



**Third Faculty
of Medicine**
Charles University

Summer School of Clinical Acid-Base and Homeostasis

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The Stewart computer modelling station: Session I

Room 523. Thursday 10 September, 13:00 to 17:00. The cases, in order.

Answers are overleaf, so do not turn over until you have one. Application: Stewart Lite v0.6.0.

Block A, 6 minutes. Tab 1: Building plasma

Do this. Build the plasma yourself, from the panel on the left: set each row of the table below by hand, in order, and after each one read the pH. (Every row is also a preset under the panel, if you would rather click than type.) Stop after the first one, while the jar is **still nothing but water**, and move the temperature: nothing is added on that row and nothing is taken away, the same litre of water is simply warmed and cooled. Then stop again at the end, on **Real plasma**, and move the pCO₂ from one end of its range to the other.

Preset	What was added	pH	Which anion is carrying the charge
1 · Pure water	nothing	6.81	nothing. [H ⁺] = [OH ⁻] = 155 nEq/L
↳ the same water, warmed and cooled	nothing. Only 37 → 25 → 0 → 43 °C	6.81 → 7.00 → 7.47 → 6.72	still nothing. [H ⁺] = [OH ⁻] at every one
2 · CO ₂ alone	pCO ₂ 39.8 mmHg / 5.3 kPa, still no ions	4.51	bicarbonate, and only 31.2 μEq/L of it. Note the axis
3 · Strong ions	Na ⁺ 140, Cl ⁻ 100, and the CO₂ back to zero	12.22	hydroxide, 40.0 mEq/L of it
4 · Strong ions + CO ₂	pCO ₂ 39.8 mmHg / 5.3 kPa	7.61	bicarbonate, 39.6. Hydroxide has collapsed
5 · Weak acids	albumin 44 g/L, phosphate 1.15	7.41	bicarbonate 25.0, and albumin now takes 12.3
6 · Real plasma	K, Ca, Mg, lactate, unmeasured	7.40	bicarbonate 24.4
↳ the same plasma, breathing	nothing. Only pCO ₂ 15 → 100	7.78 → 7.04	bicarbonate 22.2 → 26.7, and albumin hands back 14.1 → 10.1

That second row is still pure water. pK_w at those four temperatures is 14.94, 13.99, 13.62 and 13.45, and **half of each one is the pH beside it**, because the pH of neutral water is half of pK_w and nothing else.

Rung 2 is the same jar with CO₂ in it and nothing else. Both columns are 31.2 μEq/L and the axis changes unit to show them: the proton and the bicarbonate that brought it, in equal numbers, because there is no other cation in the jar.

Rung 3 puts the strong ions in and takes the CO₂ back out, so that they arrive alone. Sodium 140 against chloride 100 is 40 mEq/L of positive strong ion difference, and the only anion a jar of water can offer is hydroxide: there it is, 40.0 mEq/L of it, and the pH is 12.22. Nothing alkaline was added. The alkali is the *difference*.

Rung 4 gives the CO₂ back, and the anion column changes hands. Bicarbonate takes 39.6 of the 40 and the hydroxide collapses to nothing, at pH 7.61. Nothing removed the hydroxide and nothing competed with it for space: bicarbonate simply carries the same charge at a far lower pH, so once it is available, that is where the charge sits.

Rung 5 adds the weak acids and they take their own share, 12.3 mEq/L on the albumin and 2.1 on the phosphate, so bicarbonate falls to 25.0 and the pH to 7.41. Again nothing was removed. **Rung 6 adds what is left of a real panel** and lands on pH 7.40 with a base excess of 0.0, which is the definition of a normal plasma and is the same plasma the Gamblegram opens on, tab 2, which is the page the rest of this session works from.

And that last row is respiratory acid-base on one slider. Move $p\text{CO}_2$ and **SIDa does not move**: it is made of the ion sliders and you did not touch them. Neither does A_{TOT} . What changes is how the anion column is *divided*. CO_2 and water make a bicarbonate and a proton in equal numbers, and the proton does not stay free: albumin and phosphate take it up and their own charge falls by almost exactly what bicarbonate gains. At $p\text{CO}_2$ 15 the albumin carries 14.1 mEq/L against 22.2 of bicarbonate; at 100 it carries 10.1 against 26.7. The column total at the foot of the readout never moves at all.

Now watch the base excess on the same slide. It is supposed to be the metabolic number, the one a respiratory change does not touch, and it very nearly is: **+3.3 at $p\text{CO}_2$ 15, 0.0 at 39.8, -2.8 at 100**. Nearly, but not exactly, and nothing metabolic happened. Van Slyke's equation is a straight-line fit made at $p\text{CO}_2$ 40, and asked about a $p\text{CO}_2$ of 15 or 100 it is being extrapolated a long way past where it was fitted. Between 25 and 60 it stays within about a milliequivalent and a half, which is most patients. It is worth knowing the size of that, because on tab 3 it appears as a bar of its own.

Watch the pH strip on the right rather than the columns. It is the same scale on every rung, and the dot only reaches the normal band on the last one.

❓ SIX QUESTIONS All six can be answered from the screen, without leaving tab 1.

1. Pure water at 37 °C is pH 6.81, not 7.00. Is it acidic?
2. You cooled the water from 37 to 0 and the pH rose by 0.66. Did it become alkaline?
3. **CO_2 alone** holds 31.2 $\mu\text{Eq/L}$ of bicarbonate and plasma holds 24 mEq/L, a thousand times more, at the same $p\text{CO}_2$. What is the difference between the two jars?
4. **Strong ions** is pH 12.2. Where did the alkali come from? Nothing alkaline was added.
5. Between **Strong ions + CO_2** and **Weak acids** the bicarbonate falls from 39.6 to 25.0. What removed it?
6. On **Real plasma**, $p\text{CO}_2$ from 15 to 100 drops the pH by three quarters of a unit while SIDa and A_{TOT} do not move at all. Which two numbers are doing the work, and why must they move in opposite directions? And why does the base excess move at all, when nothing metabolic has happened?

✓ ANSWER

1. **No.** Neutral means $[H^+] = [OH^-]$, which is exactly what **Pure water** shows. pH 7.00 is the neutral point at 25 °C and has no standing at body temperature.
2. **No.** It stayed exactly neutral the whole way, because $[H^+]$ and $[OH^-]$ stayed equal. A pH means nothing until you say at what temperature, which is the entire argument for reporting a blood gas at the patient's temperature or not correcting it at all.
3. **The strong ion difference, and nothing else.** Not the CO_2 : it is the same on both rungs. Bicarbonate is an anion, and an anion needs a cation opposite it. In the jar with no strong ions the only one available is the proton that came with it, so $[H^+] = [HCO_3^-]$ and both are 31.2 $\mu\text{Eq/L}$ at pH 4.5. Plasma carries 42 mEq/L of net strong cation, and that is what the 24 mEq/L of bicarbonate is answering.
4. **40 mEq/L of positive strong ion difference was added**, and the only anion available in a jar of water is hydroxide. The pH is a consequence, not an ingredient.
5. **Nothing removed it.** Nobody competed for space. Albumin and phosphate lowered the pH, and bicarbonate answers to $[H^+]$ like everything else in the column.
6. **Bicarbonate and the albumin, and they are not free to move apart.** The height of the anion column is set by the strong ions, which you did not touch, so if bicarbonate is to take more of it something else must take less. CO_2 and water make HCO_3^- and H^+ in equal numbers; the proton is taken up by albumin and phosphate, whose charge falls from 14.1 and 2.22 to 10.1 and 1.96 while bicarbonate rises from 22.2 to 26.7. That is what non-bicarbonate buffering is in this model: the buffers are not destroying an acid, they are giving up negative charge so that bicarbonate can have it.

The base excess should not have moved and it moves a little: **+3.3, 0.0, -2.8** across that range. That is the formula, not the plasma. Van Slyke's equation is a straight line fitted at pCO_2 40, and 15 and 100 are a long way outside where it was fitted; between 25 and 60 the drift stays within about one and a half milliequivalents.

Block B, 4 minutes. Case 1

 **CLINICAL CASE** A 68-year-old man, day 1 after emergency laparotomy for a perforated sigmoid. He was resuscitated overnight with about six litres of 0.9% saline. He is warm, making urine, and the lactate is normal. The morning gas shows a base excess of -12 and the surgical team asks whether the bowel is ischaemic.

The arterial blood gas:

pH	7.18		7.35 to 7.45
pCO ₂	40.0 mmHg / 5.3 kPa		35 to 45 / 4.7 to 6.0
Na ⁺	144	mmol/L	136 to 145
K ⁺	4.0	mmol/L	3.5 to 5.1
Cl ⁻	120	mmol/L	98 to 107
Ca ²⁺ , ionised	1.20	mmol/L	1.15 to 1.30
Lactate	1.0	mmol/L	0.5 to 1.6
HCO ₃ ⁻ , calculated	14.8	mmol/L	22 to 26
Base excess, calculated	-12.0	mmol/L	-2 to 2

The italic lines are the analyser's own arithmetic: the page recomputes them, which checks your typing.

From the laboratory:

Albumin	44	g/L	35 to 50
Phosphate	1.15	mmol/L	0.8 to 1.5
Mg ²⁺	0.80	mmol/L	0.70 to 1.00

Type the panel in, or load the preset **Hyperchloraemic acidosis**: the presets are at the foot of the control panel on the left, under the last slider. Read the gauge column to the right of the figure, then switch **Anion gap**, just above the presets, to **show**.

what the page adds	Normal plasma	This patient	Reference
H ⁺	39.8	66.1	35 to 45 nmol/L
SIDa	42.0	31.0	41.1 to 45.1
A_TOT	17.8	17.8	13.8 to 20.6
A ⁻	14.8	13.4	11.6 to 17.1
Strong ion gap	+2.8	+2.8	0 to 4
Anion gap	14.6	13.2	8 to 16
Corrected for albumin	14.1	12.7	8 to 16

Change in pH from normal plasma: 7.40 to **7.18**, a fall of **0.22**.

A closer look at SIDa and A_TOT, arithmetic you can do before you touch the app:

- SIDa = $(144 + 4.0 + 2.4 + 1.6) - (120 + 1.0) = \mathbf{31.0}$, down 11.0 from 42.0. Sodium rose; chloride rose further.
- A_TOT = $0.3403 \times 44 + 2.420 \times 1.15 = \mathbf{17.75}$, unchanged.
- pCO₂, the third independent variable, has not moved either.

Both of those headings are figures under the Gamblegram.

 **QUESTION** A base excess of -12 , and the anion gap is 13.2. Is the bowel dead?

✔ **ANSWER** The answer is on the figure. Nothing was added to the anion column. Chloride grew, and because the two columns must stay the same height, bicarbonate had to give way. The apparent strong ion difference fell from 42.0 to 31.0, which is the whole of the acidosis, and it fell although the SODIUM rose: chloride rose further. The anion gap did not move because the gap only ever measured what you did not put on the figure, and chloride is measured. The strong ion gap agrees: +2.8 against a normal +2.8, so there is nothing unaccounted for.

This is the acidosis the resuscitation caused. Saline has a strong ion difference of zero, and giving enough of it drags the patient's own towards zero as well.

And the panel is that resuscitation, not an invention. Six litres of 0.9% saline, which is Na^+ and Cl^- both at 154 mmol/L, into an extracellular space of about fourteen litres in a 70 kg man gives sodium $(14 \times 140 + 6 \times 154) \div 20 = \mathbf{144}$ and chloride $(14 \times 105 + 6 \times 154) \div 20 = \mathbf{120}$. Both rise, because the fluid is more concentrated than plasma in each; chloride rises further because it started further below 154, and the gap between them is what the pH answers to.

One thing the panel does not do to itself: six litres would dilute the albumin too, to about 31 g/L. It is held at 44 here so that a single variable moves, which is what makes the case readable. Case 3 is the one where albumin is the variable.

Block C, 4 minutes. Case 2

CLINICAL CASE A 54-year-old woman, four hours into septic shock from pyelonephritis. She is on norepinephrine at 0.5 µg/kg/min. Lactate 8 mmol/L, albumin still 44, chloride 105.

The arterial blood gas:

pH	7.28		7.35 to 7.45
pCO ₂	40.0 mmHg / 5.3 kPa		35 to 45 / 4.7 to 6.0
Na ⁺	140	mmol/L	136 to 145
K ⁺	4.0	mmol/L	3.5 to 5.1
Cl ⁻	105	mmol/L	98 to 107
Ca ²⁺ , ionised	1.20	mmol/L	1.15 to 1.30
Lactate	8.0	mmol/L	0.5 to 1.6
HCO ₃ ⁻ , calculated	18.6	mmol/L	22 to 26
Base excess, calculated	-7.0	mmol/L	-2 to 2

The italic lines are the analyser's own arithmetic: the page recomputes them, which checks your typing.

From the laboratory:

Albumin	44	g/L	35 to 50
Phosphate	1.15	mmol/L	0.8 to 1.5
Mg ²⁺	0.80	mmol/L	0.70 to 1.00

Or load **Hyperlactataemia**, then **...with respiratory compensation** for the third column; by hand that column is the same panel at pH **7.38** and pCO₂ **30.0 mmHg / 4.0 kPa**. **The unmeasured anion is not on the list:** it is what the page works out.

what the page adds	Normal	Lactate 8	...and pCO ₂ 30	Reference
pH	7.40	7.28	7.38	7.35 to 7.45
SIDa	42.0	35.0	35.0	41.1 to 45.1
A_TOT	17.8	17.8	17.8	13.8 to 20.6
A ⁻	14.8	14.1	14.7	11.6 to 17.1
HCO ₃ ⁻	24.4	18.6	17.6	22 to 26
Base excess (SBE)	0.0	-7.0	-6.6	-2 to 2
Strong ion gap	+2.8	+2.3	+2.8	0 to 4
Anion gap	14.6	20.4	21.4	8 to 16
Corrected for albumin	14.1	19.9	20.9	8 to 16

Change in pH from normal plasma: 7.40 to **7.28**, a fall of **0.12**.

A closer look at SIDa and A_TOT: SIDa = (140 + 4.0 + 2.4 + 1.6) – (105 + 8.0) = **35.0**, down 7.0 from 42.0. A_TOT = **17.75**, unchanged. Neither moves when she hyperventilates: breathing is the third variable.

The same single variable as in Case 1, moved half as far and by a different anion. She has compensated in the third column; read its other rows before you call her better.

THREE QUESTIONS Both this and Case 1 are a fall in the strong ion difference of about the same size, so why does the anion gap move here and not there? Why is the strong ion gap normal, at +2.3 and +2.8? And is the compensation in the third column the one you would predict?

✔ **ANSWER** The anion gap moves because lactate is invisible to it. Lactate is on the figure and chloride is on the figure, but the anion gap counts only sodium, potassium, chloride and bicarbonate. Lactate is not among them, so it appears as a gap; chloride is, so it does not. The gap is a measure of your measurement, not of the patient.

The strong ion gap stays normal because you measured the lactate. Nothing unaccounted for has appeared. If this were ketoacidosis the SIG would rise; here it does not, and that is a real distinction the base excess alone cannot make.

The compensation is more than the rule asks for. Winter's rule says the expected $p\text{CO}_2$ is $1.5 \times \text{HCO}_3^- + 8$, in mmHg, plus or minus 2; in kPa the same rule is $\text{HCO}_3^-/5 + 1$, plus or minus 0.3. Her bicarbonate in that third column is **17.6 mmol/L**, so the prediction is **34.4 mmHg (4.5 kPa)** and she is at **30.0 mmHg (4.0 kPa)**. That is common in early sepsis and it is usually fever, pain and catecholamines rather than an acid-base signal. Tabs 2 and 3 print this line themselves, under the numbers, whenever the base excess shows a metabolic acidosis, and they predict from the bicarbonate exactly as printed, so the arithmetic can be checked by hand against the panel.

Block D, 4 minutes. Case 3

 **CLINICAL CASE** A 71-year-old man, day 6 of ICU for pneumonia. He is off vasopressors and the lactate is 1.0. Albumin has fallen from 42 on admission to 20. The gas shows pH 7.50 and a base excess of +7, and the registrar is asked to look for a diuretic or a gastric loss.

The arterial blood gas:

pH	7.50		7.35 to 7.45
pCO ₂	40.0 mmHg / 5.3 kPa		35 to 45 / 4.7 to 6.0
Na ⁺	140	mmol/L	136 to 145
K ⁺	4.0	mmol/L	3.5 to 5.1
Cl ⁻	105	mmol/L	98 to 107
Ca ²⁺ , ionised	1.20	mmol/L	1.15 to 1.30
Lactate	1.0	mmol/L	0.5 to 1.6
HCO ₃ ⁻ , calculated	30.9	mmol/L	22 to 26
Base excess, calculated	+7.4	mmol/L	-2 to 2

The italic lines are the analyser's own arithmetic: the page recomputes them, which checks your typing.

From the laboratory:

Albumin	20	g/L	35 to 50
Phosphate	1.15	mmol/L	0.8 to 1.5
Mg ²⁺	0.80	mmol/L	0.70 to 1.00

Or load the preset **Acute hypoalbuminaemia**. One line differs from normal plasma, and **it is not a strong ion**. Set the panel and read the base excess before anything else.

what the page adds	Normal plasma	This patient	Reference
SIDa	42.0	42.0	41.1 to 45.1
A_TOT	17.8	9.6	13.8 to 20.6
A ⁻	14.8	8.4	11.6 to 17.1
HCO ₃ ⁻	24.4	30.9	22 to 26
Strong ion gap	+2.8	+2.8	0 to 4
Anion gap	14.6	8.1	8 to 16
Corrected for albumin	14.1	13.6	8 to 16

Change in pH from normal plasma: 7.40 to **7.50**, a rise of **0.10**.

A closer look at SIDa and A_TOT: SIDa = (140 + 4.0 + 2.4 + 1.6) - (105 + 1.0) = **42.0**, exactly normal. A_TOT = 0.3403 × 20 + 2.420 × 1.15 = **9.59**, down 8.16. This is the case where the other variable moves. Not one strong ion did.

 **QUESTION** A metabolic alkalosis with a base excess of +7. What was given, and what was lost?

✔ **ANSWER Neither.** No strong ion moved. Albumin is a weak acid, and the second of Stewart's three independent variables is how much weak acid is present. Take 24 g/L of it away and the anion column is short by 6 mEq/L, so bicarbonate fills the space.

And the anion gap now reads 8.1, which in this patient is not reassurance, it is the same missing albumin seen from the other side. Corrected, it is 13.6: normal, which is the true answer, and only visible once you put the albumin back.

Block E, 4 minutes. Case 4

CLINICAL CASE A 47-year-old man, several weeks of very little food and a great deal of alcohol, admitted with vomiting and epigastric pain. There are ketones on his breath, and the urine dipstick is only weakly positive for them. He has had two litres of 0.9% saline in the emergency department. He is wasted, and the albumin has come back at 18 g/L. The registrar has looked at the anion gap and is not worried.

The arterial blood gas:

pH	7.30		7.35 to 7.45
pCO ₂	30.0 mmHg / 4.0 kPa		35 to 45 / 4.7 to 6.0
Na ⁺	136	mmol/L	136 to 145
K ⁺	4.0	mmol/L	3.5 to 5.1
Cl ⁻	110	mmol/L	98 to 107
Ca ²⁺ , ionised	1.20	mmol/L	1.15 to 1.30
Lactate	1.0	mmol/L	0.5 to 1.6
HCO ₃ ⁻ , calculated	14.6	mmol/L	22 to 26
Base excess, calculated	-10.5	mmol/L	-2 to 2

The italic lines are the analyser's own arithmetic: the page recomputes them, which checks your typing.

From the laboratory:

Albumin	18	g/L	35 to 50
Glucose	4.2	mmol/L	3.9 to 5.6
Phosphate	1.15	mmol/L	0.8 to 1.5
Mg ²⁺	0.80	mmol/L	0.70 to 1.00

Or load the preset **Ketoacidosis hidden by hypoalbuminaemia**.

what the page adds	Normal plasma	This patient	Reference
H ⁺	39.8	50.1	35 to 45 nmol/L
SIDa	42.0	33.0	41.1 to 45.1
A_TOT	17.8	8.9	13.8 to 20.6
A ⁻	14.8	7.3	11.6 to 17.1
Strong ion gap	+2.8	+11.1	0 to 4
Anion gap	14.6	15.4	8 to 16
Corrected for albumin	14.1	21.4	8 to 16

Change in pH from normal plasma: 7.40 to **7.30**, a fall of **0.10**.

A closer look at SIDa and A_TOT: SIDa = (136 + 4.0 + 2.4 + 1.6) – (110 + 1.0) = **33.0**, down 9.0 from 42.0. A_TOT = 0.3403 × 18 + 2.420 × 1.15 = **8.91**, down 8.8, and that one is a *base*. Two of the three independent variables have moved, in opposite directions, and the third, pCO₂, has moved as well.

QUESTION The anion gap is **15.4**, inside the 8 to 16 that everyone quotes. He is acidotic, he smells of ketones, and his anion gap is normal. Is there an unmeasured acid in this plasma or not?

✔ **ANSWER** There is, and there is a lot of it: the strong ion gap is **+11.1 mEq/L**. The page needs that much anion that nothing on the panel measures for a pH of 7.30 to be true, and in this patient it has a name: β -hydroxybutyrate and acetoacetate. The glucose is 4.2, so this is not diabetes. Starvation alone does not reach a gap of 11.1 either, which is alcoholic ketoacidosis territory: the fast started the ketogenesis and the ethanol drove it. Both push the pair towards β -hydroxybutyrate, which the nitroprusside reaction cannot see, so the urine ketone test can be weakly positive in a patient whose acid load is this large. The point-of-care blood β -hydroxybutyrate meter most units now have measures it directly and is the test to ask for.

Why the anion gap missed it. Roughly half of the normal anion gap is not a gap at all, it is albumin, sitting on the figure as negative charge that the gap arithmetic never subtracts. This man has lost 26 g/L of it, and the figure prices that exactly: the albumin bar falls from **12.3 to 4.8 mEq/L**, so 7.5 mEq/L of negative charge has left the anion column and the ketoacid load has moved into the space. The bedside correction is a little meaner: $AG + 0.25 \times (42 - 18)$ credits back 6.0 and reads **21.4**. Either way the gap is frankly abnormal, and nothing about the patient changed between 15.4 and 21.4.

Read it against the other three. Case 1 was a narrowed SIDa alone. Case 3 was a fallen A_{TOT} alone. Case 4 is both of those *and* a gap, all at once: chloride from the saline narrowed the strong ion difference by 9, starvation dropped A_{TOT} by 8.8, and the ketones opened a gap of 11.1. The base excess adds them into a single -10.5 and tells you none of it. The three-variable answer separates them, and the treatment for each of the three is different.

And the breathing is right. Winter's rule predicts $1.5 \times 14.6 + 8 = \mathbf{29.9 \text{ mmHg}}$, or $14.6/5 + 1 = \mathbf{3.9 \text{ kPa}}$, band $\pm 2 \text{ mmHg}$ ($\pm 0.3 \text{ kPa}$). He is at 30.0 mmHg, 4.0 kPa. The lung is doing its arithmetic correctly. It is the only part of this patient that is.

Block F, 3 minutes. Case 5

Reset to Normal plasma, then move pH, and only pH, to 7.55. Nothing else: not an ion, not the albumin, not the pCO₂. Every value you would measure on a patient stays exactly where it was.

what the page adds	Normal plasma	Now	Reference
SIDa	42.0	42.0	41.1 to 45.1
A_TOT	17.8	17.8	13.8 to 20.6
HCO ₃ ⁻	24.4	34.5	22 to 26
Base excess (SBE)	0.0	+11.4	-2 to 2
Strong ion gap	+2.8	-8.1	0 to 4
Anion gap	14.6	4.5	8 to 16

? QUESTION Nothing you can measure has moved and the pH is 7.55. Look at the top of the cation column. What has appeared there, and what could put it into a patient?

✓ **ANSWER 8.3 mEq/L of unmeasured cation**, and a strong ion gap of -8.1 . The two columns must be the same height, so the only way this page reaches pH 7.55 from a normal panel is to put in positive charge it cannot name. The anion gap went the other way, down to 4.5: a low anion gap is the classical footprint of the same thing, and the mirror of Case 4.

What could do it.

- **Measurement error.** Sodium and chloride each carry one to two mmol/L, and the gap is their difference. A negative gap of a couple of mEq/L is noise. This one is too big for that, but repeat the sample before you diagnose anything.
- **THAM.** An amine buffer given as an alkalinising drug. Its pK is about 7.8, so at plasma pH most of it has taken a proton and is THAM- H^+ , a cation no electrode on the panel measures. Sodium bicarbonate raises the pH by adding sodium, which *is* measured, so it widens SIDa and shows in the sodium bar; try the preset. THAM raises the pH without moving one measured ion, so the negative gap is its only trace. That is also how it works: THAM- H^+ leaves in the urine and takes the proton with it.
- **A cationic paraprotein.** IgG myeloma. IgG is cationic at pH 7.4 and IgA is anionic, so only IgG lowers the gap. It is the only thing on this list that reaches -8.1 alone.
- **Lithium, bromide, iodide.** Lithium is a real unmeasured cation, but it is lethal far below 8.3 mmol/L. Bromide and iodide are read as chloride, so the chloride is falsely high and SIDa falsely narrow: the same picture from the opposite direction.
- **Unmeasured Ca^{2+} or Mg^{2+} .** Severe hypercalcaemia, magnesium in eclampsia, but only on a panel that does not report them. Here you typed them in.