

qNet — Titration Simulator and Isoelectric Point of Peptide Sequences

José Maurício Schneedorf Ferreira da Silva

2026-02-17

The *isoelectric point* (pI) is the pH value at which a molecule carries *zero net electric charge* under an electric field, i.e., its positive and negative charges cancel each other. Experimentally, it can be estimated by kinetic or electrokinetic measurements such as *zeta potential*, isoelectric focusing, or capillary electrophoresis.

In a related sense, the *isoionic point* refers to the same condition *in the absence of an electric field*, and may be inferred from potentiometric titration, viscosity, or directly from the structural information encoded in a monomeric sequence, as in the primary sequence of proteins. The program *qNet* simulates a titration curve for peptide (and protein) sequences.

1 Equation

The net charge of a compound, $qNet$, can be expressed as the sum of its acidic (qa) and basic (qb) contributions:

$$qNet = qb + qa$$

Where:

- qb = charge in the basic form (+1, 0, or -1)

Considering the ionization of chemical groups via the Henderson–Hasselbalch equation:

$$pH = pK_a + \log \left(\frac{A^-}{HA} \right)$$

Where:

- $pK_a = -\log[H^+]$
- HA = acid form concentration
- A^- = base form concentration

For a set of ionizable groups in a molecule, an operational expression for $qNet$ can be written as:

$$qNet = \sum_{i=1}^n \left(q_{b,i} + \frac{1}{1 + 10^{pH-pK_i}} \right)$$

Thus, $qNet$ is computed from the input values of $q_{b,i}$, pK_i , and n (the multiplicity/amount of ionizable groups of type i in the sequence).

2 Use and example

Plotting is performed by an independent program, *plotF*, which allows the user to plot a mathematical function by placing the expression on the stack along with the initial and final values of the independent variable.

In this way, $qNet$ supports data input and generates a net-charge curve as a function of pH. For program execution, example inputs and outputs are:

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# Inputs
1. List with the number of ionizable groups (multiplicity):
   Example: Glu (glutamate): {1 1 0 1 0 0 0 0}

2. List with "qb", i.e., the base-form charge of each ionizable group:
   Example: Glu: {-1 0 -1 -1 0 -1 -1 0 0}

3. List with pKa values for each ionizable group:
   {2.2 9.6 3.9 4.3 6.0 8.3 10.9 10.8 12.5}
   ...or in the order:
   {C-t N-t Glu Asp His Cys Tyr Lys Arg}

# Outputs
Potentiometric titration curve of "qNet" as a function of pH (1 to 14)
Function expression, and Xi and Xf values returned for re-plotting

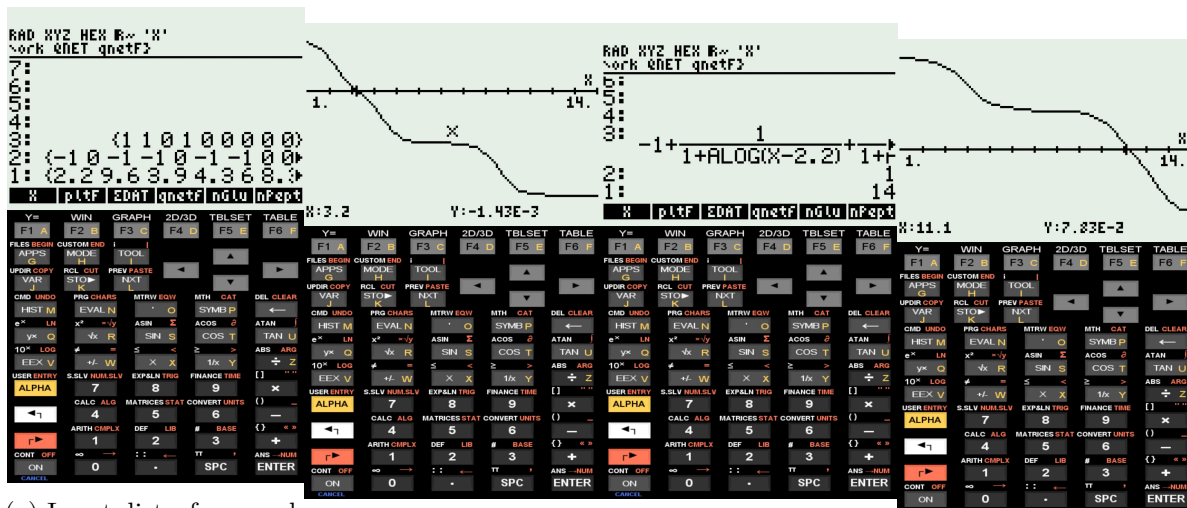
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3 Files

1. Programs (main and plot)
2. Source code
3. This tutorial

The figure below illustrates data entry and the execution of *qNet* using the examples included in the compressed file.

The simulated curves for the examples included in the compressed file, as well as the pI values computed by *qNet*, are consistent with values reported in the literature.



(a) Input lists for n , q_b , and pK_a of the sequence. Example for glutamate (Glu). (b) Glu titration curve showing the pI value (3.2). (c) Function output and X_i/X_f values for re-plotting. (d) Lysozyme titration curve and its pI value.

Figure 1: Program *qNet* running on the Android HP50G emulator ([Go49gp](#)), showing input data, function output for re-plotting, and titration curves for an amino acid (glutamate) and for lysozyme. The X coordinate corresponds to the estimated isoelectric point (pI).

References

1. Bloomfield, Victor. *Computer Simulation and Data Analysis in Molecular Biology and Biophysics: An Introduction Using R*. Springer, 2009.

Author

José Maurício Schneedorf Ferreira da Silva
Dept. Biochemistry, Institute of Biomedical Sciences
Federal University of Alfenas - UNIFAL-MG, Brazil
Email: jose.dasilva@unifal-mg.edu.br

Site: <https://bioquanti.netlify.app>

Lattes: <http://lattes.cnpq.br/0436922594542722>

ORCID: 0000-0002-2031-6315