Flowcharts to aid student comprehension of Nernst equation calculations

Angus M Brown[1,2]

[1]School of Life Sciences
University of Nottingham
Nottingham, NG7 2UH
UK

[2]Department of Neurology
University of Washington
Seattle, WA 98195
USA

Running Head: Nernst equation flowcharts

Corresponding author:
Dr Angus M Brown
School of Life Sciences
Queens Medical Centre
University of Nottingham
Nottingham, NG7 2UH, UK
Email: ambrown@nottingham.ac.uk

The ability to understand calculations involving the Nernst equation is a fundamental skill expected of all students studying excitable membranes. The typical scenario encountered by students involves an intracellular compartment separated from the extracellular fluid by a semi-permeable membrane (7). Under these conditions the Nernst equation can be expressed as:

$$E_X = \frac{RT}{zF} \ln \frac{[X]_o}{[X]_i} = \frac{61.5}{z} \log_{10} \frac{[X]_o}{[X]_i}$$

where E_X is the reversal potential, $[X]_o$ and $[X]_i$ are the extracellular and intracellular ion concentrations, respectively, z is the valence of the ion, and R, T and F have their usual meanings (7), initially reducing to the factor 26.7 mV at 37°C, then to 61.5 mV if $\log_{10}$ rather than ln is used, since $\log_{10}x = \ln x/\ln 10$. The equation and its utility in determining membrane potential is considered sufficiently important to justify dedicated chapters in textbooks (2, 8, 11, 12), and has been the subject of numerous articles in this (3-6, 9, 10, 13, 14, 16) and other journals (1, 15). Although the Nernst equation contains only 3 parameters, it is the cause of much student anguish, an issue I attempted to address in a recent publication regarding the logarithmic transformation that lies at the heart of the Nernst equation (13). Reflecting on that publication whilst teaching the topic to current 2nd year undergraduate neuroscience students prompted me to develop a flowchart to help students understand the logical sequence of steps that is required to satisfactorily implement calculations involving the Nernst equation. This chart can be used as a template to calculate any of the three parameters in the Nernst equation, providing the two other parameters are known. Thus, when $[X]_o$ and $[X]_i$

are known E_X can be calculated, and $[X]_o$ or $[X]_i$ can be calculated if E_X and the other compartmental ion concentration are known.

The flowchart, illustrated in Fig 1, requires as an initial step identifying the valence of the ion under investigation, followed by selection of the parameter to be calculated (E_X or $[X]_{o/i}$), which dictates the direction of flow. For the sake of clarity I have assumed that all calculations are carried out at 37°C. If we assume that E_X is the unknown parameter and $[X]_o$ and $[X]_i$ are known (left branch of the chart), the factor 61.5 mV must be modified according to the ions valence (i). The ratio of $[X]_o$ and $[X]_i$ is calculated (ii), the result of which is then logarithmically transformed (iii). It is then a simple matter of multiplying the result of steps (i) and (iii) to return the value for E_X (iv). This procedure works for anions and cations of any valence. The alternate calculation initially appears more complex since E_X and the ion concentration in only one compartment are known (right branch of the chart). This calculation requires rearrangement of the standard form in which the Nernst equation is usually expressed (see above), such that the ratio of $[X]_o/[X]_i$ is isolated on one side of the equation. E_X is then divided by the factor 61.5 scaled according to the valence of the ion (v), then the ratio of $[X]_o$ and $[X]_i$ that yields E_X forms the exponent of the base 10 (vi), since $\log_{10}x = a$ is equivalent to $10^a = x$. Retaining natural logarithms in the Nernst equation has two consequences in our scheme, requiring the factor 61.5 mV be divided by ln 10 to revert to 26.7 mV (see above), and transforming step (vi) to $e^{(v)}$, since $\ln x = a$ is equivalent to $e^a = x$. Whether $[X]_o$ or $[X]_i$ is the unknown quantity (vii) determines the subsequent scaling of the known ion concentration (viii) by the result calculated in (vi). When teaching students calculations involving base 10 logs I have found that maintaining an order of magnitude difference between $[X]_o$ and $[X]_i$ e.g. 20 mM and 200 mM, simplifies the arithmetic to the extent that calculators are not required.

A flowchart that allows investigation of the effect of temperature on E_X is illustrated in Fig 2. As above the initial stage is to identify the valence of the ion, followed by rearrangement of the equation to isolate T from the other constants (i). Sequential solving of R/zF (ii), calculating the ratio of $[X]_o/[X]_i$ (iii), logarithmically transforming this ratio (iv), then multiplying by (ii), produces a quantity that when multiplied by the desired temperature allows the calculation of E_X as a factor of temperature (v).

In conclusion, I suggest that these templates be used in conjunction with recently published articles in this journal that describe the concept of the Nernst equation (3), logarithmic transformation as applied to the Nernst equation (13) and the direction of ion flow that occurs when Ex is not equal to Em (5).

Figure Legends

Figure 1

The template, which follows conventional flowchart symbols, illustrates the sequence of steps and decisions required to complete the data flow process. The Roman numerals in parentheses represent the individual steps in the process, which are used to calculate any of the three parameters in the Nernst equation if the two other parameters are known. The equations, contained within the dotted boxes, are placed underneath the corresponding steps, and denote progress of the calculation. The parameters in the equation are replaced by the relevant Roman numerals upon sequential completion of the appropriate step. A $\log_{10}$ conversion scale is included to facilitate steps iii and vi.

Figure 2

A template for investigating the effect of temperature on E_X. The sequential steps are completed in the manner described for Figure 1.

Acknowledgement

I am grateful to the current cohort of 2nd Neuroscience students at the University of Nottingham whose insightful comments precipitated this paper.

References

1. **Barry PH.** Membrane potential simulation program for IBM-PC-compatible equipment for physiology and biology students. *Am J Physiol* 259: S15-23, 1990. doi: 10.1152/advances.1990.259.6.S15
2. **Bear MF, Connors BW, Paradiso MA.** The Neuronal Membrane at Rest.In: *Neuroscience: Exploring the Brain*, eds Bear MF, Connors BW, & Paradiso MA (Wolters Kluwer, Philadelphia), 4th Ed, pp 55-80, 2016
3. **Cardozo D.** An intuitive approach to understanding the resting membrane potential. *Adv Physiol Educ* 40: 543-547, 2016. doi: 10.1152/advan.00049.2016
4. **Cardozo DL.** A model for understanding membrane potential using springs. *Adv Physiol Educ* 29: 204-207, 2005. doi: 10.1152/advan.00067.2004
5. **Crowther GJ.** Which way do the ions go? A graph-drawing exercise for understanding electrochemical gradients. *Adv Physiol Educ* 41: 556-559, 2017. doi: 10.1152/advan.00111.2017
6. **Dwyer TM, Fleming J, Randall JE, Coleman TG.** Teaching physiology and the World Wide Web: Electrochemistry and electrophysiology on the Internet. *Adv Physiol Educ* 18: S2-S13, 1997. doi:
7. **Hille B.** *Ion Channels of Excitable Membranes* (Sinauer Associates Inc., Sunderland, MA, USA), 2001
8. **Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ.** Membrane Potential and the Passive Electrical Properties of the Neuron.In: *Principles of Neural Science*, eds Kandel ER, Schwartz JH,

Jessell TM, Siegelbaum SA, & Hudspeth AJ (McGraw Hill, New York), Fifth Ed, pp 126-147, 2013

9. **Milanick M.** Changes of membrane potential demonstrated by changes in solution color. *Adv Physiol Educ* 33: 230-230, 2009. doi: 10.1152/advan.00052.2009

10. **Moran WM, Denton J, Wilson K, Williams M, Runge SW.** A simple, inexpensive method for teaching how membrane potentials are generated. *Adv Physiol Educ* 22: S51-S59, 1999. doi:

11. **Nicholls JG, Martin AR, Fuchs PA, Brown DA, Diamond ME, Weisblat DA.** Ionic Basis of the Resting Potential.In: *From Neuron to Brain*, eds Nicholls JG, Martin AR, Fuchs PA, Brown DA, Diamond ME, & Weisblat DA (Sinauer Associates Inc, Sunderland, MA), Fifth Ed, pp 99-128, 2012

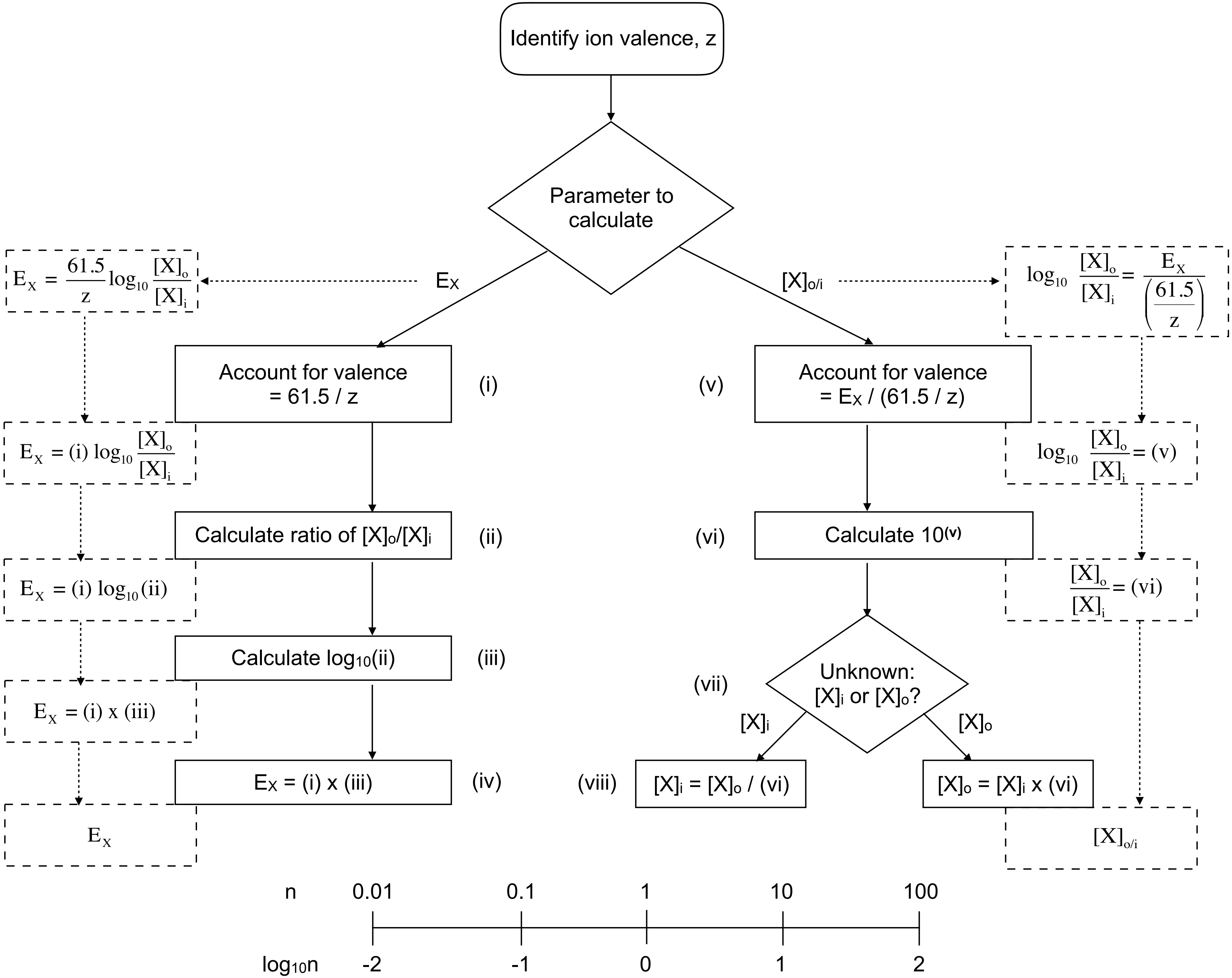
12. **Purves D, Augustine GJ, Fitzpatrick D, Hall WC, LaMantia A-S, White LE.** Electrical Signals of Nerve Cells.In: *Neuroscience*, eds Purves D, Augustine GJ, Fitzpatrick D, Hall WC, LaMantia A-S, & White LE (Sinauer Associates Inc, Sunderland, MA), Fifth Ed, pp 25-56, 2012

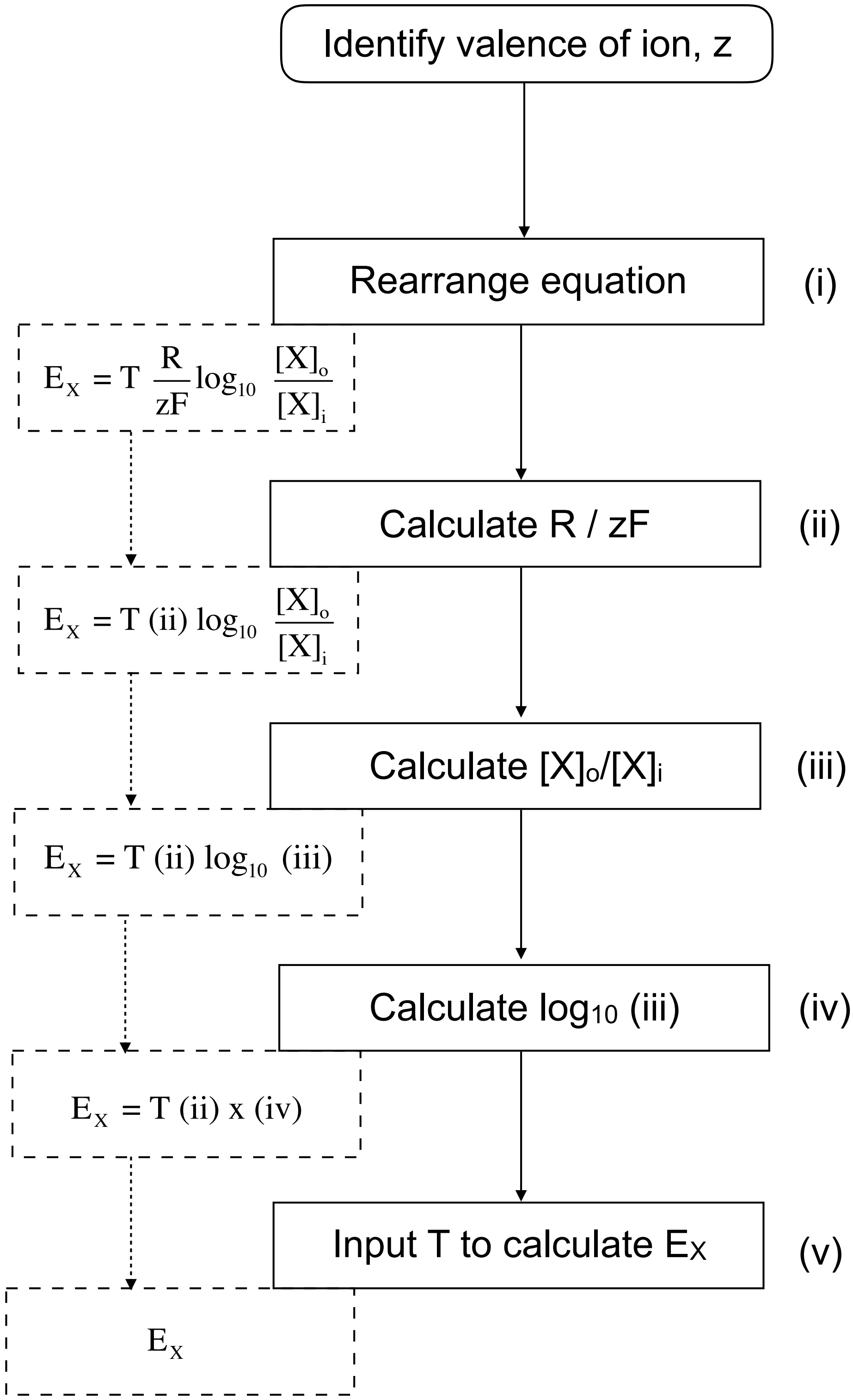
13. **Sawyer JER, Hennebry JE, Revill A, Brown AM.** The critical role of logarithmic transformation in Nernstian equilibrium potential calculations. *Adv Physiol Educ* 41: 231-238, 2017. doi: 10.1152/advan.00166.2016

14. **Silverthorn DU.** Uncovering misconceptions about the resting membrane potential. *Adv Physiol Educ* 26: 69-71, 2002. doi: 10.1152/advan.00012.2002

15. **Thurman CL.** Resting membrane potentials: a student test of alternate hypotheses. *Am J Physiol* 269: S37-41, 1995. doi: 10.1152/advances.1995.269.6.S37

16. **Wright SH.** Generation of resting membrane potential. *Adv Physiol Educ* 28: 139-142, 2004. doi: 28/4/139 [pii] 10.1152/advan.00029.2004


Identify ion valence, z
Parameter to calculate
E_X
$[X]_{o/i}$
$E_X = \frac{61.5}{z} \log_{10} \frac{[X]_o}{[X]_i}$
Account for valence = 61.5 / z
(i)
$E_X = (i) \log_{10} \frac{[X]_o}{[X]_i}$
Calculate ratio of $[X]_o/[X]_i$
(ii)
$E_X = (i) \log_{10}(ii)$
Calculate $\log_{10}$(ii)
(iii)
$E_X = (i) \times (iii)$
E_X = (i) x (iii)
(iv)
E_X
$\log_{10} \frac{[X]_o}{[X]_i} = \frac{E_X}{\left(\frac{61.5}{z}\right)}$
(v)
Account for valence = E_X / (61.5 / z)
$\log_{10} \frac{[X]_o}{[X]_i} = (v)$
(vi)
Calculate $10^{(v)}$
$\frac{[X]_o}{[X]_i} = (vi)$
(vii)
Unknown: $[X]_i$ or $[X]_o$?
$[X]_i$
$[X]_o$
(viii)
$[X]_i = [X]_o$ / (vi)
$[X]_o = [X]_i$ x (vi)
$[X]_{o/i}$
n
0.01
0.1
1
10
100
$\log_{10}$n
-2
-1
0
1
2


Identify valence of ion, z
Rearrange equation
(i)
$E_X = T \frac{R}{zF} \log_{10} \frac{[X]_o}{[X]_i}$
Calculate R / zF
(ii)
$E_X = T\ (ii) \log_{10} \frac{[X]_o}{[X]_i}$
Calculate $[X]_o/[X]_i$
(iii)
$E_X = T\ (ii) \log_{10}\ (iii)$
Calculate $\log_{10}$ (iii)
(iv)
$E_X = T\ (ii)\ x\ (iv)$
Input T to calculate E_X
(v)
E_X