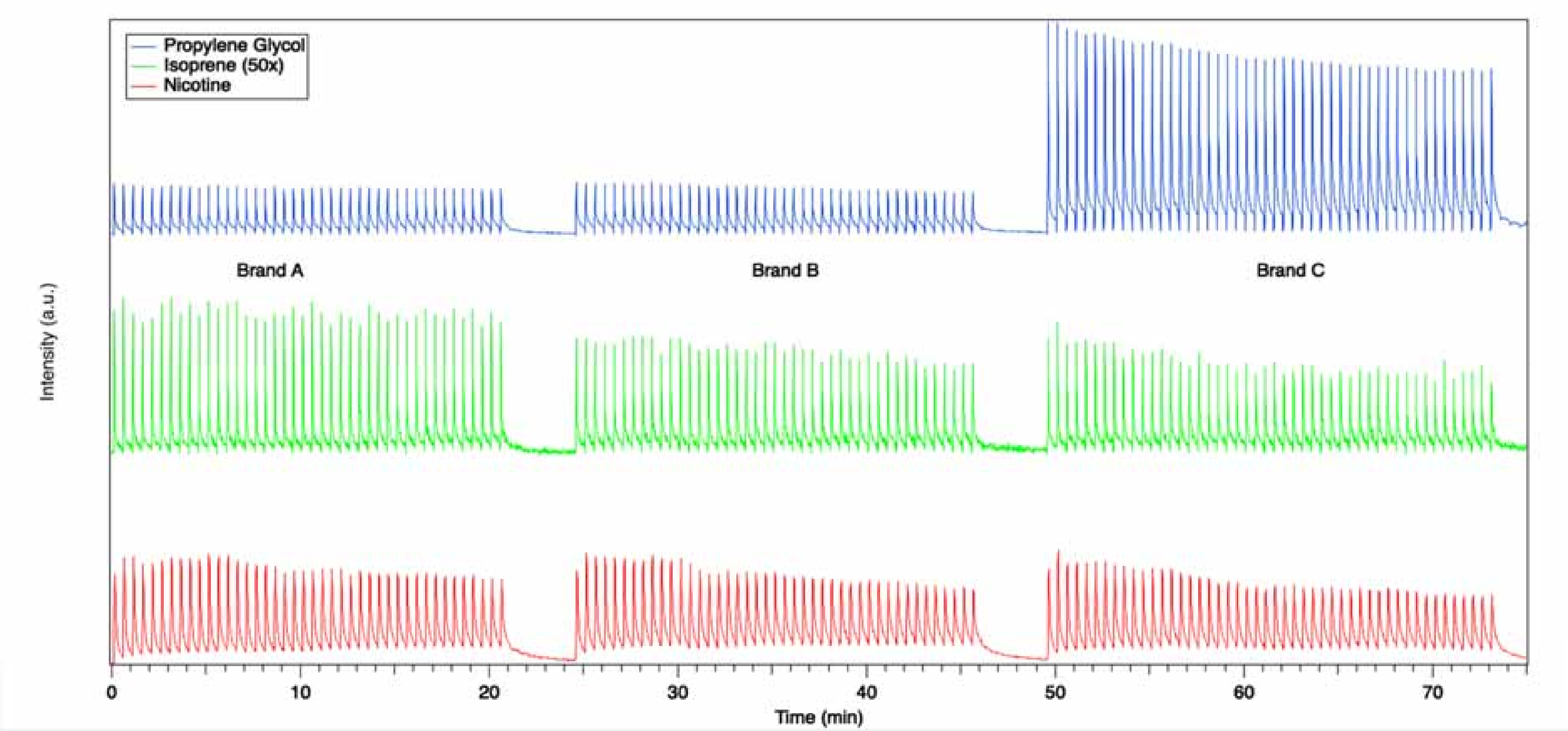
PTR-MS Method allows high resolution analysis of the puffing profile

Stability and constant delivery of nicotine



Concentrations (mg/puff) for a) nicotine, b) propylene glycol, and c) vegetable glycerin from 1st to last puff of an e-cigarette.

Stability and constant delivery of nicotine

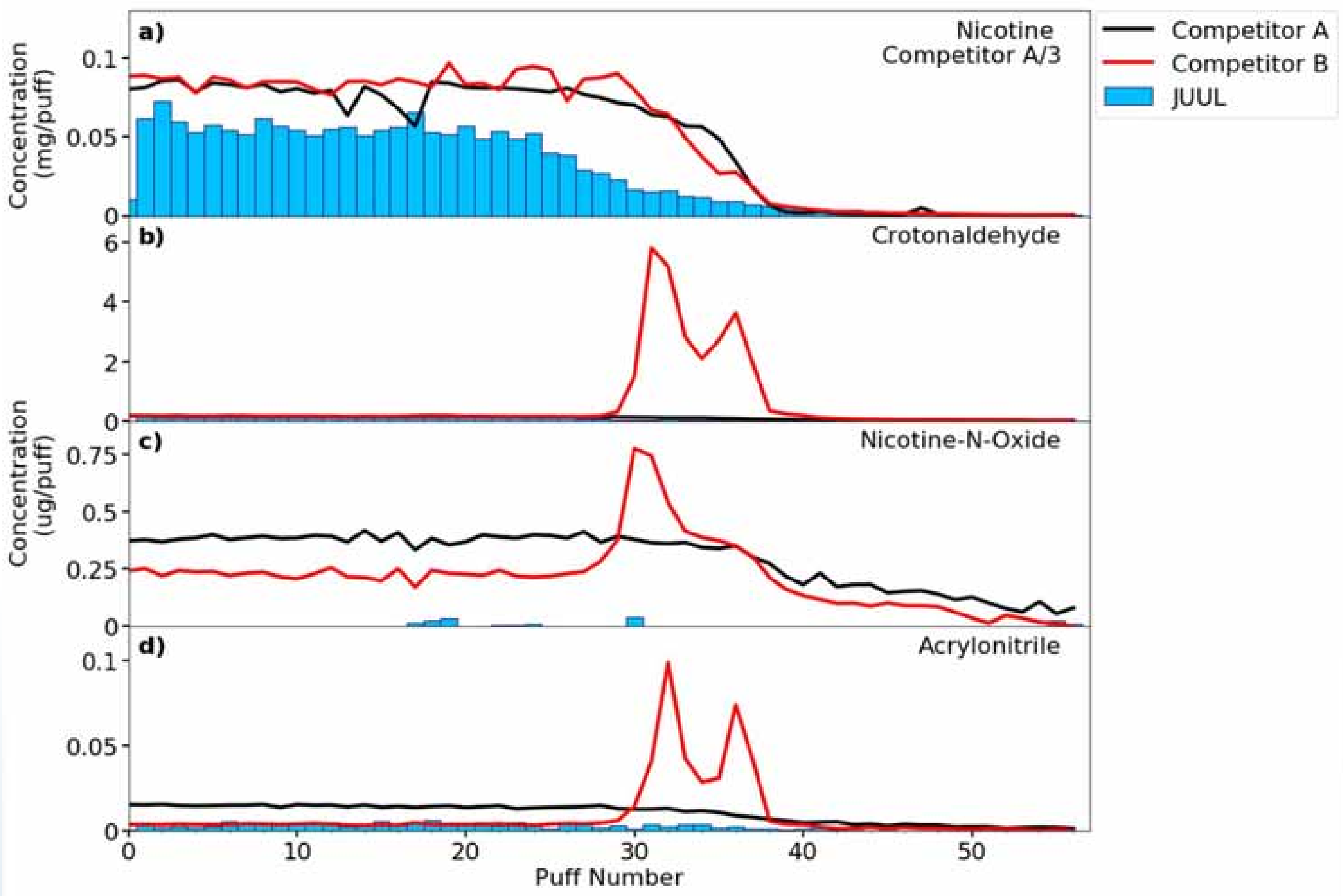


End-of-Liquid/Battery - Device comparison

Concentrations (mg and µg/puff) for last 50 puffs:

a) nicotine
b) crotonaldehyde
c) nicotine-n-oxide
d) acrylonitrile

for end-of-liquid with $\mathbf{H_3O^+}$ as primary ion.

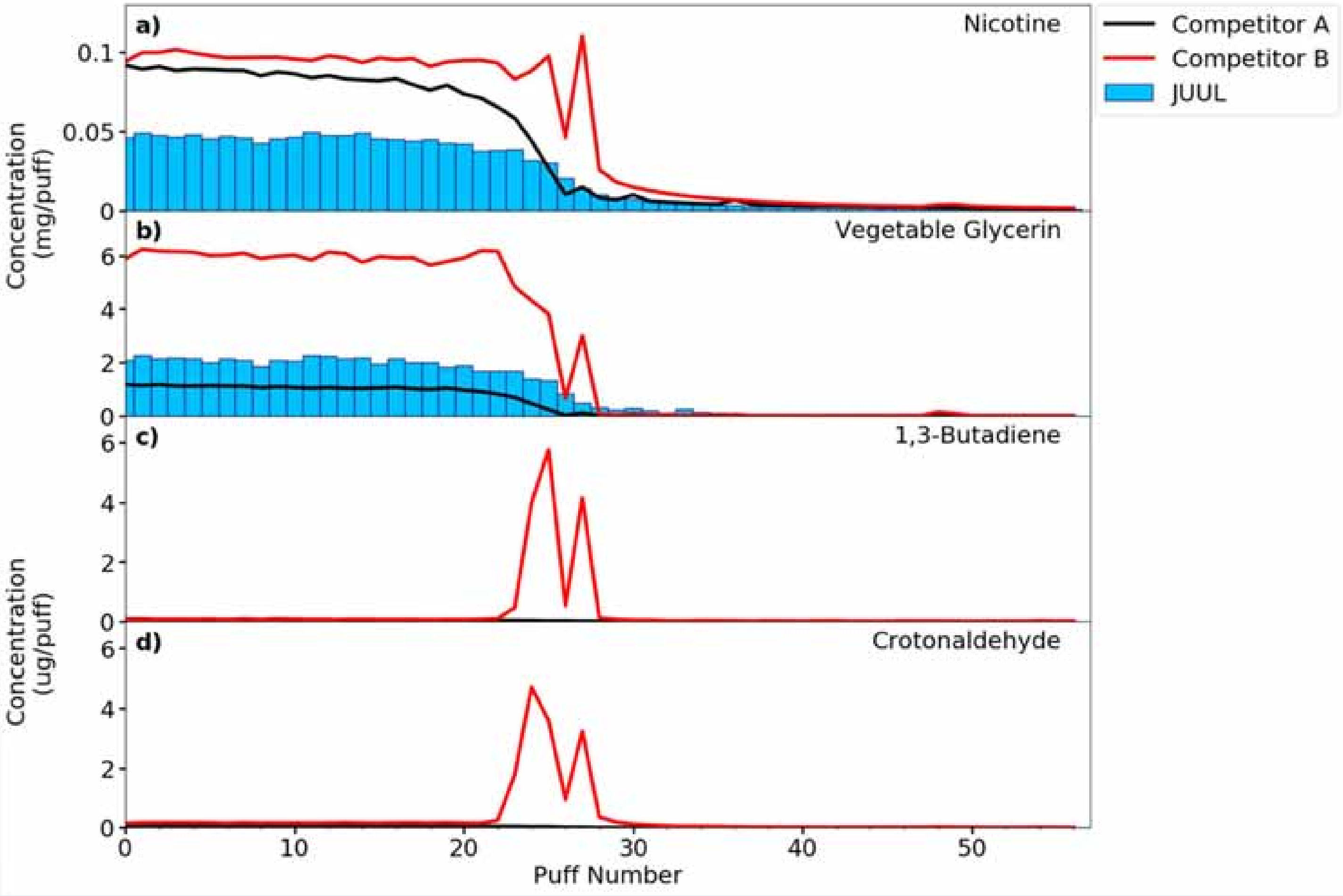


End-of-Liquid/Battery - Device comparison

Concentrations (mg and µg/puff) for last 50 puffs:

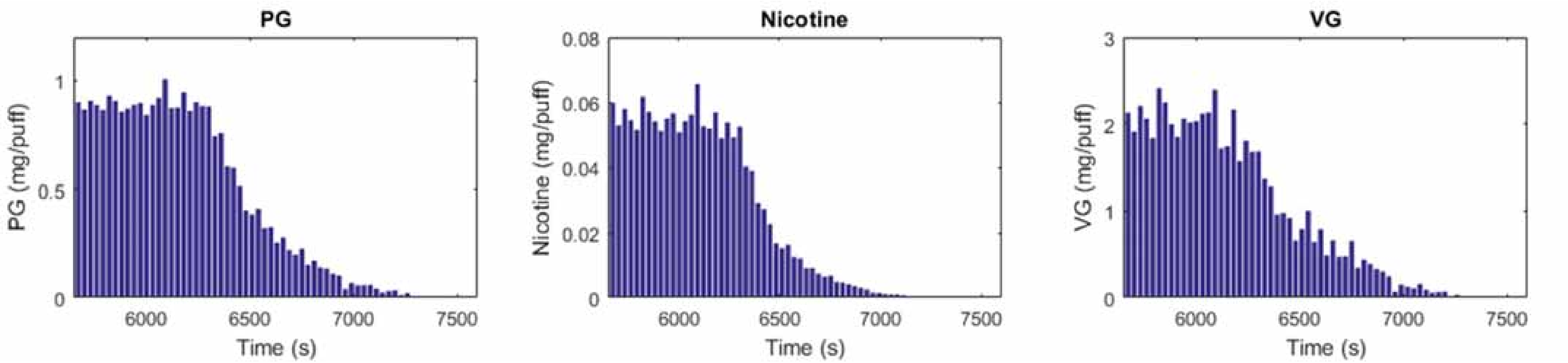
a) nicotine
b) VG
c) 1,3-Butadiene
d) crotonaldehyde

for end-of-liquid with **NO⁺** as primary ion.



Comparison with CRO/offline methods

Temperature-regulated device



1.46 mg/puff Reference (CRO/offline method)

0.052 mg/puff

1.77 mg/puff

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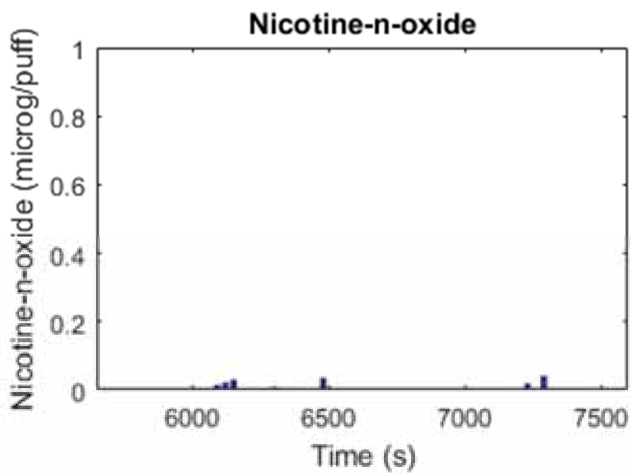
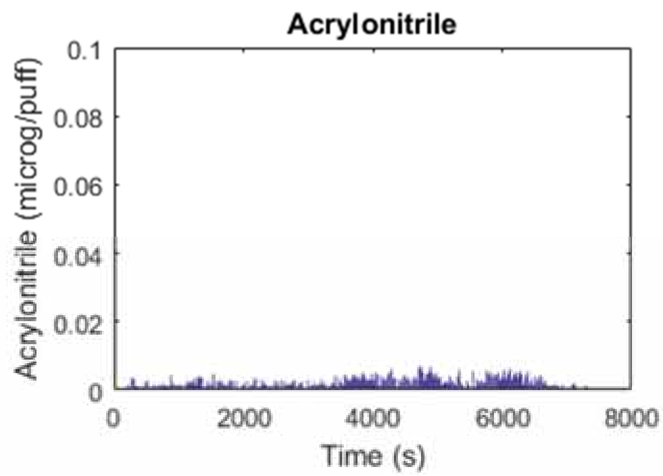
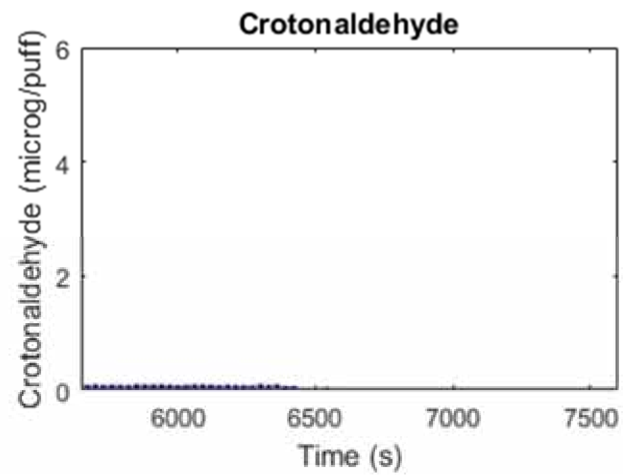
Temperature-regulated device





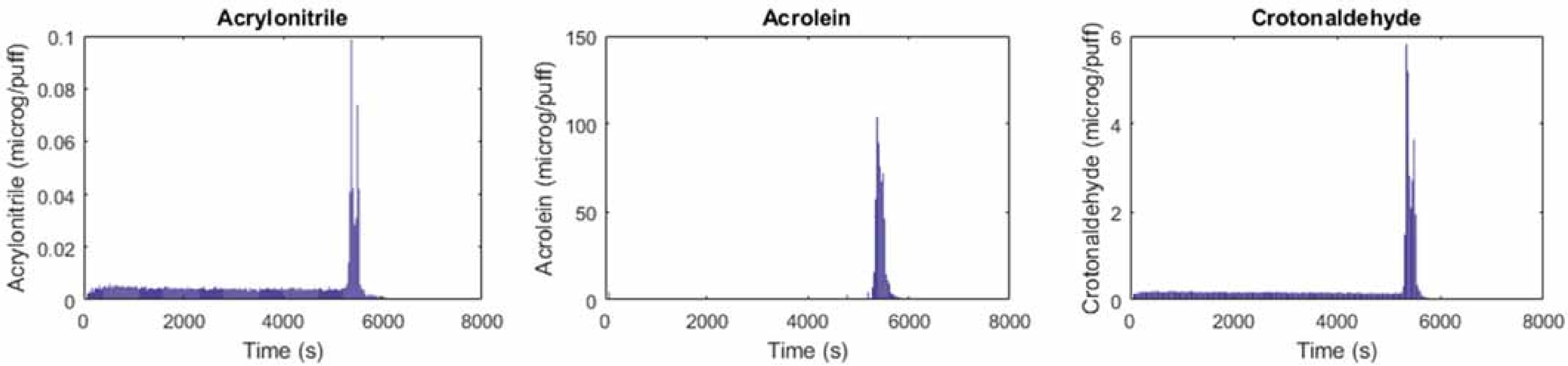


Reference (CRO/offline method)	-- -	ND (LOD = 0.03 **μ**g/puff)	ND (LOD = 0.03 **μ**g/puff)

No combustion products → no burning at end of liquid, because device regulates temperature

Comparison with CRO/offline methods

Non-temperature-regulated device



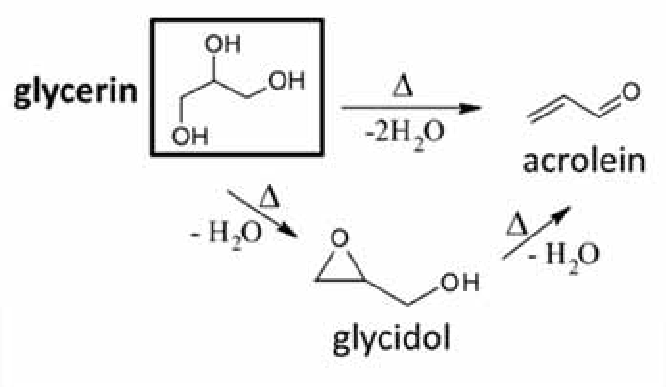
Reference (end of liquid): (CRO/offline method) 56 μg/puff 2.6 μg/puff

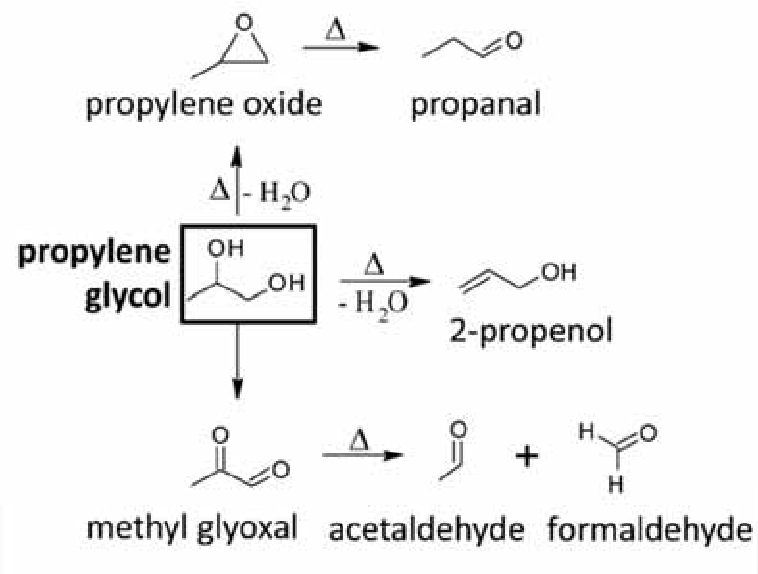
Overheating at end of liquid causes thermal decomposition of main components

Potential Pathways for Carbonyl Formation

Thermal Degradation of Main Aerosol Components

- Overheating of liquid is likely caused by uncontrolled power/ heating of device, missing or insufficient temperature control, bad device maintenance
- Known decomposition pathways:





Source: Sleiman *et al.*, ES&T **2016**, 50, 9644.

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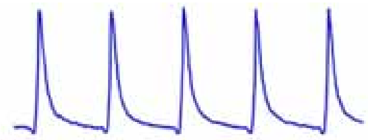

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Key Takeaways

IMPACT OF PTR-MS FOR HPHC ANALYSIS

- ✔ Quantifiable results for main aerosol components, degradants and impurities with puff-to-puff resolution
- ✔ Direct assessment of constant delivery of nicotine
- ✔ Per-puff LODs are close or below LODs of standard offline methods
- ✔ Most compounds can be detected simultaneously
- ✔ Puff-to-puff analysis enables instant online assessment of device performance

→ Improved risk assessment and potential hazard identification