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Authors	Ahmed, M. Rizwan;Vos, Bastiaan;McSweeney, Sean;Kruse, Jacob;Fitzpatrick, Dara
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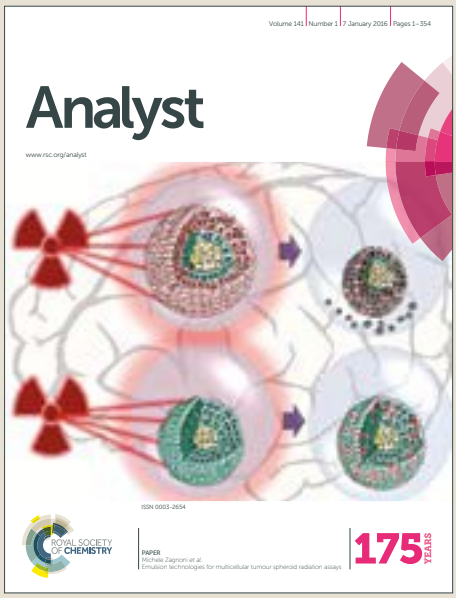
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Contactless, Probeless and Non-Titrimetric Determination of Acid-Base Reactions Using Broadband Acoustic Resonance Dissolution Spectroscopy (BARDS)

M.Rizwan Ahmed,[a] Sean McSweeney,[b] Jacob Krüse,[c] Bastiaan Vos,[a,d] Dara Fitzpatrick, [a, b,*]

[a] School of Chemistry, and Analytical and Biological Chemistry Research Facility (ABCRF), University College Cork (UCC), Cork, Ireland.

[b] BARDS Acoustic Science Labs, Cork, Ireland

[c] Kinetox, Beilen, The Netherlands.

[d] Novartis, Dublin, Ireland (current address)

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Abstract

pH determination is a routine measurement in scientific laboratories worldwide. Most major advances in pH measurement were made in the 19th and early 20th century. pH measurements are critical for the determination of acid base reactions. This study demonstrates how an acid-base reaction can be monitored without the use of a pH probe, indicator and titres of reagent. The stoichiometric reaction between carbonate and HCl acid yields specific quantities of CO2, which causes reproducible changes to the compressibility of the solvent. This in turn slows down the speed of sound in solution which is induced by a magnetic follower gently tapping the inner wall of the vessel. As a consequence the frequencies of the acoustic resonances in the vessel are reduced.

This approach is called Broadband Acoustic Resonance Dissolution Spectroscopy (BARDS) which harnesses this phenomenon for many applications. The acid-carbonate experiments have also been validated using H2SO4 acid and using both potassium and sodium counterions for the carbonate. This method can be used to

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interrogate strong acid-base reactions in a rapid and non-invasive manner using carbonate as the base. The data demonstrates the first example of a reactant also acting as an indicator. The applicability of the method to weak acids has yet to be determined. A novel conclusion from the study is that a person with a well-trained ear is capable of determining the concentration and pH of a strong acid just by listening. This brings pH measurement into the realm of human perception.

Introduction

The evolution of acid base theory is long and interesting, starting in earnest with Antoine Lavoisier in 1776,[1] with important contributions by Von Liebig in 1838,[2] to Arrhenius in the 1880's. Arrhenius along with Friedrich Ostwald established the presence of ions in solution due to the dissociation of an acidic compound.[3] Forty years later Brønsted and Lowry proposed the idea of protonation and de - protonation as a donate and accept process for acids and base.[4,5] It was Gilbert Lewis who further added to the definition of non-protic acid base reactions, which is based in terms of electron donation and acceptance.[6]

From a practical stand point, Sorensen developed a colorimetric assay for acidity in 1909 and introduced the concept of acidity as -log[H^+].[7] It was not until 1930 that the first glass electrode capable of measuring H^+ ions was developed. This was improved upon by Beckman five years later. Ultimately, this lead to the development of the modern pH meter.[8] Despite advances in pH measurements the requirement for titrimetry has remained since it was introduced by Karl Mohr in the 1850's.[9] This paper introduces a new end-point determination of an acid-base reaction in the absence of a conventional probe, indicator or titrimetry. Typically, an end-point can be determined by a colour change or by monitoring pH. However, in the method presented here an audible frequency determines the end point and the reactant itself (base) is the indicator.

Both Frank Crawford and A.B. Woods independently derived a relationship between the compressibility of a solvent and the speed of sound therein.[10,11] It has also been established by the current authors that during the dissolution of a solute there are reproducible changes in the compressibility of a solvent due to entrained

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gas and the generation of gas bubbles due to the reduction in the solubility of dissolved gas in solution. These transient changes in compressibility are due to highly ordered processes in terms of gas bubble nucleation, evolution and liberation from solution. These relationships now underpin a new platform technology called Broadband Acoustic Resonance Dissolution Spectroscopy (BARDS).[12-15]

Although, BARDS applications have focused on gas evolution during dissolution of a solute in a liquid medium, this paper focusses on gas evolution as a result of a rapid chemical reaction following the mixing of two solutions.

BARDS analysis of an induced acoustic response is focused on the lowest variable frequency time course, i.e., the fundamental resonance mode of the liquid in a vessel (Figure 1). Its frequency is determined by the sound velocity in the liquid and the approximate but fixed height of the liquid level, which corresponds to ¼ of its wavelength[10]. Thus Crawford was able to derive Equation 4.

$$freq = \frac{freq_w}{\sqrt{1+1.49x10^4.f_a}} \qquad \text{Equation 1}$$

where $freq_w$ and $freq$ are the frequencies of the fundamental resonance modes in pure and gas-filled water, respectively and f_a is the fractional volume occupied by CO_2 bubbles. The frequency minimum (f_{min}) of the BARDS response represents an equilibrium between the rate of formation of gas in solution and the rate of liberation of gas from the surface of the solvent. The solution is at its most compressible at this point. Figure 1 shows the BARDS spectrum for the 1:2 stoichiometric reaction of sodium carbonate with hydrochloric acid in 25 mL of deionised water.

Experimental

Materials

The following materials used were of Analar grade and were purchased from Sigma Aldrich and VWR international; sodium carbonate (S7795), potassium carbonate (12611) and hydrochloric acid (SZBD3160V) sulphuric acid (K47573680). Deionised water was used for preparation of all solutions used in the experiments.

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Instrumentation

A BARDS spectrometer was procured from BASL Ltd. (BARDS Acoustic Science Labs, Cork, Ireland) A typical BARDS spectrometer consists of a chamber with a custom glass tumbler, microphone and a magnetic stirrer and follower. The dissolution vessel can be accessed from the front and at the top in order to place a sample in a weighing boat on a tipper motor for introduction of the solute. However, for the experiments presented here the liquid solutions of acid or base were introduced manually. The microphone is positioned directly above the dissolution vessel within the housing. The resonances of the liquid vessel are recorded in a frequency band of 0–20 kHz. The microphone registers the acoustic resonance changes of the vessel which are monitored in real time using dedicated integrated computer software on a PC.

Method

In a typical experiment, the spectrometer records the steady state resonances of the system as a reference for thirty seconds when the stirrer is set in motion before the addition of the powder sample. However, in an acid – base experiment 5 mL of an acidic solution was mixed with 20 mL of carbonate solution which affects the reference resonance. The pitch of the resonance modes in the solution change significantly, when the acid and carbonate are added together, before gradually returning to steady state over several minutes (Figure 1). All experiments were performed in duplicate. Under standardised conditions (constant volume, concentration, temperature and stirring rate) the time courses of the observed acoustic profiles are highly reproducible.

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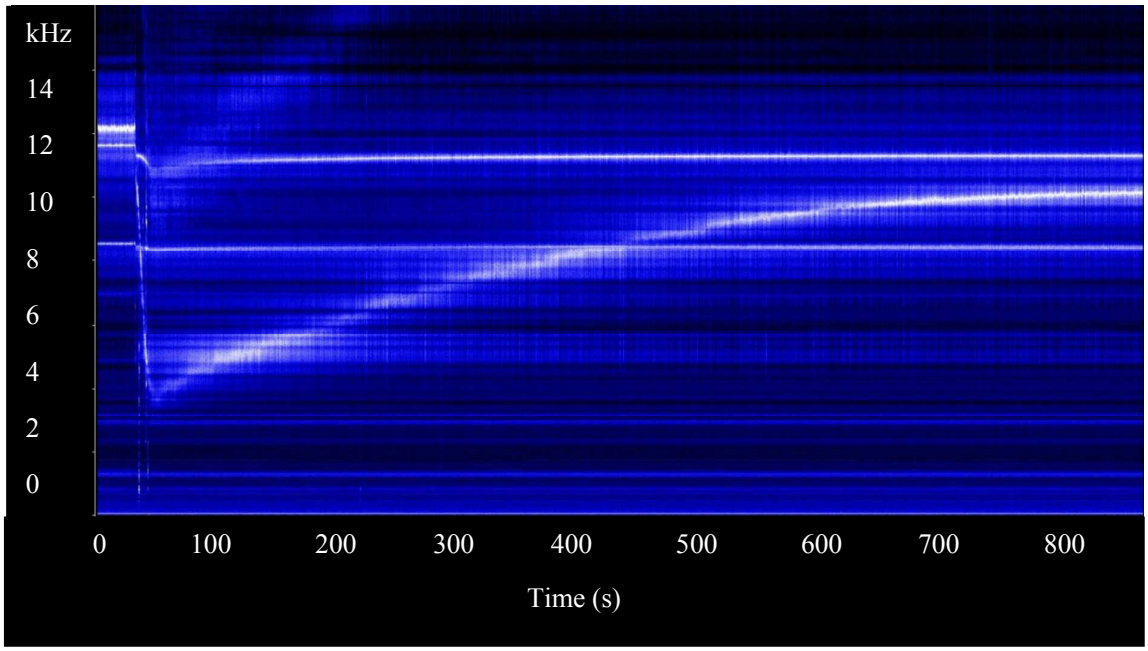


Figure 1: BARDS profile for the stoichiometric reaction between a sodium carbonate solution and a HCl solution. Note the frequency drop from 12 to 3 kHz after the addition of reactants at 30 s.

Results

The overall reaction of HCl with sodium carbonate or potassium carbonate takes the form of Equation 2 and the stoichiometry is the same irrespective of the counter cation being sodium or potassium.

$$2HCl + Na_2CO_3 \longrightarrow H_2O + CO_2 + 2NaCl \qquad \text{Equation 2}$$

In fact there are several equilibria involved as shown in Equation 3-5.

$$CO_3^{2-} + H^+ <=> HCO_3^- \qquad \text{Equation 3}$$

$$HCO_3^- + H^+ <=> H_2CO_3 \qquad \text{Equation 4}$$

$$H_2CO_3 <=> H_2O + CO_2 \text{ (dissolved or gaseous)} \qquad \text{Equation 5}$$

Figure 2 (A) shows the BARDS spectra for the addition of 5 mL of HCl acid to 20 mL sodium carbonate base and also a reverse experiment with the addition of the base to the acid. Note the volume line has a value of 12.0 kHz for 20 mL of sodium carbonate before the acid is added. Alternately, 5 mL of acid in the vessel produces and resonant frequency >of 14 kHz. The 1:2 reaction results in a decrease in the

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resonant frequency of the volume line to a value of 3.9 kHz irrespective of the initial resonant frequency. This is due to the production of CO_2 as a product of the reaction which changes the compressibility of the reaction. The experiment demonstrates that CO_2 production is independent of the sequence of addition of the acid to the base or vice versa.

The return to steady state of 10.2 kHz at 800 s is the same for all four spectra in Figure 2 (A) due to the final volume of 25 mL being the same for all the experiments. The frequency decrease after the addition of either acid or base is due to gas evolution in the solution as a result of the rapid reaction. The frequency minima (f_{min}) is reached almost instantaneously after the reactants are added together at 30 s.

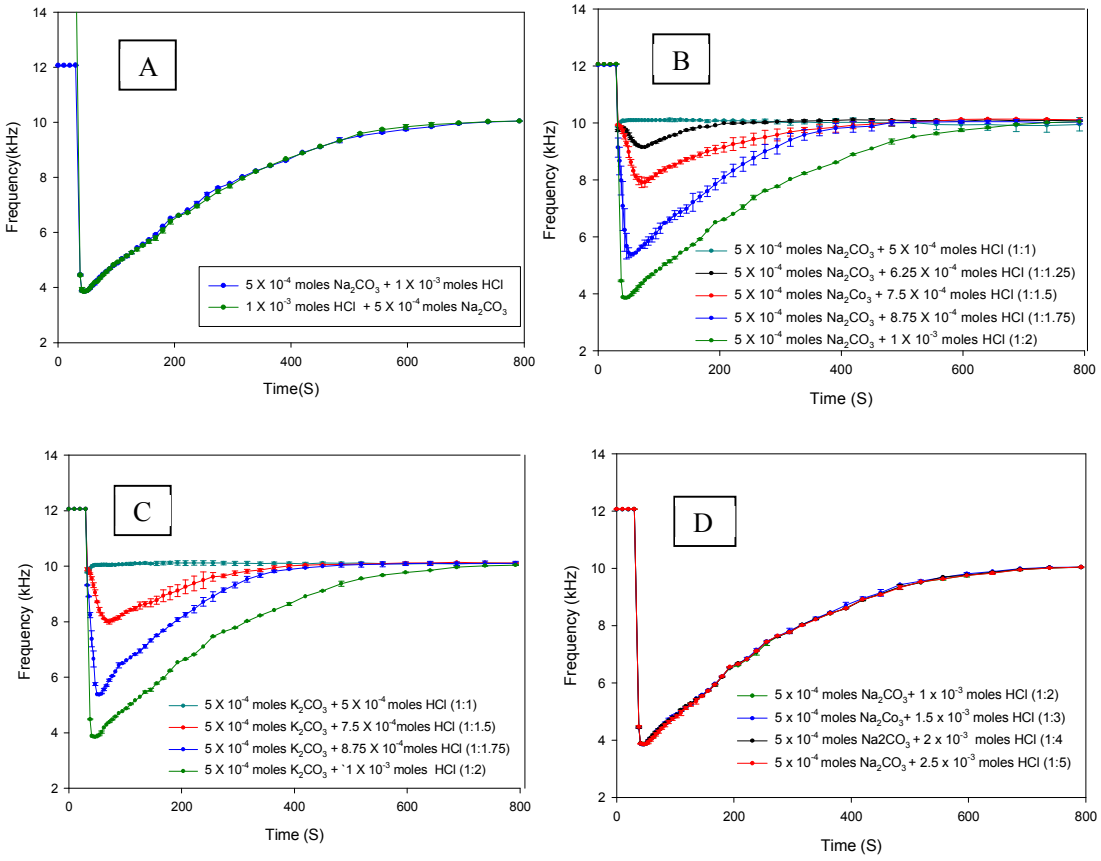


Figure 2: (A) BARDS spectra for the reaction of 20 mL sodium carbonate and 5 mL of hydrochloric acid. The blue profile represents addition of 5mL of HCl to 20 mL of sodium carbonate. The green profile represents the opposite sequence of addition. (B) The changing BARDS response upon decreasing the HCl amount below 1:2 stoichiometry. (C) The changing of the counter ions from sodium to potassium has no effect on the resulting spectra

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for the acid base reaction. (D) BARDS spectra of increasing amount of HCl where sodium carbonate is the limiting reagent.

HCl as limiting reagent

The next logical step was to vary the amounts of the reactants to establish if there is an associated change in the acoustic response (f_{min}). Figure 2(B) shows BARDS spectra for the addition of decreasing amounts of HCl to a fixed amount of sodium carbonate. These spectra show a reduction in the volume of CO_2 gas produced which corresponds to an increase in the f_{min} values with decreasing amounts of HCl. When the stoichiometry reduces to 1:1 there is a flat line response, which suggests that no CO_2 gas bubbles are liberated into the solution at this ratio. The change of the sodium cation to potassium results in the spectra in Figure 2 (C). The spectra are identical to those for the reaction between sodium carbonate and HCl. Therefore, this data strongly supports the hypothesis that the spectra solely represent the CO_2 gas production due to the acid base reaction.

Sodium Carbonate as limiting reagent

The data in Figure 2 (D) shows the BARDS response upon increasing the amounts of HCl sequentially. There is no difference in all four BARDS spectra, showing that the amount of sodium carbonate is limiting.

Until now tests were carried out with a maximum amount of 5×10^{-4} moles Na_2CO_3, whereby the maximum gas evolution was attained at an amount of 1×10^{-3} moles HCl (1:2 stoichiometry). In a subsequent experiment an amount of 5×10^{-3} moles HCl was used and a range of amounts of Na_2CO_3 was tested. Figure 3 (A) presents the results whereby HCl is in excess and carbonate is the limiting reagent. A six fold increase in amount of carbonate results in a decrease of 6.5 kHz in the frequency minima.

The reaction at the highest amount of Na_2CO_3 in Figures 3 (A) were observed to 'fizz' as the reaction became more vigorous in solution. Therefore, it was decided not to increase the concentrations any further to avoid less favourable conditions for

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BARDS experiments. Vigorous gas evolution causes disruption of the liquid surface which causes interference in the BARDS signal. Therefore, the highest concentration is defined as the upper limit of detection for the reaction and the data in Figure 2 (B) and (C) determine the lower limit of detection.

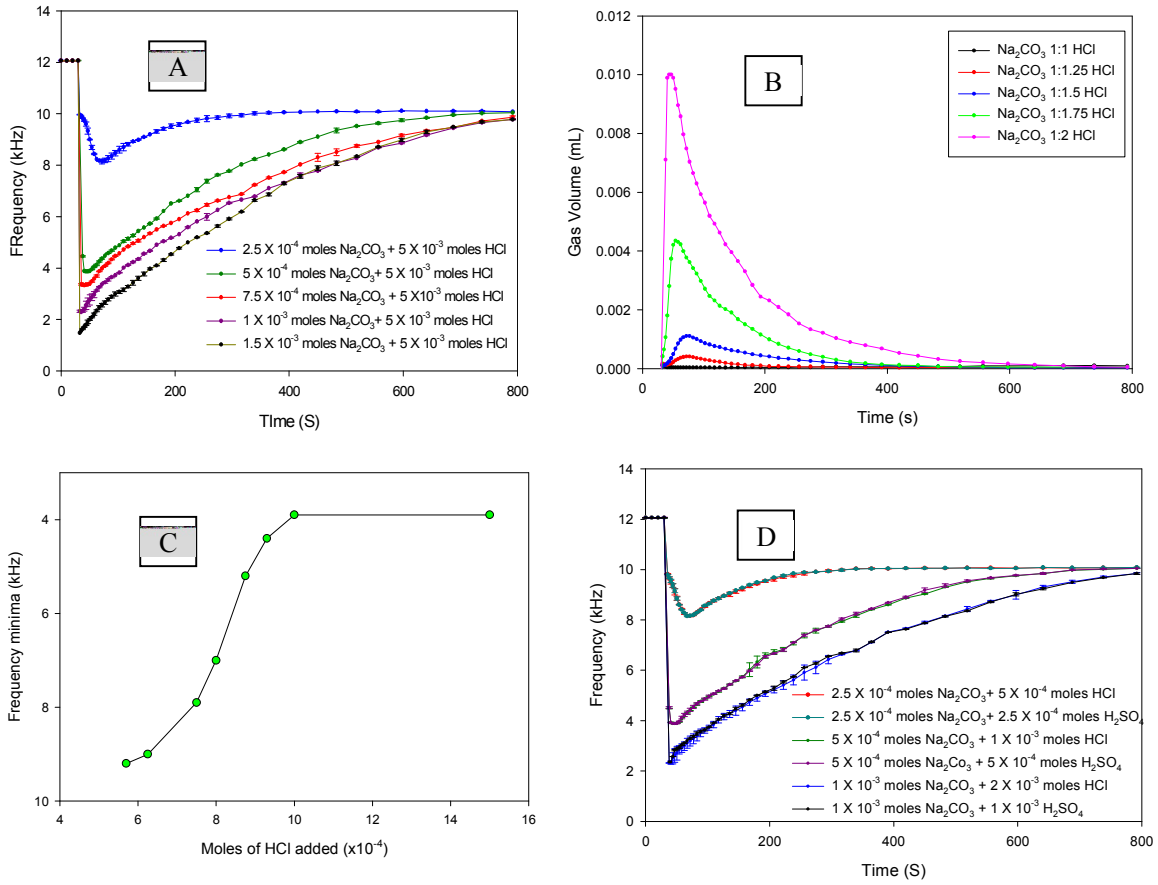


Figure 3: (A) BARDS spectra of increasing concentration of sodium carbonate as the limiting reagent with excess HCl. (B) Gas volume plot for the reaction of sodium carbonate with hydrochloric acid. The data in Figure 2(B) was used. (C) f_{min} values v acid concentration from data in Figure 2 (B) with some data added from additional experimens. (D) Comparison of BARDS profiles of mono-protic and di-protic acid base reactions.

Di-protic Acid Base Reactions

A further confirmation that the BARDS response is due to the reaction and gas evolution is shown when half the amount of a di-protic acid was used. Figure 3 (D)

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shows that half the concentration of sulphuric acid yields the same BARDS response as twice the concentration of HCl.

Gas Volume Calculations

The Crawford equation allows the conversion of frequency data in Figure 2 (B) into gas volume data. Figure 3 (B) shows the non-linear production of CO_2 and the data suggests that a 1.6 fold increase in the amount of HCl results in a 29 fold increase in gas production. In the simple assumption that for the 1:2 reaction ratio the conversion into CO_2 gas bubbles is instant and complete, the maximum gas volume (which was reached almost immediately after mixing) should correspond to the total amount of CO_2 gas that can be produced by 5.0×10^{-4} moles of Na_2CO_3. This yields a volume of $(5\times10^{-4}) \times (24 \times10^{3})$ mL = 12 mL for the expected volume of CO_2 to be produced with a molar gas volume of 24 L. In Figure 3 (B), the maximum volume attained immediately after addition of the acid is 10×10^{-3} mL, which is 1200 times less than theoretically produced. The assumption that the conversion into CO_2 gas bubbles is instant and complete may not be correct. If, for example, 12 mL of gas were added instantaneously to 25 mL of solution by syringe, there would be a vigorous deployment of gas mimicking 100% gas evolution of the acid base reaction. However, this vigorous gas evolution is not observed. A BARDS test for oversaturation has been previously presented (Fitzpatrick *et al.*, 2014) whereby the dissolution of a compound in a saturated solution will produce an over-response (lower f_{min}). This experiment was performed on the acid base solutions, post reaction, and there was no such over-response observed. Therefore, it is hypothesised that just a fraction of the CO_2 product exists in the gaseous state and that the majority of the CO_2 remains dissolved until it is exchanged at the liquid/air interface without BARDS detection.

The data in Figure 3 (C) shows the inverse relationship between f_{min} and moles of HCl added in the experiments shown in Figure 2(B). Additional experiments were conducted to define the curve. The data reaches a plateau at 4 kHz due to the limiting concentration of Na_2CO_3 which is reached when the HCl concentration reaches 1.0×10^{-3} M. It is therefore possible to determine the concentration and pH of

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a strong acid from the curve by obtaining the f_{min} during a standardised reaction using BARDS.

FurtherAnalysis of the CO_2 gas Volume Response.

Figure 4 (A) shows a log plot of the gas volume calculated using the Crawford equation. There is a linear decay yielding a kinetic rate constants for the CO_2 escape / release from solution. The release of gas is independent of the stoiciometry of the reaction (see supplementary information). The rate constant (k_d) for decrease of compressible gas in the solution is given by the descending slope in Figure 4 (B) with a k_d value of 7.2×10^{-3} s^{-1} obtained.

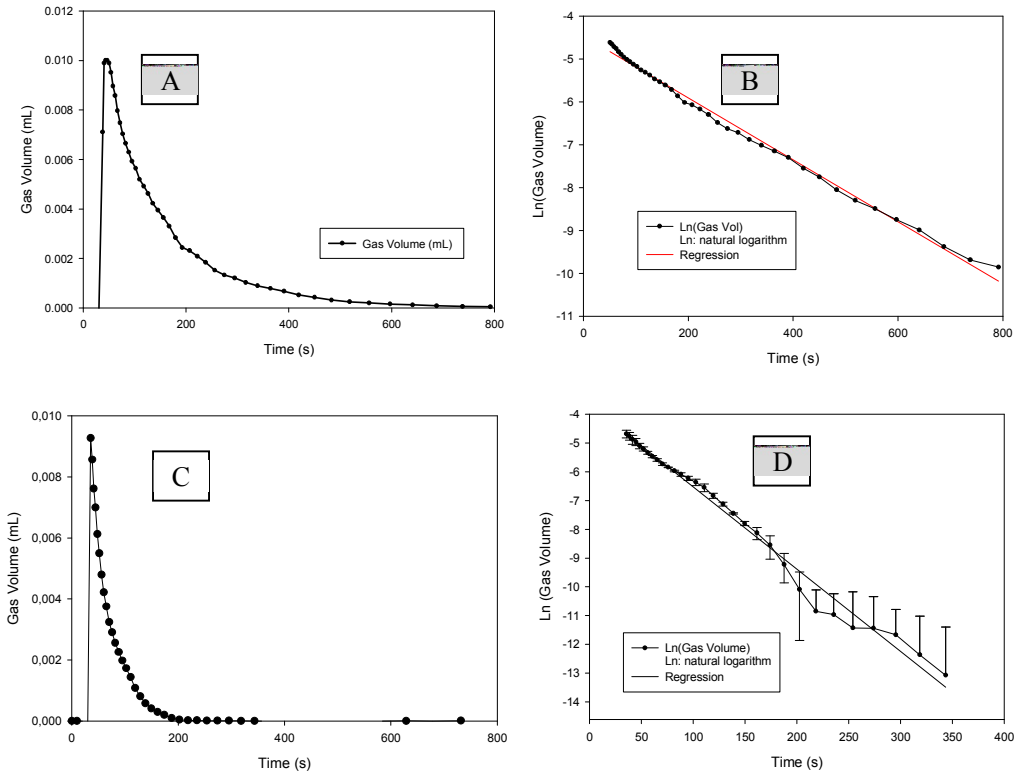


Figure 4: (A) Gas volume plot of the stoichiometric acid base reaction. (B) Natural log plot of the data in (A) with regression line shown. (C) Gas volume plot of the dissolution of 0.5 M KCl in water (D) Natural log plot of the data in (C).

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Assuming that the decrease rate (k_d) of compressible gas represents the bubble escape/elimination rate (k_{el}) from the solution (thus $k_d = k_{el}$) we can estimate the total amount of CO_2 gas produced (D_{gas}) upon addition of HCl to the Na_2CO_3 solution or vice versa as follows: D_{gas} = AUV x k_{el}, where AUV (mL.s) is the total area under the gas volume/time course and k_{el} (s^{-1}) is the rate constant for the first order gas elimination process. Therefore, AUV= 1.24 mL.s and k_{el} = 7.2x 10^{-3} s^{-1} yielding a volume of 8.9x 10^{-3} mL (1350 times less than theoretically produced).

However, it may well be that the decrease rate of the compressible gas is not determined by the elimination rate of gas bubbles from the solution, but by the generation of compressible gas. This might then be attributed to e.g. slow dehydration of carbonic acid (H_2CO_3 -> CO_2 + H_2O) or the low gas bubble nucleation rate, when two liquids are mixed.

A BARDS experiment was performed in which a small amount of KCl was dissolved in water to determine the bubble elimination rate constant correctly. It is assumed that the gas volume disappearance rate is determined by the gas elimination process. In this case a value of 2.86 x 10^{-2} s^{-1} was obtained for k_{el}. Since this k_{el} is four times higher than the earlier determined k_d it is indeed shown that the gas bubble volume generation rate is rate determining in the decrease of compressible gas from the solution. An improved estimate for the total amount of CO_2 gas produced (Dgas) is D_{gas} = AUV x k_{el} = 1.24 mL.s x 2.86 x 10^{-2} s^{-1} = 35 x 10-3 mL, which is 343 times less than theoretically produced.

Discussion

The data demonstrates remarkable new insights into acid - carbonate base reactions. The compressiblity of the reaction solution changes in a very ordered way which has not been understood or studied before. The data also presents many questions regarding the fate of CO_2 produced during the acid base reactions. Crawfords equations indicates that just ~0.1% of the expected CO_2 exists as gas in solution as the reactions proceeds. Carbon dioxide is soluble in water, in which it reversibly forms H_2CO_3, which is a weak acid. The majority of the carbon dioxide is not

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converted into carbonic acid, but remains as CO_2 molecules, not affecting the pH. However, as the reaction ratio changes from 1:1 to 1:1.75 the pH drops from 7.5 to 6.0, respectively which indicates an increase in ionised carbonic acid(see supplementary information). There is a further significant decrease to pH 3 observed for the 1:2 reaction. This low value is attributable to a slight excess of the hydrochloric acid.

Fordtran *et al*. (1984)[16] designed an experiment to measure the amount of CO_2 produced during the reaction of HCl and bicarbonate. However, there are major differences in the experimental setup which make detailed comparisons with BARDS data difficult.

The presence or role of nano-bubbles of CO_2 cannot be ruled out given the growing knowledge of their existence and persistence in solution (Leroy *et al*., 2016). [17]

Conclusions

The relationship between moles of acid added and the compressibility of the solution during an acid base reaction is clearly demonstrated. The bulk compressibility changes are associated with the generation of CO_2 gas. The measurement can be achieved without the need for a submerged probe, indicators or consecutive titres. Given the audible nature of the resonant reaction vessel, it is possible to determine the pH acoustically.

The fate of CO_2 produced during the reaction of acid and carbonate is determined to be about 0.1% gaseous which is conducive to BARDS quantitative measurement. The bulk of CO_2 produced remains largely dissolved probably followed by slow release over time.

CO_2 plays a vital role in many biological and environmental processes. BARDS data provides new insights into its fate in aqueous solutions in terms of gas evolution and loss in the presence of a chemical reaction.

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The concentration ranges of acid and base within which BARDS measurement can be made is narrow for routine applications. However, the method is simple and elegant.

Future work will focus on weak acid and base reactions. Experiments will also demonstrate how BARDS elucidates quantitatively the hydrogen production in an electrolytic cell and also its production during the synthesis of gold nanoparticles using gold chloride and borohydride.

References:

1. Antoine de Lavoisier. Elements of Chemistry In a New Systematic order, containing all Modern Discoveries .Second Edition, (1806) page 116-121.

2. J. von Liebig. Ueber die Constitution der Organischen Säuren, (1838) page 41-45.

3. Savante Arrhenius "Textbook of Electrochemistry" Translated by John McCrae, (1902), page 110-121.

4. Brønsted, J. N.. "Einige Bemerkungen über den Begriff der Säuren und Basen" [Some observations about the concept of acids and bases]. Recueil des Travaux Chimiques des Pays-Bas. 42 (8), (1923) page 718–728.

5. Lowry, T. M. "The uniqueness of hydrogen". Journal of the Society of Chemical Industry. 42 (3), (1923), page 43–47.

6. Lewis G.N Valence and The Structure of Atoms and Molecules, (1923), page 141-142.

7. Sørensen, S. P. L.. "Enzymstudien. II: Mitteilung. Über die Messung und die Bedeutung der Wasserstoffionenkoncentration bei enzymatischen Prozessen". Biochemische Zeitschrift (in German), (1909), 21: 131–304.

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DOI: 10.1039/C7AN01447C

Published on 15 January 2018. Downloaded by University College Cork on 24/01/2018 12:46:16.

8. Thackray & Minor Myers, Jr. . Arnold O. Beckman : one hundred years of excellence. (2002), page 23.

9. Oesper, Ralph E., 'Karl Friedrich Mohr', Journal of Chemical Education, 4 (11), (1927), page 1357.

10. Crawford, F. S., 'The hot chocolate effect', American Journal of Physics, 50 (5), (1982), page 398-404.

11. Wood,A.B A text book of sound, 1st ed; MacMillan:New York,(1930).

12. Fitzpatrick, D., et al., 'Principles and applications of broadband acoustic resonance dissolution spectroscopy (BARDS): A sound approach for the analysis of compounds', Analytical Chemistry, 84 (5), (2012), page 2202-2210.

13. Fitzpatrick, D., E. Scanlon, et al.. Fitzpatrick, D., E. Scanlon, et al. (2012). "Blend uniformity analysis of pharmaceutical products by Broadband Acoustic Resonance Dissolution Spectroscopy (BARDS)." International Journal of Pharmaceutics 438(1-2), (2012), page 134-139.

14. Fitzpatrick, D., R. Evans-Hurson, et al. Fitzpatrick, D., R. Evans-Hurson, et al.. "The relationship between dissolution, gas oversaturation and outgassing of solutions determined by Broadband Acoustic Resonance Dissolution Spectroscopy (BARDS)." Analyst 138(17), (2013), page 5005-5010.

15. Bastiaan Vos , Shane V. Crowley , Jonathan O'Sullivan , Rachel Evans-Hurson, Seán McSweeney, Jacob Krüse, M. Rizwan Ahmed, Dara Fitzpatrick, James A. O'Mahony New insights into the mechanism of rehydration of milk protein concentrate powders determined by Broadband Acoustic Resonance Dissolution Spectroscopy (BARDS). 61, (2016), page 933–945.

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View Article Online
DOI: 10.1039/C7AN01447C

Published on 16 January 2018. Downloaded by University College Cork on 24/01/2018 12:46:16.

16. Fordtran JS, Morawski SG, Santa Ana CA, Rector FC Jr., Gas production after reaction of sodium bicarbonate and hydrochloric acid. Gastroenterology. 87(5), (1984), page 1014-21.

17. Leroy, V.; Norisuye, T., Investigating the existence of bulk nanobubbles with ultrasound. ChemPhysChem , 19;17(18), (2016), page 2787-90.

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Author Contributions

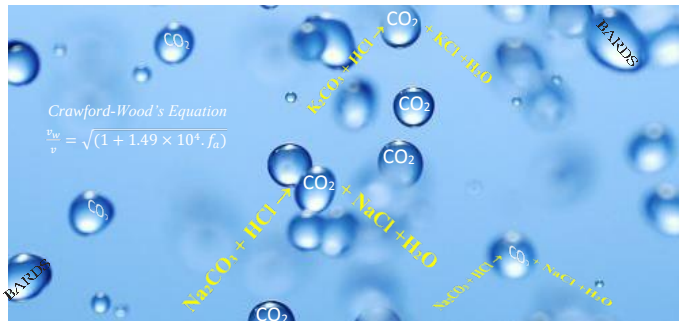
Dr. Dara Fitzpatrick is the originator of BARDS and supervised the study. Rizwan Ahmed is a Ph.D. candidate and carried out the experimental measurements. Dr. Seán McSweeney developed the BARDS instrument and Jacob Kruse is responsible for the modelling of the data.

Competing Financial Interests

Seán McSweeney and Dara Fitzpatrick are directors of BARDS Acoustic Science Labs Ltd. The application presented in this paper has no likely commercial application.

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