

# Multi-parameter estimation in voltammetry when an electron transfer process is coupled to a chemical reaction

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**ABSTRACT.** Estimation of thermodynamic and kinetic parameters in electrochemical studies is usually undertaken *via* comparison of the experimental results with theory based on a model that mimics the experiment. The present study examines the credibility of transient d.c. and a.c. voltammetric theory-experiment comparisons for recovery of the parameters needed to model the ubiquitous mechanism when an electron transfer (**E**) reaction is followed by a chemical (**C**) step in the **EC** process ( $A \pm e^- \xrightleftharpoons{E^0, k^0, \alpha} B \xrightleftharpoons[k^b]{k^f} C$ ). The data analysis has been undertaken using data optimisation methods facilitated in some cases by grid computing. These techniques have been applied to the simulated (5% noise added) and experimental (reduction of *trans*-stilbene) voltammograms to assess the capabilities of parameter recovery of  $E^0$  (reversible potential for the **E** step),  $k^0$  (heterogeneous electron transfer rate constant at  $E^0$ ),  $\alpha$  (charge transfer coefficient for the **E** step),  $k^f$  and  $k^b$  (forward and backward rate constants for the **C** step) under different kinetic regimes. The advantages provided by the use of a.c. instead of d.c. voltammetry and data optimisation methods over heuristic approaches to ‘experiment’-theory comparisons are discussed, as are the limitations in the efficient recovery of a unique set of parameters for the **EC** mechanism. In the particular experimental case examined herein, results for the protonation of the electrochemically generated stilbene di-anion demonstrate that notwithstanding significant advances in experiment and theory of voltammetric analysis, reliable recovery of the parameters for the **EC** mechanism with a fast chemical process remains a stiff problem.

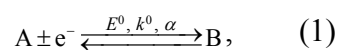
## INTRODUCTION

In quantitative studies of complex problems in physical chemistry, experimental results usually are compared with those derived from simulations of a model designed to mimic the experiment. In the often used heuristic approach, a collection of unknown parameter inputs used in the simulations are varied systematically until the experimentalist decides that satisfactory agreement between experiment and theory has been achieved. The parameters reported from this experimenter-determined 'best fit' scenario are then assumed to accurately describe the experimental data. In more advanced methods of data analysis, the level of agreement between experiment and theory is optimised computationally and quantitative reports of the level of agreement are provided.

An area of science that includes a highly formalised mandatory description of the agreement level achieved between experimental and modelled data is structural analysis by X-ray diffraction. This technique has a major advantage in that the number of possible space groups and hence models available for testing is finite, although of course there are many nuances that can lead to ambiguities in solving the so-called inverse problem needed to propose a unique crystal structure. In contrast, in dynamic forms of electrochemistry, an infinite number of mechanisms involving electron transfer and coupled chemical reactions are theoretically possible so that automation of data analysis is extremely difficult. In voltammetry, readers of papers are therefore still usually reliant on the experience of the experimentalist to correctly define the mechanism and provide reliable values of the parameters that describe the electrode reaction of interest. However, this leads to the unsatisfactory outcome of experimenter dependent reports of parameters. Presumably because of the difficulty of routinely obtaining uniquely defined solutions, use of statistically optimised parameter recovery is rare in voltammetry. Nevertheless,

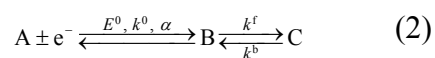
optimised data analysis approaches should advance the fidelity of parameter recovery in electrode kinetics, as demonstrated in detailed d.c. voltammetric studies with data optimisation by Speiser *et al.*<sup>1-6</sup>

In recent work,<sup>7,8</sup> we have implemented data optimisation strategies for parameter recovery for quasi-reversible and reversible electrode processes using the a.c. instead of d.c. cyclic voltammetry. The experimental results have been compared with data derived from modelling the electrode process described by the equation (1).



where the upper and lower of the alternative  $\pm$  signs apply to reduction and oxidation, respectively. For this electrode process, values of parameters such as reversible potential ( $E^0$ ), the heterogeneous charge transfer rate constant ( $k^0$ ) at  $E^0$ , the charge transfer coefficient ( $\alpha$ ) (assuming Butler-Volmer kinetics apply), the uncompensated resistance ( $R_u$ ) and the capacitance of the double layer ( $C_{dl}$ ) in a potential dependent form are optimised by establishing the best possible fit of theory to the experimental data.<sup>7-9</sup> However, even application of sophisticated forms of data analysis to this relatively simple class of electrode reaction can be problematic.<sup>8</sup>

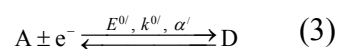
In the present paper we explore the application of multi-parameter recovery methods in transient voltammetry to a commonly encountered mechanism where electron transfer is followed by a chemical reaction in the so-called **EC** process. This reaction scheme is summarised in equation 2 with the chemical reaction  $B \rightleftharpoons C$  (**C** step) occurring after the electron transfer (**E** step). For simplicity, we consider a first order chemical step with a forward ( $k^f / s^{-1}$ ) and backward ( $k^b / s^{-1}$ ) homogeneous chemical rate constants and hence an equilibrium constant  $K = k^f / k^b$ .



For this **EC** process, all the parameters needed to describe the electron transfer reaction (**E** step) included in equations 1 and 2, viz.  $E^0$ ,  $k^0$ , and  $\alpha$  as well as  $k^f$  and  $k^b$  (from the **C** step) along with  $R_u$  and  $C_{dl}$  may need to be optimised, giving rise to even more possibilities for non-unique solutions to be available within experimental uncertainty.

From an experimental perspective, when using d.c. cyclic voltammetry to quantify the thermodynamics and kinetics, data sets derived from a range of potential sweep rates ( $\nu$ ) are typically obtained, with each one providing a different level of sensitivity of the response to the unknown parameters. This approach has been well developed and widely applied over many years.<sup>10</sup> In a.c. voltammetry, when a periodic sine wave of amplitude,  $\Delta E$  / V, and frequency,  $f$  / Hz, is superimposed onto the d.c. ramp, variation in  $f$  achieves an analogous impact to altering  $\nu$  in the d.c. method. If  $\Delta E$  is large enough, the aperiodic component (similar properties to those available in the d.c. method<sup>11</sup>), along with series of a.c. harmonics can be resolved by application of Fourier transform (FT) methods.<sup>9,12,13</sup> Large amplitude a.c. voltammetry therefore provides different levels of kinetic sensitivity in each harmonic, available from single rather than multiple experiments. Furthermore, other advantages are available. For example, the second and higher harmonics have minimal charging current even at high  $f$ , while the d.c. method usually suffers from dominant non-faradaic contribution at very high  $\nu$ .

Prospects for ambiguities in reporting electrode kinetic data or having a non-unique solution (within experimental error) are known to abound under d.c. voltammetric conditions with the **EC** mechanism.<sup>14</sup> For example, if  $k^f$  and  $k^b$  are both sufficiently fast then the process can be chemically reversible (**C<sub>rev</sub>**). To all intents and purposes the process will therefore appear to be exactly equivalent to that in equation 3,



but with a different combination of  $E^{0'}$ ,  $k^{0'}$  and  $\alpha'$  being fitted to the data, relative to those of  $E^0$ ,  $k^0$  and  $\alpha$  in equation 2, if the experimentalist is unaware of the presence of the C step. In this scenario, the potential shift and hence apparent  $E^{0'}$  value is governed by the values  $k^f$  and  $k^b$ . A second region of potential ambiguity arises when the E step is slow and  $k^f$  is fast in an  $E_{irrev}C_{irrev}$  case to give what Feldberg<sup>15</sup> calls the ‘heterogeneous equivalent region’ where the heterogeneous  $k^0$  and homogeneous  $k^f$  parameters have become intimately coupled so that the origin of irreversibility is not readily discerned. Analogous ambiguities that can potentially lead to non-unique thermodynamic or kinetic parameter evaluation in d.c. voltammetry must also arise in a.c. methods.

The discussion above implies that the E step can be fully reversible ( $E_{fr}$  case), quasi-reversible ( $E_{qr}$ ) or irreversible ( $E_{irrev}$ ) and also that the C step can likewise be reversible ( $C_{rev}$ ) or irreversible ( $C_{irrev}$ ) to give  $E_{fr}C_{rev}$ ,  $E_{fr}C_{irrev}$ ,  $E_{qr}C_{rev}$ ,  $E_{qr}C_{irrev}$ ,  $E_{irrev}C_{rev}$  and  $E_{irrev}C_{irrev}$  sub-categories of reaction. Making a careful distinction as to which sub-category of EC mechanism applies can be very useful in voltammetry when undertaking heuristic forms of data analysis. A problem is that the sub-category of reaction that applies can vary with  $v$  in d.c. method, or  $f$ , or the harmonic component in a.c. voltammetry.

Saveant *et al.*<sup>10,16,17</sup> early on in the modern era of quantitative electrode kinetics with d.c. cyclic voltammetry, characterised the EC and CE type reactions in linear sweep or cyclic d.c. voltammetry into kinetic regimes by introducing dimensionless parameters such as  $\lambda = \frac{(k^f + k^b)RT}{Fv}$  and defined regions of the experimental parameter space that could be purely diffusion controlled, diffusion controlled but modified by the equilibrium constant or completely kinetically controlled. In the case of  $E_{fr}C$  reaction with small values of  $\lambda$ , essentially reversible behaviour is expected. For large values of  $\lambda$ , no d.c. current is observed on reversing the potential

scan direction in a d.c. cyclic experiment and the shape of the d.c. linear sweep voltammogram is similar to that of a totally irreversible charge transfer process predicted for an  $E_{\text{irrev}}$  reaction. The dependence of the peak position in linear sweep voltammetry on scan rate is complex, but in the one-electron transfer  $E_{\text{r}}C$  case for oxidation, shifts towards more negative potentials by about 0.03 V at 298 K for a tenfold increase in  $\lambda$  are expected. Nicholson and Shain<sup>18</sup> developed working curves for the ratio of reduction to oxidation peak currents in cyclic voltammetry, which have been widely used to calculate  $k^f$ , but are only applicable to a small range of  $\lambda$ .

The ubiquitous EC mechanism has been studied extensively for many decades using dynamic electrochemical techniques. Bard and Faulkner<sup>10</sup> have comprehensively reviewed the many permutations and combinations that may arise in EC mechanisms in d.c. voltammetry. In the a.c. version of the technique, the frequency becomes the key parameter determining the EC mechanistic regime that applies, with  $\lambda$  now being defined as  $\frac{(k^f + k^b)}{2\pi f}$ . A number of reports on EC behaviour with a.c. techniques are available, with parameter evaluations relying on heuristic methods of data analysis.<sup>10,19-23</sup>

Given the ambiguities that can arise in parameter estimation, comparisons with theoretical predictions are best undertaken with experimental data obtained over a wide range of timescales:  $\nu$  in d.c. methods,  $f$  or harmonics in a.c. methods, as well as concentration, and where appropriate, temperature. The complexity of quantitative data analysis with the EC mechanism is such that the reliable use of heuristic methods for parameter estimation in d.c. or a.c. voltammetry is always tedious if not impossible and computationally intensive approaches, sometimes facilitated by utilising high-end computational resources, need to be introduced to enhance the probability that a unique solution has been obtained for all parameters that are relevant. In this paper, it will be shown how application of data optimisation methods assists in

disentangling some of the ambiguities that can make the reporting of a unique set of  $E^0$ ,  $k^0$ ,  $\alpha$ ,  $R_u$ ,  $C_{dl}$ ,  $k^f$  and  $k^b$  parameter values more probable than is currently likely to be achieved with experimenter dependent heuristic methods. The initial data analysis is based on parameter estimation from d.c. and a.c. simulations with added noise. Further, d.c. and a.c. voltammetric experimental data for the reduction of *trans*-stilbene<sup>21</sup> are also re-examined with the aid of data optimisation methods. The reaction involves the initial reduction of *trans*-stilbene to the anion-radical and then to the dianion, which is rapidly protonated, and represents a ‘stiff’ problem of the  $E_{qr}E_{qr}C_{irrev}$  kind where full parameter recovery is not possible with d.c. methods, but is amenable to recovery of  $E^0$ ,  $k^0$  and  $k^f$  values by analysis of the a.c. harmonics available with Fourier transformed large amplitude a.c. voltammetry and data optimisation methods.

## SIMULATIONS AND DATA ANALYSIS

Details on the simulation methods employed are provided in Appendix A of the Supporting Information.

The ‘Global Method’ (GM) used at Oxford in the analysis of d.c. or total current a.c. voltammetry<sup>7,8</sup> recovers the unknown parameters with the aid of a Quasi-Newton method,<sup>24</sup> which minimises the difference ( $\Psi_{GM}$ ) between the experimental ( $f^{Exp}$ ) and simulated ( $f^{Sim}$ ) data expressed as:

$$\Psi_{GM} = \sum_{i=1}^N (f^{Exp}(x_i) - f^{Sim}(x_i))^2. \quad (4)$$

This form of data analysis is conveniently undertaken with a standard laptop computer.

In the case of the Nimrod/O-based analysis used in FT based a.c. voltammetry at Monash,<sup>7,8</sup> parameter recovery is based on the Simplex method, and the objective function  $\Psi_{Nim}$  is defined as



$$\Psi_{\text{Nim}} = \frac{1}{H} \cdot \sum_{h=1}^H \sqrt{\frac{\sum_{i=1}^N (f_h^{\text{Exp}}(x_i) - f_h^{\text{Sim}}(x_i))^2}{\sum_{i=1}^N f_h^{\text{Exp}}(x_i)^2}}, \quad (5)$$

where  $h$  is the number of the aperiodic d.c. or a.c. harmonic component,  $H$  is the total number of the components evaluated,  $f_h^{\text{Exp}}(x)$  and  $f_h^{\text{Sim}}(x)$  are the experimental and simulated functions in the corresponding component, respectively, and  $N$  is the number of data points. The procedure used to obtain the harmonics prior to the data optimisation exercises is as follows. Fourier transformation of total a.c. current data in the time domain gives the power spectrum in the frequency domain. Band selection followed by inverse Fourier transformation is then used to resolve the experimental data into the d.c. aperiodic and a.c. harmonic components in the time domain.<sup>7-9,12,13,25</sup>

The Nimrod/G parameter sweep tool used in experiment-simulation comparisons allows the quality of the fit of the individual harmonics or total a.c. data (calculated using equation 5) to be defined as a function of combinations of variables,<sup>9,13</sup> and because it requires substantially more calculations to be undertaken than in the GM approach, was used in conjunction with grid computing.

## RESULTS AND DISCUSSION

**Analysis of simulated data: examples of successful and unsuccessful parameter recovery outcomes.** As a starting point for identifying limitations in parameter recovery for the EC mechanism, the efficiency of the data optimisation methods was assessed with respect to simulated d.c. and a.c. voltammetric data modelled on the basis of the mechanism in equation 2 and using dimensional parameters that are typical of those used in experimental studies. The underlying reason for initially replacing an actual experiment with simulations is that precise

values of the parameters sought are known, whereas with real **EC** experimental data, this knowledge is not available. This procedure also allows avoiding obfuscation of the analysis by the effects of uncompensated resistance ( $R_u$ ) and double-layer capacitance ( $C_{dl}$ ). However, the impact of these terms will be critical in the analysis of the *trans*-stilbene electrochemistry employed subsequently as a practical example.

In the absence of added noise, both GM and Nimrod/O almost invariably derive correct input parameters from the simulated voltammograms within machine tolerance for all values and their combinations referred to in this paper. To make our analysis of the simulated data sensible with respect to an experimental scenario, 5% noise was added to the simulated data (Fig. S1) using a well-documented procedure.<sup>7</sup> This level of noise is significantly higher than that present in experimental data (Fig. S1), but was deliberately used to severely challenge the ability of the algorithms to achieve reliable recovery of some of the parameters. The same rationale for adding noise to simulated data as part of the test of the efficacy of data optimisation protocols also has been used by Speiser *et al.*<sup>6</sup> It has already been established that even with addition of 5% noise, both GM and Nimrod/O are able to recover the correct values of  $E^0$ ,  $k^0$  and  $\alpha$  from the d.c. and a.c. voltammograms simulated for a simple case of the **E** mechanism<sup>7</sup> unless the reversible limit is approached.<sup>8</sup> On this basis, limitations in estimation of  $E^0$ ,  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$  disclosed in the discussion provided below with respect to analysis of ‘noisy’ simulated data are confidently attributed to ambiguities introduced by coupling of the heterogeneous and homogeneous parameters intrinsic to the voltammetry of the **EC** mechanism.

A wide range of scan rates are employed in a typical d.c. cyclic voltammetric study of an **EC** process and also an extensive range of kinetics parameters can be encountered. The combinations of scan rate and electrode kinetic parameters ultimately chosen for use in the analysis of ‘noisy’

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3 simulated data was governed by wishing to address a.c. parameter recovery scenarios that are  
4 shown to be ‘stiff’ in d.c. voltammetry, typically where ambiguities in a sub-category of  
5 mechanism in the d.c. context increase the risk of major uncertainties in parameter estimation. In  
6 order to simplify the presentation of results, a fixed scan rate of  $0.10 \text{ V s}^{-1}$  was selected for use in  
7 all simulations with 5% added noise. Implications with respect to regimes where recovery of  $E^0$ ,  
8  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$  are difficult when this particular scan rate and noise level are discussed in detail in  
9 Appendix B using  $k^0$ ,  $k^f$  and  $k^b$  values encompassing the ranges of  $10^{-6}$  to  $10^3 \text{ cm s}^{-1}$ , 0 to  $100 \text{ s}^{-1}$   
10 and 0 to  $100 \text{ s}^{-1}$  respectively.  $\alpha$  was fixed at 0.5. Parameters such as diffusion coefficient,  $D$ ,  
11 electrode area,  $A$ , were fixed at values relevant to the *trans*-stilbene experimental exercise  
12 presented later.  
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16 In Appendix B, simulated a.c. voltammograms employing identical parameter combinations  
17 relevant to the previously established d.c. ‘stiff’ conditions were then examined but with  
18 superimposition of a low frequency ( $f = 9 \text{ Hz}$ ) sinusoidal perturbation with an amplitude of  
19 0.08 V onto the d.c. waveform. The detailed analysis presented in Appendix B reveals a much  
20 lower risk of ambiguity with respect to parameter estimation when using a.c. voltammetry within  
21 the chosen parameter regime, even though the d.c. and a.c. timescales are not widely different.  
22 Advantageously, in the a.c. method, and as shown in Appendix B, the current magnitude is a far  
23 more sensitive function of the kinetics associated with the **E** and **C** steps in the **EC** mechanism  
24 than it is in the d.c. method and it is predominantly this feature that allows the kinetic regime for  
25 reliable parameter estimation to be extended when using the a.c. method. Advantages of analysis  
26 of a.c. data at higher frequencies are also included in Appendix B. Results of analogous exercises  
27 using other d.c. scan rates, and electrode kinetic parameters would scale with  $\lambda$ , the  
28 dimensionless parameter referred to in the Introduction.  
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The outcomes of the data optimisation analysis applied to the simulated EC reaction (equation 2) with 5% added noise in kinetically stiff parameter recovery regimes are summarised in Tables 1-3. Before examining these outcomes, it needs to be noted that when using the Nimrod/O toolkit with the Simplex algorithm it is customary to undertake a series of data optimisation runs starting from different points in the selected parameter space. In the presence of 5% random noise, non-unique localised minima produce a slightly different set of optimised parameters from each run. This problem can be unveiled by examination of contour plots introduced in Refs.<sup>9,13</sup> In the initial series of exercises, the average values of parameters and standard deviations obtained from 15 runs are reported when the Simplex method is used. Only one GM data optimisation run was performed to provide the data in Tables 1-3, and of course the absolute proximity of this particular result to an ‘optimal outcome’ is uncertain. Results generated for 1000 runs in a GM-based bootstrapping exercise are available in Appendix C of the Supporting Information and reveal that the single GM data optimisation run is adequate for the present purposes, but also that superior parameter recovery can be achieved by this computationally intensive approach and that recovery of some parameters is far easier than others under specified circumstances.

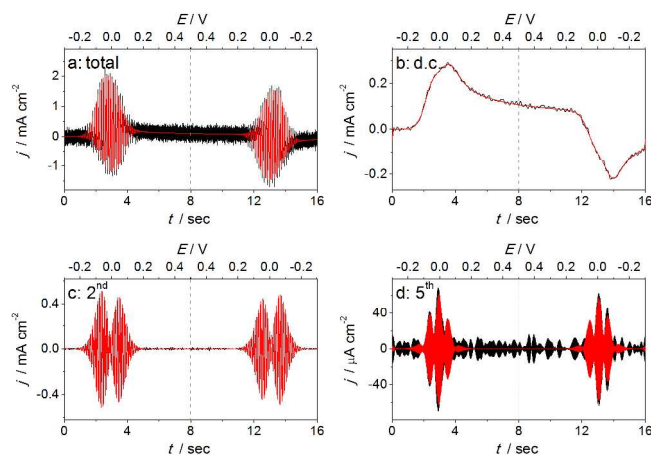
In the first exercise with 5% added noise considered (Table 1; Figs. 1 and S2), a fully reversible  $E_{fr}$  step (simulated as  $E_{qr}$  with  $k^0 = 10^3 \text{ cm s}^{-1}$  and  $\alpha = 0.50$ ) was coupled to a chemical transformation ( $C_{rev}$  step) having an equilibrium constant,  $K = 1$  with  $k^f = k^b = 100 \text{ s}^{-1}$ . This represents an essentially untenable situation for the parameter recovery from d.c. cyclic voltammetric data on the relevant time scale ( $\nu = 0.10 \text{ V s}^{-1}$ ). Under this set of conditions, the d.c. cyclic voltammogram exhibits an oxidation to reduction peak current ratio  $I_{Ox}^p/I_{Red}^p = 0.99$  which is hardly distinguishable from 1.00 predicted for an  $E_{fr}$  mechanism, but with an ‘incorrect’

value of  $E^0$  that differs by *ca* 0.016 V from the true  $E^0$  value used to simulate the  $\mathbf{E_{fr}C_{rev}}$  mechanism. Thus as shown in Table 1, the ‘noisy’ simulated data for the  $\mathbf{E_{fr}C_{rev}}$  mechanism having an  $E^0$  value of 0.000 V can be almost perfectly represented by an  $\mathbf{E_{fr}}$  reaction with  $E^0$  of *ca* 0.016 V. In all probability, such an outcome in a real experiment would be interpreted to mean that the system under study is a simple electron transfer process, unless an independent analytical method argues for the presence of coupled chemical reaction. Furthermore, the known input parameters for the mechanism are not recovered in the presence of 5% noise from d.c. cyclic voltammograms under the conditions of Table 1 by the Nimrod/O tool even with the use of this ‘correct’  $\mathbf{E_{fr}C_{rev}}$  model. The significant variation found in individual Nimrod-assisted data optimisation runs (Table 1) provides a warning that a data optimisation exercise may be of limited value without a computationally very intense effort of the kind described in the bootstrapping exercise presented in Appendix C. Nevertheless, the levels of theory-‘experiment’ agreement, reflected by the magnitudes of objectives,  $\Psi$ , achieved by fitting either  $\mathbf{E}$  or  $\mathbf{EC}$  models to the d.c. cyclic voltammograms simulated for the  $\mathbf{E_{fr}C_{rev}}$  mechanism with  $k^f = k^b = 100 \text{ s}^{-1}$  are identical (Table 1) and achieve what most likely would be considered to be a ‘perfect’ fit in a heuristic form of data analysis (Fig. S2).

**Table 1.** Examples of parameters ( $E^0$ ,  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$ ) and objectives ( $\Psi$ ) recovered by Global Method (GM) and Nimrod/O (Nim) <sup>a</sup> from fitting different models to d.c. and a.c. voltammetric data simulated with an  $E_{fr}C_{rev}$  mechanism (equation 2) with  $E^0 = 0.000$  V;  $\alpha = 0.50$ ,  $k^0 = 10^3$  cm s<sup>-1</sup> and  $k^f = k^b = 100$  s<sup>-1</sup> with added noise (5% of the peak current).<sup>b</sup>

Mode	Model	$\pm E^0$ / V		$10^{-3} \cdot k^0$ / cm s <sup>-1</sup>		$\alpha$		$k^f$ / s <sup>-1</sup>		$k^b$ / s <sup>-1</sup>		$\Psi$	
		GM	Nim	GM	Nim	GM	Nim <sup>c</sup>	GM	Nim	GM	Nim	GM <sup>d</sup>	Nim <sup>a</sup>
d.c.	$E_{fr}$		0.016 $\pm 0.001$		n.a. <sup>e</sup>		n.a.		n.a.		n.a.		0.13
	$E_{fr}C_{rev}$		-0.004 $\pm 0.009$		n.a.		n.a.	500	572 $\pm 300$		493 $\pm 284$		0.12
	$E_{qr}C_{rev}$		-0.002 $\pm 0.011$		5.6 $\pm 3.4$		0.52 $\pm 0.07$		487 $\pm 316$		511 $\pm 289$		0.12
a.c.	$E_{fr}$	-0.011	0.007 $\pm 0.001$		n.a.		n.a.		n.a.		n.a.	8.8	0.26
	$E_{qr}$	-0.017	0.007 $\pm 0.000$	$6.5 \cdot 10^{-5}$	3.9 $\pm 3.1$	0.00	0.49 $\pm 0.07$		n.a.		n.a.	4.2	0.26
	$E_{fr}C_{rev}$	0.000	-0.012 $\pm 0.005$ (-0.001) <sup>f</sup>		n.a.		n.a.	115	678 $\pm 316$ (121) <sup>f</sup>	111	288 $\pm 87$ (114) <sup>f</sup>	4.2	0.098  (0.096) <sup>f</sup>
	$E_{qr}C_{rev}$	0.000	-0.011 $\pm 0.004$ (-0.004) <sup>f</sup>	$2.0 \cdot 10^{-3}$	4.5 $\pm 3.2$ (6.5) <sup>f</sup>	0.61	0.50 $\pm 0.08$ (0.56) <sup>f</sup>	98	595 $\pm 270$ (190) <sup>f</sup>	99	272 $\pm 73$ (146) <sup>f</sup>	4.2	0.098  (0.096) <sup>f</sup>

<sup>a</sup> Mean values and standard deviations of the parameters and objectives (calculated using equation 5 for d.c. component and 1<sup>st</sup> to 5<sup>th</sup> a.c. harmonic components) derived from 15 optimisation runs. <sup>b</sup> Other simulation parameters:  $c_A = 1.00$  mM,  $c_B = c_C = 0$  mM;  $D_A = D_B = D_C = 2.00 \cdot 10^{-5}$  cm<sup>2</sup> s<sup>-1</sup>;  $A = 0.0700$  cm<sup>2</sup>;  $T = 296$  K;  $R_u = 0$   $\Omega$ ;  $C_{dl} = 0$   $\mu$ F cm<sup>2</sup>;  $E_{start} = E_{final} = \pm 0.300$  V,  $E_{switch} = \mp 0.500$  V,  $\nu = 0.100$  V s<sup>-1</sup>, and for a.c. voltammetry,  $f = 9.00$  Hz,  $\Delta E = 0.080$  V. <sup>c</sup> Simulations are insensitive to variation in  $\alpha$ . The close proximity to 0.50 is an artefact of the data optimisation method employed. <sup>d</sup> Calculated using equation 4 and multiplied by  $10^7$ . <sup>e</sup> n.a. = not applicable. <sup>f</sup> Parameters in brackets were derived from the optimisation run with the lowest value of  $\Psi_{Nim}$ .



**Figure 1.** (a) Total current, (b) aperiodic component, (c) 2<sup>nd</sup> and (d) 5<sup>th</sup> a.c. harmonic components of an a.c. cyclic voltammogram ( $f = 9.00$  Hz;  $\Delta E = 0.080$  V;  $\nu = 0.100$  V s<sup>-1</sup>) simulated for an  $E_{fr}C_{rev}$  mechanism (equation 2,  $E$  as oxidation;  $k^0 = 10^3$  cm s<sup>-1</sup>,  $k^f = k^b = 100$  s<sup>-1</sup>) without (red) and with added noise (5% of the peak current) (black). Other simulation parameters are specified in Table 1. Currents are normalised to the electrode surface area. Dashed lines (----) indicate the time at which the direction of the d.c. potential ramp is reversed.

The higher kinetic sensitivity, particularly of the current magnitude available in a.c. voltammetry, allows more efficient analysis of the  $E_{fr}C_{rev}$  case and also allows a distinction to be made with the  $E_{fr}$  mechanism. False  $E_{fr}$  models are now rejectable after examination of results reported by both Nimrod/O and GM analysis on the basis of excessively large  $\Psi$  values as compared to those derived with the true  $E_{fr}C_{rev}$  scheme, although caution needs to be exercised in reaching this conclusion since fewer parameters need to be fitted in the  $E_{fr}$  model than in the  $E_{fr}C_{rev}$  case. The low a.c. frequency ( $f = 9$  Hz) employed (Fig. 1) does not allow quantification of the charge transfer kinetics with the process being essentially reversible ( $k^0 = 10^3$  cm s<sup>-1</sup>),<sup>8</sup> but is appropriate under some circumstances to recover an authentic  $E^0$  value for the  $E$  step and very close to correct  $k^f$  and  $k^b$  values for the  $C$  stage when either the total current is analysed by the GM or the a.c. harmonic content is assessed from the data optimisation runs that produce the

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2  
3 minimum value of  $\Psi_{\text{Nim}}$  ( $\Psi_{\text{min}}$ ) (Table 1). Use of a higher frequency also may be advantageous  
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5 (Appendix B). For the a.c. case, the level of theory-‘experiment’ that can be achieved by fitting  
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7 simulated data for the  $\text{E}_{\text{fr}}\text{C}_{\text{rev}}$  mechanism also can represent a situation that might be viewed as  
8  
9 corresponding to a ‘perfect’ fit in a heuristic form of data analysis (Fig. S3).  
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12  
13 The less successful outcome found with the Nimrod/O-assisted analysis of the filtered  
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15 components of the a.c. voltammograms are explained by the relatively greater interference from  
16  
17 5% noise leading to corrupted higher order a.c. harmonics (Fig. 1d). The 6<sup>th</sup> and higher order a.c.  
18  
19 harmonic components in the example considered in Table 1 are significantly masked by the  
20  
21 introduced noise and are therefore not useful for analysis. Nevertheless, when the correct  $\text{E}_{\text{fr}}\text{C}_{\text{rev}}$   
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23 model is used and recovered parameters are reported with  $\Psi_{\text{min}}$ , their values are close to the  
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25 expected ones (Table 1). However, these results could hardly be identified as the ‘correct  
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27 solution’ when only marginal differences are found with  $\Psi_{\text{min}}$  (0.096) and the average  $\Psi_{\text{Nim}}$  value  
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29 (0.098) calculated from 15 optimisation runs. Nevertheless, Nimrod/O-assisted data analysis of  
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31 the kind described above and using a.c. harmonics is able to discriminate unambiguously  
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33 between **E** and **EC** scenarios even under these highly adverse noisy conditions. Another merit of  
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35 parameter recovery achieved *via* analysis of the filtered a.c. components is unmistakable  
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37 identification of the presence of a fully reversible  $\text{E}_{\text{fr}}$  step. This is reflected in the data  
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39 optimisation exercises by the very large and highly variable  $k^0$  values recovered (Table 1) and  
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41 insensitivity of  $\Psi_{\text{Nim}}$  to  $\alpha$ .<sup>8</sup>  
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48 Results of the data optimisation analysis applied to  $\text{E}_{\text{qr}}\text{C}_{\text{rev}}$  and  $\text{E}_{\text{qr}}\text{C}_{\text{irrev}}$  mechanisms with  
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50  $k^0 = 10^{-2} \text{ cm s}^{-1}$  and slower homogeneous kinetics than  $k^{\text{f}}$  and  $k^{\text{b}}$  of  $100 \text{ s}^{-1}$  used above also  
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52 emphasise the superiority of the a.c. voltammetric method over the d.c. one for recovery of the  
53  
54 **EC** mechanism parameters (Tables 2 and 3). In these cases, the inappropriateness of the  $\text{E}_{\text{fr}}$   
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mechanism is readily deduced by visual inspection of both d.c. and a.c. voltammograms (Figs. S4 and S5), which reveal profiles that are clearly inconsistent with this scenario.

**Table 2.** Parameters ( $E^0$ ,  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$ ) and objectives ( $\Psi$ ) recovered by the Global Method (GM) and Nimrod/O (Nim) from fitting  $\mathbf{E}_{qr}\mathbf{C}_{rev}$  model to d.c. and a.c. voltammetric data simulated for an EC process (equation 2) with  $E^0 = 0.000$  V;  $\alpha = 0.50$ ,  $k^0 = 1.0 \cdot 10^{-2}$  cm s<sup>-1</sup>,  $k^f = 10$  s<sup>-1</sup> and  $k^b = 1.0$  s<sup>-1</sup> with added noise (5% of the peak current).<sup>a</sup>

Mode	$\pm E^0$ / V		$10^2 \cdot k^0$ / cm s <sup>-1</sup>		$\alpha$		$k^f$ / s <sup>-1</sup>		$k^b$ / s <sup>-1</sup>		$\Psi$	
	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM <sup>c</sup>	Nim <sup>b</sup>
d.c.	0.004	-0.011 ±0.006	0.89	1.3 ±0.2	0.49	0.51 ±0.04	7.0	30 ±13	0.83	1.7 ±0.4	0.12	0.15
a.c.	0.000	0.001 ±0.005	0.99	1.0 ±0.1	0.50	0.50 ±0.03	9.9	10 ±1.2	0.99	1.0 ±0.0	1.0	0.11

<sup>a</sup> Other simulation parameters are as defined in Table 1. <sup>b</sup> Mean values and standard deviations of parameters and objectives (calculated using equation 5 for the d.c. case and 1<sup>st</sup> to 3<sup>rd</sup> harmonics for the a.c. case) derived from 15 optimisation runs. <sup>c</sup> calculated using equation 4 and multiplied by 10<sup>7</sup>.

GM and Nimrod/O assisted fitting of the  $\mathbf{E}_{qr}\mathbf{C}_{rev}$  model to the a.c. voltammetric data simulated for equation 2 with quasi-reversible  $\mathbf{E}_{qr}$  ( $k^0 = 1.0 \cdot 10^{-2}$  cm s<sup>-1</sup>,  $\alpha = 0.50$ ) and  $\mathbf{C}_{rev}$  with  $K = 10$  ( $k^f = 10$  s<sup>-1</sup>,  $k^b = 1.0$  s<sup>-1</sup>) allows unmistakably close to correct recovery of the input values of  $E^0$ ,  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$  from a multi-parameter fit (Table 2) when a.c data are analysed. In this exercise, the combination of parameter values were chosen so that the d.c. voltammetry lies just outside the problematic regime (see Appendix B in Supporting Information). When the C step is irreversible ( $k^f = 10$  s<sup>-1</sup>,  $k^b = 0$  s<sup>-1</sup>), while neither of the automated parameter recovery methods are able to distinguish between the incorrect  $\mathbf{E}_{qr}\mathbf{C}_{rev}$  and correct  $\mathbf{E}_{qr}\mathbf{C}_{irrev}$  models on the basis of  $\Psi$  values, it is noted that  $k^b$  derived in the former case is very low relative to  $k^f$  (Table 3), especially when total current data are analysed *via* the GM. In the context of a.c. voltammetry, notable

differences in the values of the parameters recovered by the GM and Nimrod/O again most probably reflect advantages provided by parameter recovery from the total current when the higher order a.c. harmonics currents are small and hence significantly distorted by the 5% noise.

**Table 3.** Parameters ( $E^0$ ,  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$ ) and objectives ( $\Psi$ ) recovered by Global Method (GM) and Nimrod/O (Nim) from fitting different models to d.c. and a.c. voltammetric data simulated for an  $E_{qr}C_{irrev}$  mechanism (equation 2) with  $E^0 = 0.000$  V;  $\alpha = 0.50$ ,  $k^0 = 1.0 \cdot 10^{-2}$  cm s<sup>-1</sup>,  $k^f = 10$  s<sup>-1</sup> and  $k^b = 0$  s<sup>-1</sup> with added noise (5% of the peak current).<sup>a</sup>

Model	$\pm E^0$ / V		$10^2 \cdot k^0$ / cm s <sup>-1</sup>		$\alpha$		$k^f$ / s <sup>-1</sup>		$10^2 \cdot k^b$ / s <sup>-1</sup>		$\Psi$	
	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM	Nim <sup>b</sup>	GM <sup>c</sup>	Nim <sup>b</sup>
$E_{qr}C_{rev}$	-0.003	-0.012 $\pm 0.008$	0.94	1.3 $\pm 0.00$	0.49	0.51 $\pm 0.03$	8.2	32 $\pm 14$	0.24	0.9 $\pm 2.0$	0.12	0.15
$E_{qr}C_{irrev}$	0.002	-0.008 $\pm 0.009$	0.92	2.1 $\pm 2.6$	0.49	0.50 $\pm 0.04$	9.6	23 $\pm 16$	n.a. <sup>d</sup>		0.12	0.15
$E_{qr}C_{rev}$	-0.001	0.000 $\pm 0.001$	1.0	0.99 $\pm 0.02$	0.50	0.51 $\pm 0.01$	11	9.8 $\pm 0.2$	0.11	2.1 $\pm 2.3$	0.99	0.11
$E_{qr}C_{irrev}$	0.001	0.000 $\pm 0.001$	0.99	0.99 $\pm 0.02$	0.50	0.51 $\pm 0.01$	9.4	9.8 $\pm 0.1$	n.a. <sup>d</sup>		0.99	0.11

<sup>a</sup> Other simulation parameters are as defined in Table 1. <sup>b</sup> Mean values of parameters and objectives (calculated using equation 5 for d.c. component and 1<sup>st</sup> to 3<sup>rd</sup> a.c. harmonic components) derived from 15 optimisation runs. <sup>c</sup> Calculated using equation 4 and multiplied by  $10^7$ . <sup>d</sup> n.a. = not applicable.

The above exercise is artificial in the sense that the added noise is random whereas systematic error also will be present in real experimental data. Furthermore, the model used is perfect whereas in practice background faradaic processes and radial diffusion for example may also be present but be neglected when using a model based on purely capacitive background and linear diffusion, respectively. Systematic errors in values of uncompensated resistance, electrode area and concentration also will arise in a real experiment vs. theory comparison exercise. However,

in the context of purely random noise applied to a given model, if enough data optimisation runs are undertaken, then the use of computationally intensive bootstrapping types of methods can be expected to improve the fidelity of parameter recovery to the point of achieving a near perfect outcome. Details of bootstrapping exercises based on 1000 GM data optimisation runs with 5% random noise are provided in Appendix C (Supporting Information) for a series of scenarios relevant to Tables 1-3. In particular, it can be noted from examination of results in Table S1 that the average of recovered parameter values are now very close to known input values in all cases when the correct EC model is applied. However, variability of recovered  $k^f$  and  $k^b$  values from individual runs for the  $E_{fr}C_{rev}$  case under ‘stiff’ conditions is substantial as displayed in Fig. S6 and also readily apparent from inspection of the magnitude of the standard deviation values present in Table S1.

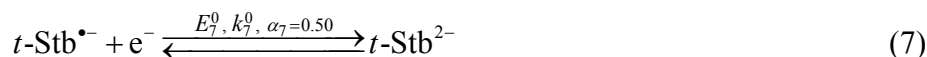
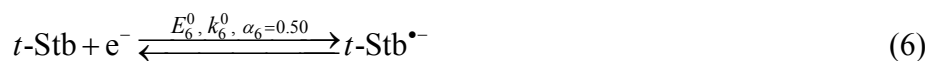
In summary, a.c. voltammetry is shown to be advantageous relative to the d.c. version for thermodynamic and kinetic parameter recovery in the presence of random noise for mechanisms involving electron transfer coupled to a chemical reaction. In particular, with 5% added noise, reliable estimates of  $E^0$ ,  $k^0$ ,  $\alpha$ ,  $k^f$  and  $k^b$  for the  $E_{qr}C_{rev}$  mechanism are available *via* application of data optimisation methods, provided that the kinetics are not too fast or too slow, relevant to the experiment timescale ( $\nu$  in d.c. method and  $f$  for a.c. technique).

**Analysis of experimental data: addressing the problematic regime arising from a very fast  $k^f$  value.** In experimental studies, fast kinetics associated with a chemical reaction coupled to the charge transfer process is the regime most likely to be encountered where the prospect for recovery of ‘true’ parameter values and even the correct mechanism is most likely to be problematic. Random noise can be accommodated by data optimisation as described above if sufficient computer time is employed (Appendix C). However, in a practical problem, the model

used in simulations will not be perfect as systematic error, radial diffusion (if model based on planar diffusion is used), background current (faradaic and non-faradaic) and  $iR_u$  drop will be imperfectly mimicked.

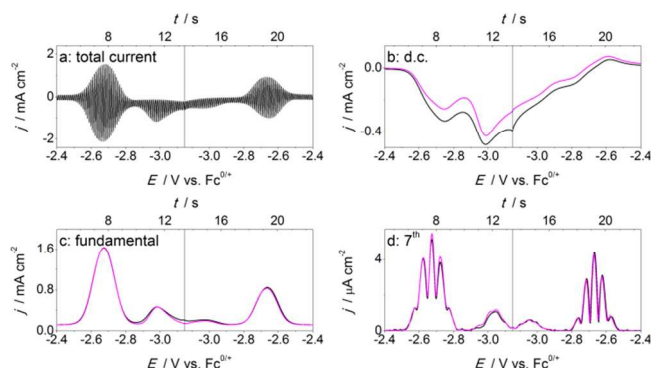
The dilemma of how to undertake a valid multi-parameter recovery exercise in a ‘stiff’ problem is encountered in the voltammetric reduction of *trans*-stilbene (*t*-Stb) in acetonitrile (0.10 M Bu<sub>4</sub>NPF<sub>6</sub>) (equations 6-8).<sup>21</sup> In this solvent (electrolyte) and using d.c. cyclic voltammetry at a glassy carbon (GC) macrodisk electrode with a scan rate of 0.10 V s<sup>-1</sup>, *t*-Stb initially undergoes a close to reversible one electron reduction to its anion radical (*t*-Stb<sup>•-</sup>) (reaction 6). Subsequently, in a second well-resolved process at more negative potentials, *t*-Stb<sup>•-</sup> is reduced to the dianion (*t*-Stb<sup>2-</sup>) (reaction 7), which in acetonitrile undergoes very fast and irreversible protonation to produce bibenzyl (StbH<sub>2</sub>) *via* a pseudo first order chemical reaction (reaction 8) with a value of  $k^f$  well above the maximum 100 s<sup>-1</sup> value regarded as recoverable in the simulated examples presented above with a scan rate of 0.10 V s<sup>-1</sup> and 5% added noise. It might be anticipated that use of much faster d.c. scan rate would allow chemical reversibility to be achieved and  $k^f$  calculated from data obtained in a suitable scan rate regime. However, as shown in Appendix D, the impact of the diffusion based  $I \sim t^{-1/2}$  tail of the initial electron transfer step on the second process, increased background current from double-layer capacitance, overlap with the solvent limit reduction processes in the very negative potential region where the process of interest occurs and significant  $iR_u$  drop at fast rates, all combine to preclude any level of chemical reversibility being achieved. Thus, a scan rate regime where the electrode kinetics can be estimated reliably by conventional approaches described in the introduction is not available nor can detailed modelling fully mimic the experiment. Appendix D also shows why the second *trans*-stilbene reduction process under slow scan rate near steady

state conditions in d.c. voltammetry at a microdisk electrode and rotating disk electrode voltammetry at fast rotation rates also are not suitable for quantitative analysis.



Since application of the d.c. methods has significant limitations, the question arises as to whether the a.c. method can be employed for quantitative studies of the reaction in equation 7 and under what circumstances. The a.c. voltammetry for reduction of *trans*-stilbene is provided in Fig. 2 with a slow d.c. scan rate (0.082 V s<sup>-1</sup>), and with a 9 Hz sinusoidal perturbation with an amplitude of 0.080 V superimposed onto the d.c. ramp. As anticipated, a complete multi-parameter fit of  $R_u$ ,  $C_{dl}$  and electrode kinetics as needed to recover all parameters relevant to equations 6-8 was found to generate unreliable and not always chemically sensible parameter values. However, the Fourier transform version with access to harmonics, as shown in Figure 4, greatly assists the modelling for the following reasons: background arc faradaic current from solvent reduction are absent (kinetics are very slow); no overlap of arc current from the first reduction step occurs; the background charging current is absent in higher harmonics, but well enough defined in fundamental harmonic to be modelled; mains frequency and other noise is filtered out. Additionally, contributions from radial diffusion are less than in d.c. methods so errors from this source in the model are minimised. The probability of having a reliable a.c. model for use in simulations, after removal or minimisation of some of the complications present in the d.c. voltammetry is helpful, but still not enough to allow quantitative electrode kinetic

analysis to be achieved. This requires further simplification of the number of parameters to be simulated.



**Figure 2.** Total current (a), aperiodic component (b), 1<sup>st</sup> (c) and 7<sup>th</sup> a.c. harmonic components (d) of an experimental a.c. cyclic voltammogram ( $f = 9.02$  Hz) obtained for reduction of 0.99 mM *trans*-stilbene in  $\text{CH}_3\text{CN}$  (0.10 M  $\text{Bu}_4\text{NPF}_6$ ) at a glassy carbon electrode (black) and simulated data with  $\Psi_{\text{Nim}} = 0.17$  (calculated for 1<sup>st</sup> to 8<sup>th</sup> harmonics using equation 5) (magenta). Note that potentials in this figure are referred to the reversible potential of the ferrocene<sup>0/+</sup> process measured in the same solution. Other parameters are as in Table 4.

The complete irreversibility of the protonation reaction and other features discussed below allows a decrease to three in the number of parameters that need to be quantified in the data optimisation exercise. First of all,  $k^b$  can be neglected and set to zero or any sufficiently small value. The mechanism can therefore be modelled as an  $\text{E}_{\text{qr}}\text{E}_{\text{qr}}\text{C}_{\text{irrev}}$  reaction. The significant separation in  $E^0$  values for reactions 6 and 7 also allows the first reduction step to be studied in isolation (Fig. 2)<sup>21,22</sup> in a separate exercise as an  $\text{E}_{\text{qr}}$  process, which allows independent determination and then inclusion of the values of  $D$  for *trans*-stilbene ( $D_{\text{t-Stb}}$ ),  $E^0_6$ ,  $k^0_6$  and  $\alpha_6$  (0.50 assumed) as known parameters (Table 4) allowing an  $\text{E}_{\text{qr}}\text{C}_{\text{irrev}}$  model to be used to describe the second process, with the first process effectively available for use as an internal standard. A reliable  $R_u$  parameter can be derived from electrochemical impedance analysis and

$C_{dl}$  can be assumed to be potential independent.<sup>21</sup> To provide another reasonable simplification,  $\alpha_7$  was also set equal to 0.50. Nevertheless, even with the advantage of being able to restrict the number of unknown variables to a maximum of three *via* the above strategy, the parameter recovery exercise using data optimisation remains ‘stiff’ even under a.c. conditions.

Significant interference of the background current detected in d.c. voltammograms for reduction of *t*-Stb at very negative potentials near to the solvent limit (Fig. 2)<sup>22</sup> also restricts quantitative use of the aperiodic d.c. component in the FT a.c. voltammetry and also hinders the analysis of the total a.c. current format, which includes a d.c. contribution. However, the resolved a.c. harmonics are very insensitive to the background process at potentials where reactions 7 and 8 occur and eight well defined a.c. harmonics are available for data analysis. On this basis, it was found that if an adequate number of the parameter optimisation runs with the Nimrod/O algorithm were employed, then it was possible to simultaneously recover plausible  $E^0_7$ ,  $k^0_7$  and  $k^f_8$  values from analysis of all experimentally available a.c. harmonic components (fundamental to eighth) for reactions 6-8 at two frequencies ( $f = 9$  and 72 Hz) (Table 4). Measured random noise levels were 0.1% at 9 Hz and 0.05% at 72 Hz and hence well below that of 5% used in the above simulated data analysis (Fig. S1).

**Table 4.**  $E^0_7$  and  $k^0_7$  (reaction 7) and  $k^f_8$  (reaction 8) and corresponding objective ( $\Psi_{\text{Nim}}$ ) recovered by Nimrod/O<sup>a</sup> from fitting the simulations based on reactions 7-8<sup>a</sup> to harmonics of FT a.c. cyclic voltammograms ( $f = 9$  or  $72$  Hz) for the second process in the reduction of  $0.99$  mM *trans*-stilbene in  $\text{CH}_3\text{CN}$  ( $0.10$  M  $\text{Bu}_4\text{NPF}_6$ ).<sup>b</sup>

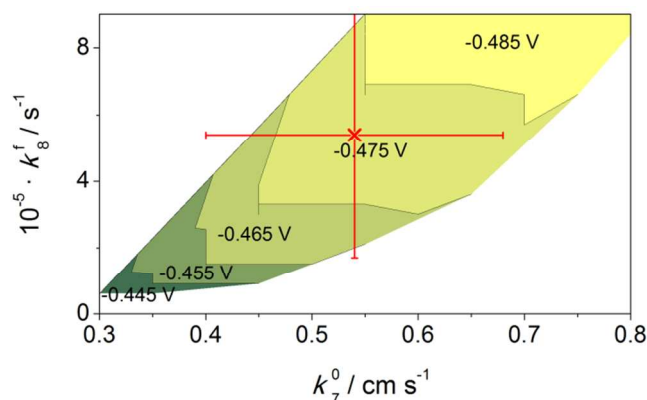
$f / \text{Hz}$	$E^0_7 / \text{V vs. } E^0_6$	$k^0_7 / \text{cm s}^{-1}$	$10^{-4} \cdot k^f_8 / \text{s}^{-1}$	$\Psi_{\text{Nim}}^c$
9	-0.476 $\pm 0.014$	0.54 $\pm 0.14$	54 $\pm 37$	0.13
9	-0.440 <sup>d</sup>	0.26 $\pm 0.00$	3.6 $\pm 0.06$	0.17
72	-0.492 $\pm 0.009$	0.51 $\pm 0.08$	56 $\pm 34$	0.21

<sup>a</sup> Mean values and standard deviations of the parameters derived from 30 ( $f = 9$  Hz) and 14 ( $f = 72$  Hz) optimisation runs for 1<sup>st</sup> to 8<sup>th</sup> a.c. harmonic components. <sup>b</sup> Other experimental parameters used in simulations with known values were:  $k^b_8 = 1.0 \cdot 10^{-20} \text{ s}^{-1}$ ;  $E^0_6 = 0.000 \text{ V}$ ;  $k^0_6 = 1.5 \text{ cm s}^{-1}$ ;  $\alpha_6 = \alpha_7 = 0.50$ ;  $D_{t\text{-Stb}} = 2.2 \cdot 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ ,  $D_{t\text{-Stb}(\bullet\cdot)} = D_{t\text{-Stb}(2\cdot)} = 1.9 \cdot 10^{-5} \text{ cm}^2 \text{ s}^{-1}$ ;  $A = 0.067 \text{ cm}^2$ ;  $T = 295 \text{ K}$ ;  $R_u = 62 \text{ }\Omega$ ;  $C_{\text{dl}} = 28 \text{ }\mu\text{F cm}^{-2}$ ;  $E_{\text{start}} = E_{\text{final}} = 0.625 \text{ V vs. } E^0_6$ ,  $E_{\text{switch}} = -0.475 \text{ V vs. } E^0_6$ ,  $v = 0.08196 \text{ V s}^{-1}$ ,  $f = 9.02$  or  $72.0 \text{ Hz}$ ,  $\Delta E = 0.080 \text{ V}$ . Further experimental details are available in Refs.<sup>21,22</sup>. <sup>c</sup> Calculated using equation 5 for 1<sup>st</sup> to 8<sup>th</sup> a.c. harmonic components. <sup>d</sup>  $E^0_7$  was fixed as  $-0.440 \text{ V vs. } E^0_6$  and only  $k^0_7$  and  $k^f_8$  were optimised by Nimrod/O.

No reliable quantitative estimation of  $E^0_7$ ,  $k^0_7$  and  $k^f_8$  was achieved when the parameter recovery *via* experiment-theory comparisons was attempted heuristically in Ref.<sup>21</sup> In contrast, Nimrod/O assisted data analysis allows recovery of plausible values of  $E^0_7$  and  $k^0_7$  (Table 4). Uncertainty in recovered  $k^f_8$  is substantial, though incomparably better than the 4 orders of magnitude uncertainty reported when the same data were analysed heuristically.<sup>21</sup> The fact that the  $E^0_7$ ,  $k^0_7$  and  $k^f_8$  values recovered *via* use of the Nimrod/O-assisted parameter optimisation do not demonstrate any significant frequency dependence (Table 4), adds confidence in the credibility of the derived values.



Another form of data analysis useful in the present context is the Nimrod/G parameter sweep tool,<sup>8,9</sup> that allows comparisons of the objectives to be made on the basis of different combinations of  $E_7^0$ ,  $k_7^0$  and  $k_8^f$ . Overall, 9920 combinations of these parameters employing search spaces of  $-0.5 < E_7^0 / \text{V} \text{ vs. } E_6^0 < -0.4$ ,  $0.05 < k_7^0 / \text{cm s}^{-1} < 1.0$  and  $10^3 < k_8^f / \text{s}^{-1} < 10^5$  were used to produce simulated a.c. voltammograms, which were then compared to the experimental data in terms of  $\Psi_{\text{Nim}}$  for the 1<sup>st</sup> to 8<sup>th</sup> harmonic components. The complexity associated with displaying the results of this analysis of the EC process in the form of a four-dimensional  $[\Psi, E_7^0, k_7^0, k_8^f]$  plot is overcome by provision of contour map (Fig. 3) that reveals the dependence of  $E_7^0$  on combinations of  $k_7^0$  and  $k_8^f$ , thereby allowing ‘the best’ experiment-theory agreement combinations to be visually identified. Differently coloured sections in Fig. 3 show the optimal values  $E_7^0$  for a given combination of  $k_7^0$  and  $k_8^f$  that allow the simulated voltammogram to mimic the experiment at the level of accuracy corresponding to  $\Psi$  below 0.17 ( $\Psi_{\text{min}}$  was 0.13 in the parameter optimisation exercise). The choice of  $\Psi = 0.17$  as a measure of ‘the best fit’ reflects an estimated best possible plausible accuracy of parameter recovery available *via* the heuristic approach when implemented by the authors of reference.<sup>21</sup> However, this heuristically based limit could significantly differ when implemented by other scientists in other laboratories, thus emphasising the disadvantage of heuristic approaches in voltammetric data analysis and the high risk of laboratory-to-laboratory irreproducibility. As an example of potential variability in reporting parameters, Fig. S5 shows the data from Fig. 3 but with  $\Psi = 0.15$  and 0.14 used as the criteria for the ‘best fit’.



**Figure 3.** Correlation of the ‘optimal’ values of  $k_7^0$  and  $k_8^f$  providing the lowest objective ( $\Psi_{\text{Nim}} < 0.17$ ) for fitting the simulation based on reactions 6-8 to the 1<sup>st</sup> to 8<sup>th</sup> harmonic components of the experimental a.c. cyclic voltammogram for the second reduction step of 0.99 mM *trans*-stilbene in CH<sub>3</sub>CN (0.10 M Bu<sub>4</sub>NPF<sub>6</sub>) derived from the Nimrod/G parameter sweep analysis on  $\Psi$  as a function of  $E_7^0$ ,  $k_7^0$  and  $k_8^f$ . Values and coloured sections show corresponding ‘optimal’  $E_7^0$  values.  $k_7^0$  and  $k_8^f$  values outside the coloured regions correspond to  $\Psi \gg 0.17$ . Other experimental and simulation parameters are as in Table 4. The data point labelled with a cross (x) and associated confidence intervals show the  $[k_7^0, k_8^f]$  combination and standard deviations derived from the Nimrod/O optimisation studies (Table 4).

The outcomes of the EC mechanism parameter optimisation (Table 4) and sweep analysis (Fig. 3) vividly demonstrate the limitations in reports of parameters derived from voltammetric experiment-simulation comparisons of reactions involving electron transfer and a fast coupled chemical reaction. Despite some success for the *t*-Stb case, substantial uncertainties remain present in values derived from the data optimisation exercise.

A remedy to minimise the large uncertainty in parameters emerging from a 3 parameter fitting exercise when  $k^f$  is fast, is to try to determine independently one of the  $E_7^0$ ,  $k_7^0$  or  $k_8^f$  parameters and then apply data optimisation methodology to the remaining two. This strategy facilitates

conversion of the remaining two unknowns towards unique values. One possibility sometimes available is to outrun the  $C_{\text{irrev}}$  step by use of very high  $\nu$  (d.c. method) or  $f$  (a.c. method) and hence simplify the process so it closely approximates an **E** reaction thereby allowing reliable estimates of  $E^0_7$  and sometimes  $k^0_7$  to become available. In the *t*-Stb case, this was not feasible experimentally as shown in Appendix D. In d.c. voltammetry, the large background current masks the required faradaic current at high  $\nu$ . In the a.c. method, the results of simulations suggested that experiments would have to be undertaken at  $f$  above 1 kHz. This would result in significant ohmic losses (with macrodisk electrodes) leading to significant distortion and insufficiently fast kinetics for the **E<sub>qr</sub>** step, thereby precluding attainment of an extensive series of a.c. harmonics. In the case being considered, inhibition of the  $C_{\text{irrev}}$  step *via* change of solvent is a viable approach. As demonstrated previously,<sup>21,22</sup> the second step in the reduction of *t*-Stb (reaction 7) is chemically reversible in highly aprotic ionic liquids, which allows the direct determination of  $E^0_7$  as -0.44 V *vs.*  $E^0_6$ . The assumption can be made that the difference of 0.44 V in  $E^0$  values remains valid in the CH<sub>3</sub>CN (0.10 M Bu<sub>4</sub>NPF<sub>6</sub>) medium, although with provision that ion-pairing which contributes to the  $E^0_7$  and  $E^0_6$  values<sup>22</sup> are similar in acetonitrile and ionic liquid environments. However, somewhat reassuringly, it is noted that a similar  $E^0_7$  *vs.*  $E^0_6$  difference to that reported in Ref.<sup>21</sup> has been demonstrated in low-temperature voltammetric studies in other solvents.<sup>26,27</sup>

Inclusion of an  $E^0_7$  value of -0.44 V as a known parameter in the Nimrod/O assisted optimisation analysis leads to recovery of a much narrower range of values of  $k^0_7$  and  $k^f_8$  (Table 4), which are in reasonable agreement from those obtained by a direct 3 parameter fit. Importantly, the  $\Psi$  value of 0.17 with optimisation of 2 unknowns is higher than  $\Psi_{\text{min}} = 0.13$  produced by Nimrod/O when optimisation was undertaken with 3 unknown parameters, *viz.*  $E^0_7$ ,

$k_7^0$  and  $k_8^f$ . However, also noteworthy is that the difference in fits with  $\Psi = 0.17$  and  $0.13$  are barely distinguishable when graphical outputs of experiment and simulation are examined visually. This observation emphasises that the use of the lowest value of the objective as a guarantee that the best solution has been found is fraught with risk, particularly when the experimental data reside in a ‘kinetically unfavourable’ regime and the numbers of parameters used in the compared models differ. Attention to the risks of model over-parameterisation has been drawn in the analysis of **E** processes under conditions that approach the reversible limit.<sup>8,28</sup> The risk is likely to be even higher for the more parameter-sensitive **EC** case, for example, in the fast electron-transfer and reversible homogeneous kinetics regimes.

In summary, use of data optimisation methods significantly improves the reliability of parameter estimation, but the outcome still depends on how data optimisation is implemented. In the *trans*-stilbene case, the use of a.c. voltammetry and data optimisation methods has allowed significant progress to be made in quantifying the values of parameters needed to describe the **E<sub>qr</sub>C<sub>irrev</sub>** reaction relative to the use of the heuristic methods employed in the initial study.<sup>21</sup>

Future work needs to generate different model outcomes in terms of relative probabilities as it is clear that comparisons of magnitudes of objectives for data optimisation do not give the complete picture. To achieve this goal, the use of Bayesian inference<sup>29</sup> or other more sophisticated forms of data analysis may be required to decide if a model is actually identifiable on the basis of data optimisation results, as pointed out by Vikhansky *et al.*<sup>28</sup> in their studies on the simple **E** case.

## CONCLUSION

Analysis of the simulated and experimental data for the **EC** mechanism demonstrates a range of advantages provided by the use of a.c. voltammetry over the d.c. method. Implementation of

data optimisation methods needed to assist in parameter estimation also improves the reliability of reporting thermodynamic and kinetic parameters associated with the **E** and **C** steps. However, notwithstanding significant advances in experimental and data processing techniques available for application in voltammetric analysis,<sup>9,13</sup> reliable recovery of the kinetic and thermodynamic parameters for an electron transfer reaction coupled to a fast chemical process remains a stiff problem.

## ASSOCIATED CONTENT

**Supporting Information.** Appendices A, B, C and D. Fig. S1 noise magnitude distribution. Figs. S2 and S3 comparing input d.c. and a.c. voltammetric data for the  $E_{fr}C_{rev}$  mechanism with simulations based on the parameters derived by fitting the  $E_{qr}C_{rev}$  model to these data. Figs. S4 and S5 showing simulated a.c. voltammograms relevant to Tables 2 and 3. Fig. S6 showing scatter plot of  $k^f$  and  $k^b$  recovered from the bootstrapping experiments. Tables S1 and S2 showing parameters and their standard deviations recovered from the bootstrapping experiments. Figs. S7 showing the data from Fig. 2 as a function of  $\Psi$ . This material is available free of charge via the Internet at <http://pubs.acs.org>.

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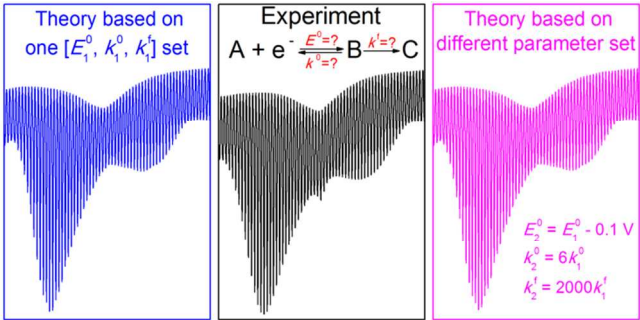
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Add Table of Contents Diagram



Which recovered parameters are correct?