Main text

1. Title: Change “Metabolome” to “The Metabolome”
2. Line 8: Change “80% of the metabolome” to “80% of the metabolome by concentration”
3. Line 20: Delete “the” in “Eco80 reflects the RNA function”
4. Line 28: Delete “the”. Change “the RNA structure and function in cells.” to “RNA structure and function in cells.”
5. Line 34: Delete “the”. Change “the so called *in vivo-*like” to “so called *in vivo-*like”
6. Line 35: Delete “the” in “experiments that probe the”
7. Line 37: Add a comma. Change “tractable biologically” to “tractable, biologically”
8. Line 44: References 1-5 should actually be references 56-59. This will require a reordering of references.
9. Line 50: Change “RNA helix” to “RNA and DNA helix”
10. Line 76: Change “reported at” to “often reported at”
11. Line 79: Change “metabolites,” to “metabolites by concentration,”
12. Line 91: Change “Metabolites” to “Metabolites by Concentration”
13. Line 96: Change “containing biological” to :containing the biological”
14. Line 99: Delete “a” in “at a 2x”
15. Line 109: Change “was recorded” to “was again regorded”
16. Line 130: Change “KDs” to “KD”
17. Line 137: Change “top black data” to “top rows black data”
18. Line 143: Change “bottom)” to “bottom rows)”
19. Line 145: Change delete “were” in “data were right-shifted”
20. Line 146: Change “by metabolite” to “ by a metabolite”
21. Line 170: Change “metabolites based” to “metabolites, based”
22. Line 173: Change “this method was that” to “this method is that”
23. Line 178: Change “estimates of Mg2+” to “calculates Mg2+”
24. Line 180: Change “method was that” to “method is that”
25. Line 194: eq 1. The values above and below SIGMA are flipped. I noted it. But should Kd be Kd’ like in the SI?
26. Line 195: Remove indent.
27. Line 231: Change “WMCM cytoplasms” to WMCM artificial cytoplasms”
28. Line 251: Change “3’-quencher labeled” tp 3’-quencher-labeled”
29. Line 269: Change “(Figure 3C)” to “(Figure 2C)”
30. Line 273: Change “folding energies” to “folding free energies”
31. Line 281: Change “van’t Hoff plot” to “van’t Hoff plots”
32. Line 291: Change “destabilization” to destabilization in Eco80”
33. Line 301: Change “0.64” to “0.60”
34. Line 302: Change “0.23” to “0.22”
35. Line 303: Change “NTPCM appeared” to “NTPCM appears”
36. Line 307: Change “could be caused” to “linear relationship could be caused”
37. Line 325: Change “metabolites reduced” to “metabolites reduce”
38. Line 337: Delete “a” in “providing a”
39. Line 338: Change “resolution of RNA” to “resolution for RNA”
40. Line 352: Delete extra period
41. Line 354: Change “trimmed” to “removed”
42. Line 392: Change “paired-distance distribution” to “paired-distance, p(r), distribution”
43. Line 394: Change “adapts” to “adopts”
44. Line 406: Change “to compaction” to “to macromolecular shape”
45. Line 406: Delete “due to”
46. Line 411: Are the numbers correct?
47. Line 411: Change “Å” to “Å3” for volume
48. Line 412: Change “Eco80 was similar” to “Eco80 is similar”
49. Line 464 & 465: Its better the way we had it
50. Line 468: Change “condition, and degradation rates recovered” to “condition, while degradation rates once again recovered”
51. Line 499: Delete “(Table 2)”
52. Line 507: Change “2 mM free” to “25 mM free”
53. Line 508: I want to leave it the way it was
54. Line 534: Change “or weak Mg2+” to “or weak (WMCM) Mg2+”
55. Line 576: Change “metabolites, 20%” to “metabolites, the 20%”
56. Line 585: Change “remaining metabolites” to “remaining 228 metabolites”
57. Line 594: Change “indicated” to “indicate”
58. Line 611: Change “0.2” to “0.12”
59. Line 620: Change “as secondary” to “as concomitant secondary”
60. Line 683: Change “respectively, in” to “respectively, than Cs and Gs in”
61. Line 729: Change “the RNA” to “RNA”
62. Line 743: Superscript “2+” in “Mg2+”
63. Line 759: Add “; orcid.org/0000-0001-5414-1667”
64. Line 764: Add “; orcid.org/0000-0002-3937-3811”
65. Line 770: Delete “the” in “The Pennsylvania State University”
66. Line 792: Change “SAXS” to “SEC-MALS”
67. Line 795: Change “deoxynucleic” to “deoxyribonucleic”
68. Line 797: Change “of *E. coli”* to “of all *E. coli*”
69. Line 821: Change “49.” to “49: e10.”
70. Line 858: Capitalize “In” in “In Vitro”
71. Line 904 & 905: Please use this capitalization in the title, "Critical Evaluation of the Stability Constants of Metal Complexes of Amino Acids with Polar Side Chains"
72. Line 911: superscript the "2+"
73. Line 914: Delete “[22]”
74. Line 920: Delete the cross symbol
75. Line 943: Delete the cross symbol
76. Line 962: this should be "tRNA at 3 Å". Lowercase “t” on “tRNA”.
77. Line 994: Change “*RNA* 202228, rna.079196.122 . 994. DOI: 10.1261/rna.079196.122.” to ““*RNA* 2022, 28, 1197-1209.”

Main text figures and tables

1. Figure 1: Insert the updated PNG
2. Some of the DDG in Table 3 are bigger than error?  e.g. +1.17 should be +1.14.  Please check all entries in this table.
3. Fig. 5A. You do realize that there is almost no teal showing (I see 2). Just to confirm, Mg2+ changes color in this figure? It is teal in A and green in B, D. Is that correct?  (We have to live with it but just confirming.)
4. Table 3: Add the correct sequence for sequence 2, “5’CGCAUCCU3’/5’AGGAUGCG3’
5. Table 3: Change the dG for “CCAUAUUA/UAAUAUGG” in WMCM from “-9.94” to “-9.96”

Main text figure and table legend

1. Figure 1 legend: Change “which comprise 80% of the E. coli metabolome” to “which comprise 80% of the E. coli metabolome by concentration”
2. Figure 1 legend: Change “Effect of Mg2+ on HQS emission” to “Effect of Mg2+ concentration on HQS emission”
3. Figure 2 legend: Change “mixtures destabilized RNA helices.” to “mixtures destabilize RNA helices.”
4. Figure 2 legend: Change “2:CGCAUCCU/AGGAUGCG” to “2:5´-CGCAUCCU-3´/5´-AGGAUGCG-3´”
5. Figure 2 legend: Change “from the fit (using MeltR).” to “from the fit using MeltR.”
6. Table 2 legend: Change “Mg2+ Concentrations” to “Total Mg2+ Concentrations”
7. Figure 3 legend: Change “Mg2+(OH-)” to “Mg2+-OH-”
8. Figure 3 legend: Change “(C) Degradation rate at each” to “(C) Degradation rate for the guanine riboswitch aptamer at each”
9. Figure 3 legend: Change “analysis of crystal structures.” to “analysis of crystal structures (Table S7).”
10. Figure 4 legend: Change “free Mg2+ concentration.” to “free Mg2+ concentration (Table 2).”
11. Figure 4 legend: Change “chelate Mg2+ with KDs greater than 2 mM.” to “chelate Mg2+, with KDs greater than 2 mM.”

We made the following corrections to the supplemental files:

Supplemental file 1

1. Page 1: Change “Lauren McKinley” to “Lauren N. McKinley”
2. Page 1: Change “Melanie Huot” to “Melanie J. Huot”
3. Page 3: Change “(SI) table 1” to “Table S1”
4. Page 4: Change “using Fnorm and KHQS.” to “using Fnorm and KHQS.3”
5. Page 6: Minor formatting changes to equations 11 and 12.
6. Page 7: Change “200, 400, 800” to “200, 250, 400, 600”
7. Page 10: Change “X = 1.To” to “X = 1. To”
8. Page 10: Minor algebraic rearrangement of equation 22.
9. Page 11: Change “(Supplementary table 8)” to “(Table S8)”
10. Page 12: Add an indent after “*In-line probing chemical degradation assay”*
11. Page 18: Add “Modeled SAXS and p(r) curves, shown as the black curve in panels A and B, are from the crystal structure of the guanine aptamer (PDB 4FE5) with an explicit solvent shell modeled using WAXSiS.” to the legend of Figure S7.
12. Lowercase the “E” on “Equation”
13. Page 20: Change “2 mM Mg2+” to “2 mM Mg2+”
14. Page 22: Change “electro mobility” to “electrophoretic mobility”
15. Page 22: Reorder gel images in Figure S11 to match the rest of the manuscript.
16. Page 30: Table S7 footnote, add “Groupings are provided only for these positions with good resolution on the gels.”
17. Table S4. Should the units on KHQS be mM? They are currently mM-1.

Supplemental file 2

1. Page 1: Change “Lauren McKinley” to “Lauren N. McKinley”
2. Page 1: Change “Melanie Huot” to “Melanie J. Huot”
3. Page 2: Change “cytoplasm and the impact of such errors” to “cytoplasm, and the impact of such errors,”
4. Page 2: Lowercase the “S” in “Supplement”
5. Page 2: Change “(SI-2 Figure 1A) to “(Figure S2-1A)”
6. Page 2: Change “(SI-2 Figure 1B) to “(Figure S2-1B)”
7. Page 2: Change “given errors in of the total Mg2+.” to “given errors in the total Mg2+ concentration.”
8. Page 2: Change “1 mM increase in total” to “1 mM change in total”
9. Page 2: Change “+0.69 +/- 0.12 we” to “+0.69 +/- 0.12 kcal/mol we”
10. Page 3: Change “SI-2 Figure S1” to “Figure S2-1”