COMPARISON OF RESULTS FROM THREE TECHNIQUES FOR THE ESTIMATION OF E-LIQUID pH-VALUES

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Quotations from Pagano *et al*., 2016

- E-Cigs can vary the delivery of nicotine in the free-base form. True pK_a values are not known across the solvent matrices and temperature gradients of the e-liquids and aerosols throughout the puffing procedure used on the products in this study, so it is not possible to extrapolate the portion of free-base nicotine delivered to the pads.
- In fact, there is currently very little information on actual nicotine pK_a profiles of aerosolized e-liquids during the vaping process, but we believe that this is an important area for future research in the field.

Outline for presentation

- Objectives for research
- Experimental details
- Experimental results
- Estimate of extent of gas-particle partition-ing of nicotine in e-cigarette aerosols
- Conclusions

Objectives for research

1. Compare results from three techniques for determining e-liquid pH-values
2. Determine effects on e-liquid pH-values caused by acidic additive with and without a menthol-based flavor
3. Provide estimates of extent of gas-particle partitioning in aerosols generated from e-liquids (based on 250 mL oral cavity)

Experimental – Formulations tested

- Commercial
  - V2 Red (tobacco) and Green (menthol), 2.4%
  - NicVape 50 mg/mL nicotine in PG
- Experimental
  - NicVape 50 mg/mL nicotine in PG + equimolar propionic acid (PA)
  - NicVape 50 mg/mL nicotine in PG + equimolar propionic acid (PA) 2:1 with L&ALLC proprietary menthol flavor concentrate in PG

Experimental – pH instrumentation

- Hach H260G meter with Hach SmartLogger II software (v. 1.0.14), OS Win 10 64 Pro
- pH electrodes (all Hanna Instruments)
  - HI1053B Conical Tip (low impedance, triple ceramic junction, high electrolyte flow rate)
  - HI1083B Micro Bulb (gel filled)
  - HI1413B Flat Tip (gel filled, low impedance)
- Low impedance electrodes make the technique work with aerosols

Experimental – Vaping machine

- L&ALLC Model IIIb µ-processor-controlled, constant-vacuum, square-wave e-cigarette puffing system; puffing regimen of 55/3/30
- Flow control by Swagelok SS-4MG-SL metering valve acting as critical flow orifice
- Flow checked with SIAL 20414 500-mL bubble meter with Cerulean SC#59138 Restrictor 10CSM (calibrated)(1 kPa)

Results – pH of undiluted e-liquids

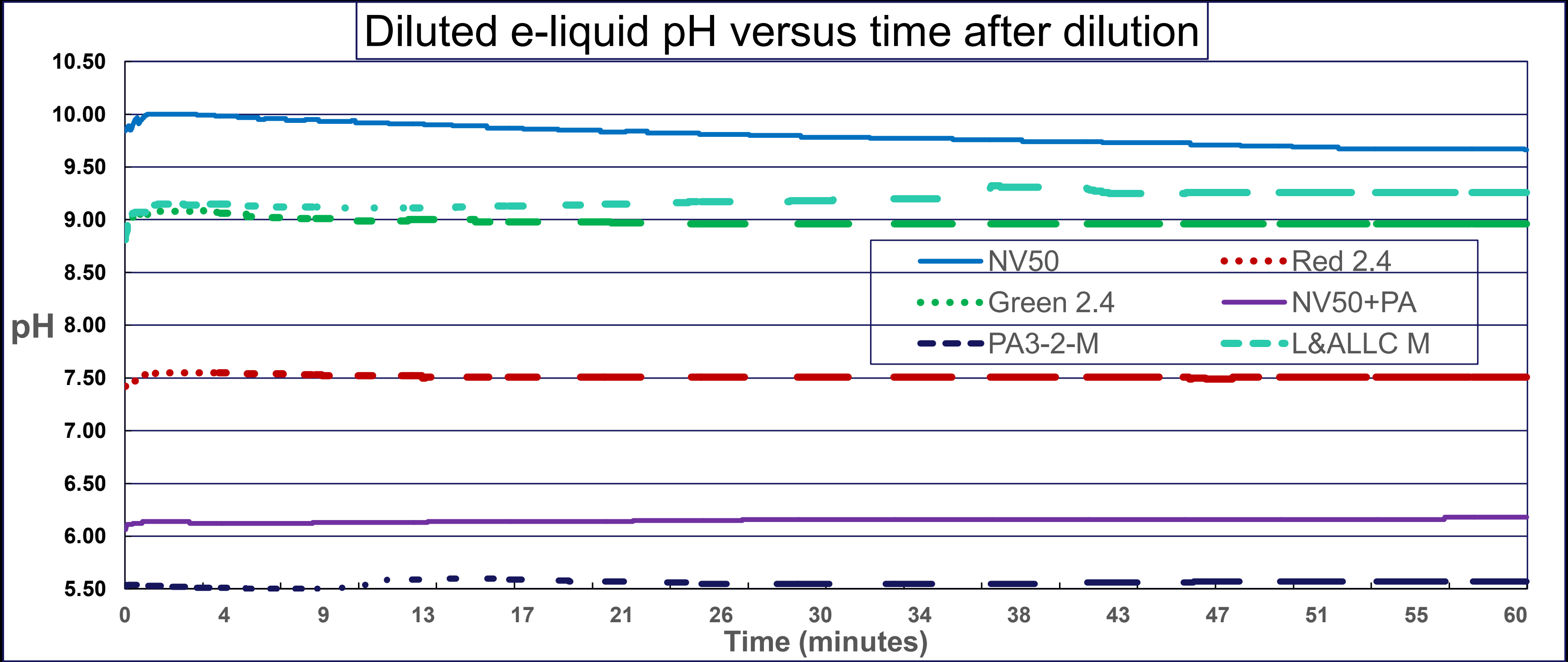
Results depend on technique used

Sample	NV50	PA1	PA2	PA1-M	PA2-M	PA3-1	PA3-2	PA3-2M	PA3-3
Electrode									
Micro Bulb	9.17	6.50	6.41	NM	NM	6.27	6.26	NM	6.19
Flat Tip	9.35	6.27	6.34	6.27	6.25	6.28	6.19	6.10	6.10

Samples are as described previously; NM = not measured
Response time for Micro Bulb electrode is very slow and easily influenced by static electricity; Flat Tip is better
Menthol has **little effect** on pH of undiluted e-liquids

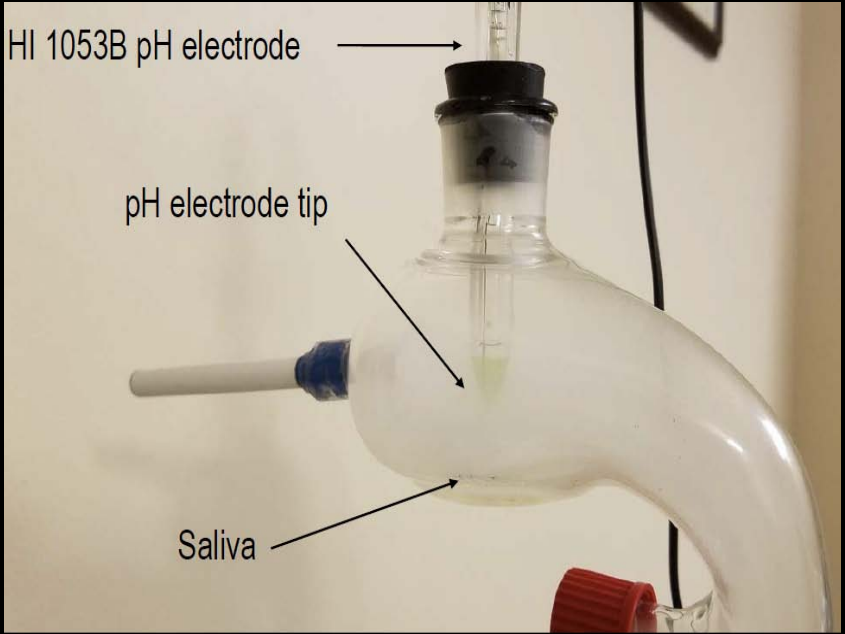
Results – pH of diluted e-liquids

500 mg sample plus 5 g ASTM Type I water



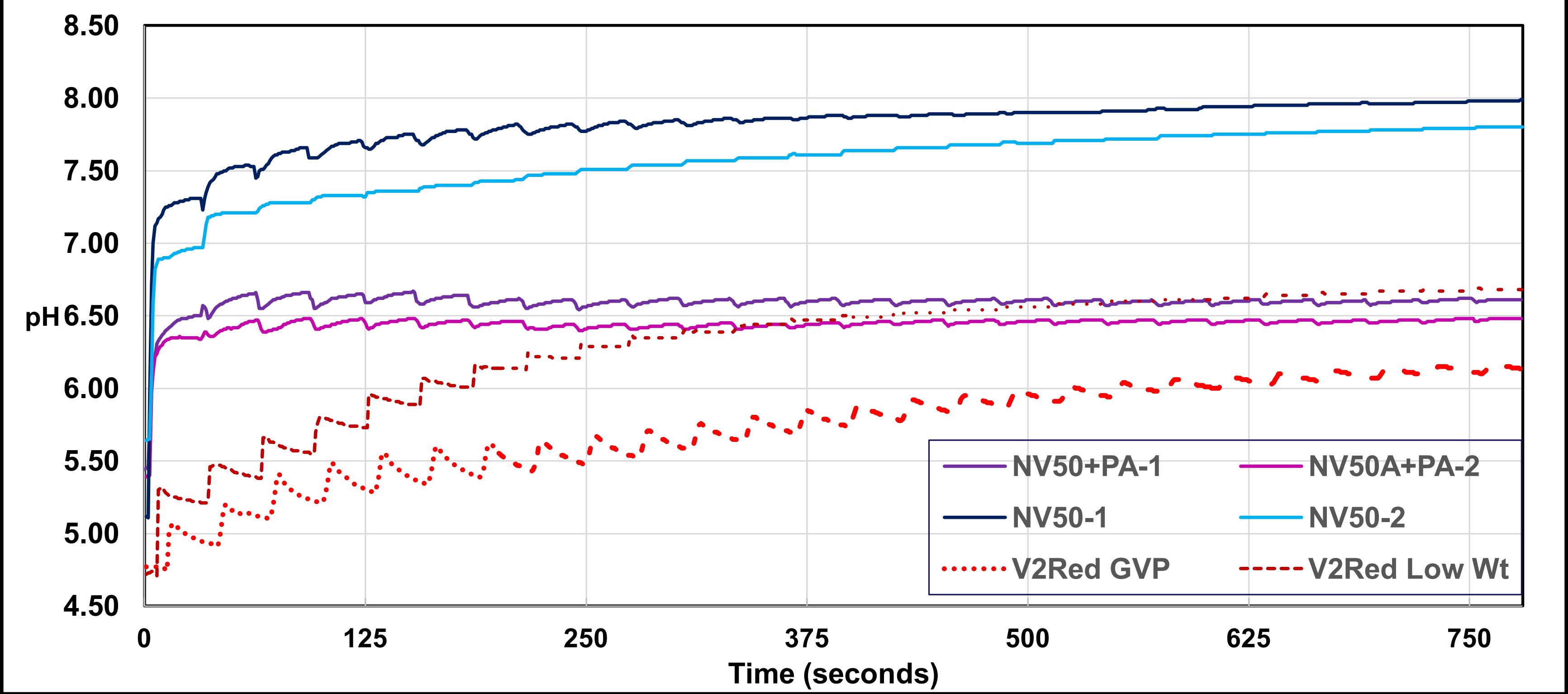
Experimental – Aerosol traps

H-C T-113 trap with HI Flat Tip electrode

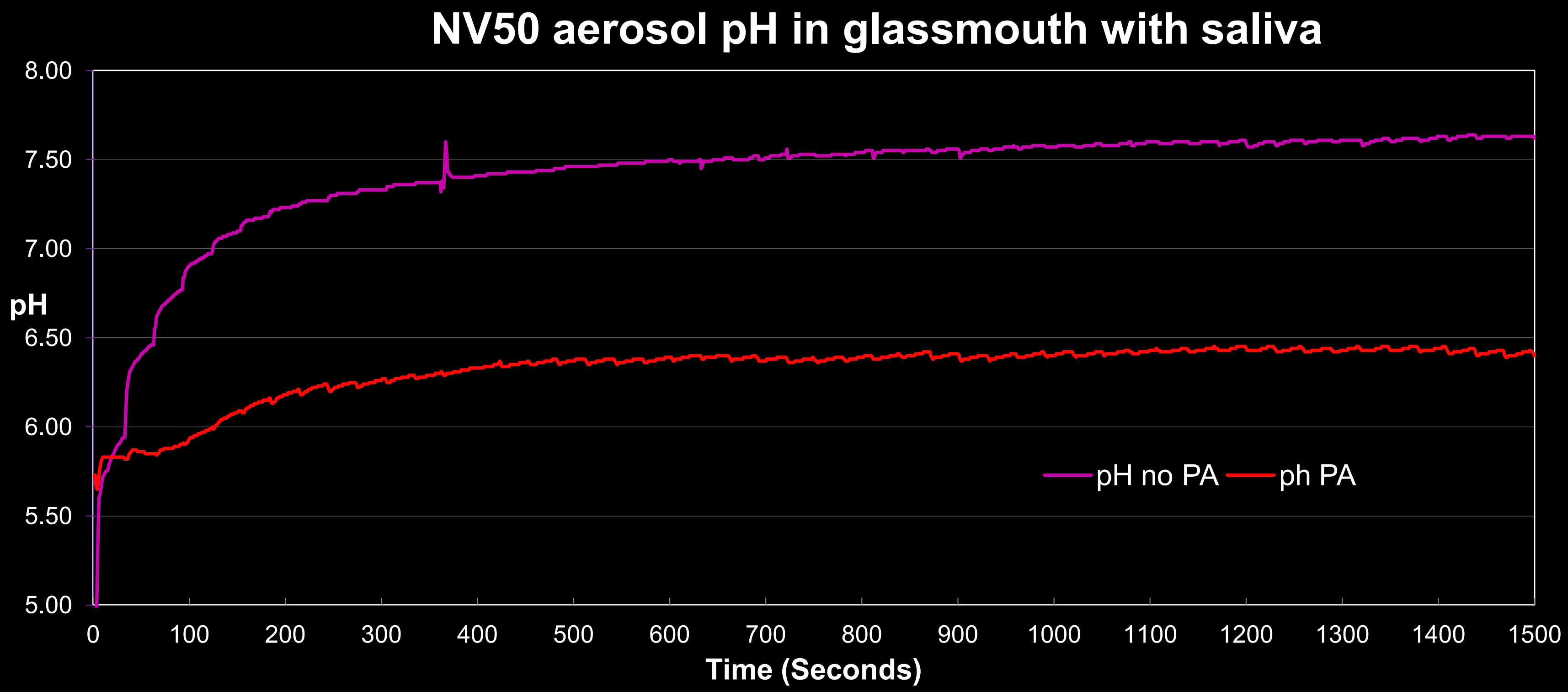


Glassmouth trap with Conical tip electrode

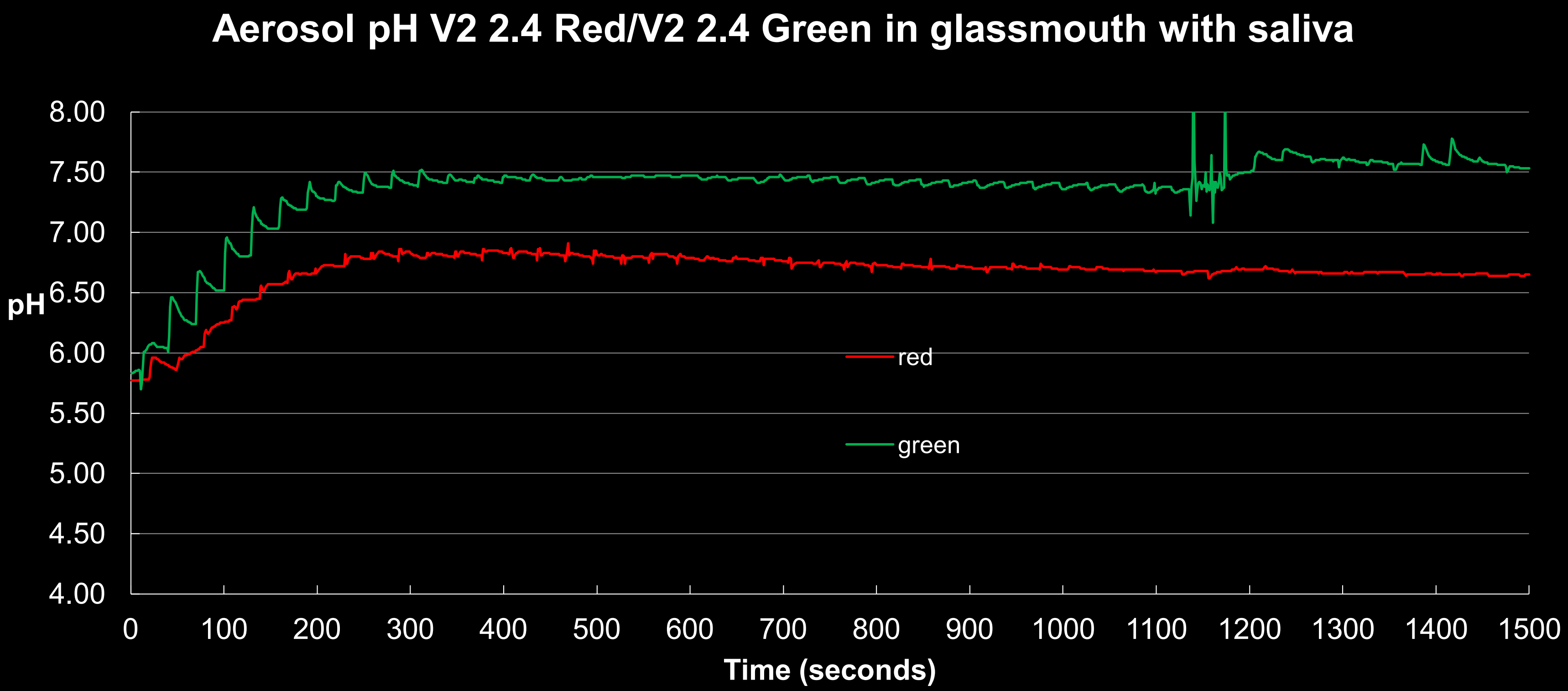
Results – aerosol pH in H-C trap



Results – effect of propionic acid on aerosol pH



Results – effect of menthol on aerosol pH



Gas-particle partitioning (GPP) -- 1

- Claims of nicotine GPP in cigarette smoke
  - Not valid for mainstream smoke from most products (Lauterbach *et al.*, 2010)
  - Exception of highly ventilated 1-mg products
    - Very dilute, very dry, high MW_{om} aerosol (FTC smoke)
    - Confirmed by experiment (Kinser *et al.*, 1999 TCRC)
    - Results consistent with Pankow's theory of absorptive partitioning (Pankow *et al.*, 1997, and later references)
  - EL-Hellani just claimed FBN in e-cig aerosols in part on pH-data from Stepanov and Fujioka

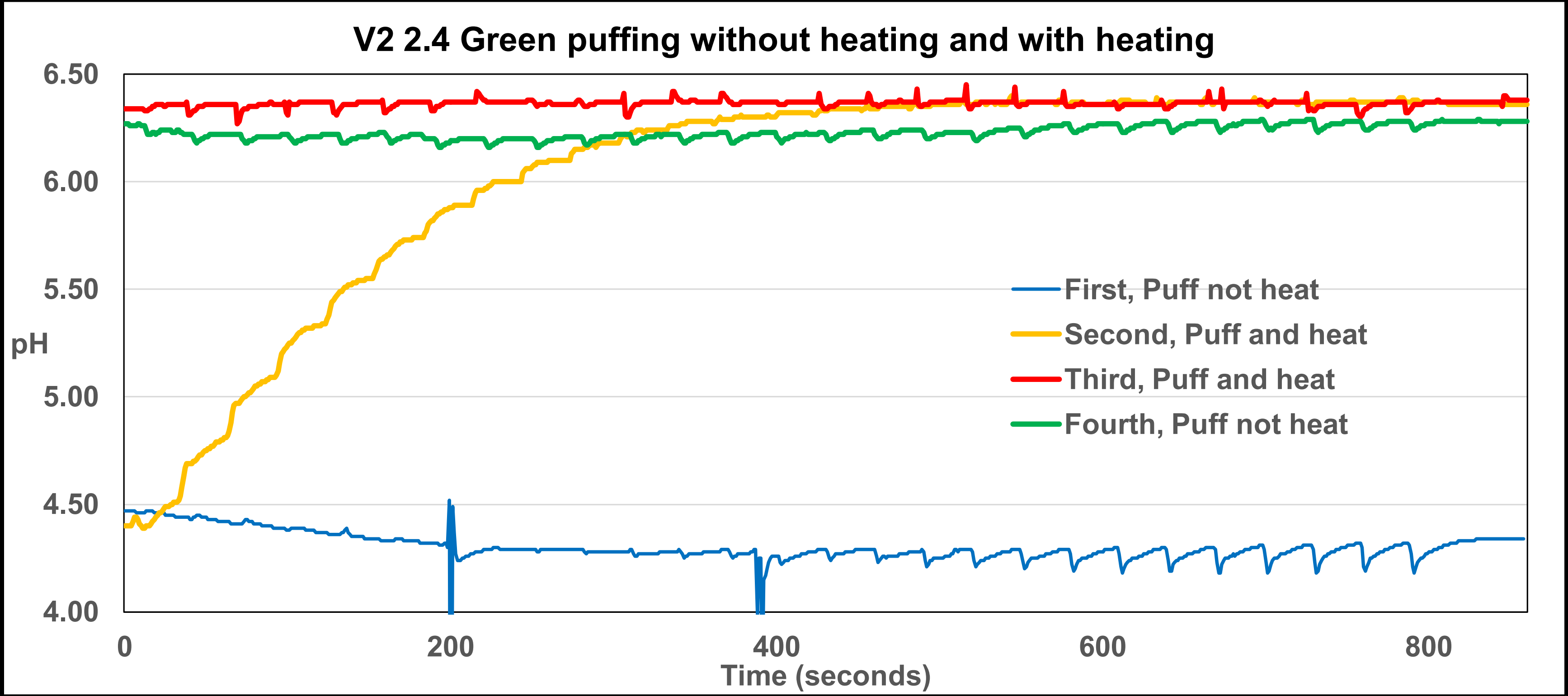
Gas-particle partitioning (GPP) – 2

- Stepanov and Fujioka used 1:10 water dilution based on pH technique for moist snuff
  - Has been shown to give cloudy mixtures and pH-values that drift (Lauterbach *et al.*, 2014)
  - Has been shown to result in overly high pH-values due to dilution with water (St. Charles *et al.*, 2016)
  - Even with limited water of dilution, it is still not aerosol that is being evaluated
- This is why aerosol pH is so important

Gas-particle partitioning (GPP) – 3

- Aerosol pH using glassmouth with saliva appears to represent equilibrium conditions once steady-state aerosol concentration achieved
  - pH electrodes appear to respond to both gas-vapor and particulate phases
  - Demonstrate by puffing when cartomizer not heated, heated twice, vacuumed and then not heated
- Data shows estimated pH for V2 2.4 Green (menthol) is LT 6.5, not GT 9.4 as reported

Gas-particle partitioning (GPP) – 4



Gas-particle partitioning (GPP) – 5

- To make an estimate of extent of GPP, we need
  - pH of the aerosol (~6.4, this work)
  - pK_{a2} for nicotine (~7.3, Clayton, CORESTA 2014, for VG)
  - TSP (concentration of aerosol in glassmouth) ~ 600 µg/m^3, 150 mg/250 mL)
  - MW_{om} , number average MW of particulate matter, assume all PG, 76 g/mol
  - p_{li} vapor pressure of nicotine, 0.021 torr @ 298°K
  - γ_i activity coefficient for nicotine, assume 0.01
  - R Gas constant (8.2×10^{-5} m^3 atm mol^{-1} T^{-1})

Gas-particle partitioning (GPP) – 6

- And the following formulae
  - $K_{p;nic} = (f_{om}760RT)/(MW_{om}\gamma_i p_{li}10^6)$
  - $P_{g;nic}(\%) = 100\%\{1/(1 + K_{p;i}TSP)\}$
- Calculations result in
  - $K_{p;nic}$ = 1.16E-03 $m^3/\mu g$
  - $P_{g;nic}(\%)$ = 59%
- Results based on assumption of "bone dry" aerosol, added water will decrease $P_{g;nic}(\%)$

Conclusions

- Methods to determine e-liquid pH using techniques that involve water dilution or direct measurement are error prone
- Only good way is to determine aerosol pH
  - Need special pH electrodes
  - Glassmouth appears to give “equilibrium” pH
- Estimates based on glassmouth pH work show likelihood of some nicotine in GVP