

SUPPLEMENTARY INFORMATION

Alternative Explanation for the Effect of *myo*-Inositol Trispyrophosphate on Normal Human Erythrocytes: ^{31}P NMR Studies

...*Mathematica* simulations

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Overview of the *Mathematica* Notebook

Here we provide a Wolfram Language (*Mathematica*) [1] implementation of the quantitative Donnan-equilibrium analysis used in the accompanying manuscript. The calculations evaluate the expected effects of extracellular *myo*-inositol trispyrophosphate (ITPP) on RBC intracellular pH, membrane potential, and cell volume under the assumption that ITPP behaves as an extracellular impermeant hexaanion. The theoretical framework is based on the classical membrane-equilibrium treatment of Donnan (1911) [2], while the quantitative RBC calibration is derived from the measurements of pH gradients and membrane potentials reported by Kirk, Kuchel and Labotka (1988) [3].

The Notebook first verifies the internal consistency of the Kirk et al. data [3] and then derives an empirical relationship between extracellular impermeant charge and intracellular alkalisation. This calibration is subsequently applied to ITPP concentrations used in the present work and in previously published studies, including those of Schneider et al., (2019) [4] Duarte et al. (2010) [5], and Koj et al. (2025) [6].

Predicted Donnan-induced pH changes are compared with the ^{31}P NMR observations reported by Koj et al. [6] and with the oxygen-affinity effects reported by Duarte et al. [5]. The analysis further examines whether the reported changes in haemoglobin oxygen affinity might be explained by Donnan equilibria alone and quantifies the osmotic consequences of exposing RBCs to high extracellular concentrations of ITPP.

All constants, assumptions, intermediate calculations and graphical outputs are explicitly defined, allowing complete transparency and reproducibility of the analysis.

Summary of Key Findings from the Notebook

1. The RBC Donnan response is quantitatively validated by the data of Kirk, Kuchel and Labotka (1988) [3]. The proton distribution ratios calculated from measured intracellular and extracellular pH values closely match the independently measured hypophosphite distribution ratios, confirming the applicability of the Donnan framework over membrane potentials spanning approximately -8 to $+12$ mV.
2. The calibrated Donnan response corresponds to approximately 0.105 pH units per 100 mEq L⁻¹ of extracellular impermeant anionic charge. Over the experimentally relevant range (0-153 mEq L⁻¹), the relationship between extracellular impermeant charge and intracellular alkalinisation is approximately linear.
3. At the ITPP concentration used in the present study (0.9 mM), the predicted Donnan-induced alkalinisation is negligible. The calculated intracellular pH increase is only about +0.006 pH units.
4. At the ITPP concentration used by Koj et al. [6] (approximately 4.1 mM), the Donnan model predicts a small intracellular alkalinisation of about +0.026 pH units.
5. The direction of the pH change observed by Koj et al. [6] is consistent with the Donnan prediction. Analysis of the reported ³¹P NMR chemical-shift changes yields an estimated intracellular alkalinisation of approximately +0.083 pH units, compared with a predicted value of +0.026 pH units. Thus, experiment and theory agree in sign and are of the same order of magnitude.
6. If ITPP were completely impermeant, very large extracellular ITPP concentrations would be predicted to produce substantial intracellular alkalinisation. Predicted values are approximately +0.49 pH units at 78 mM ITPP, +0.75 pH units at 120 mM ITPP, and +1.51 pH units at 240 mM ITPP.
7. The 34% increase in P50 reported for 120 mM ITPP cannot be explained by a Donnan mechanism alone. The observed right-shift of the oxygen-equilibrium curve requires intracellular acidification of approximately 0.26 pH units, whereas the Donnan model predicts alkalinisation of approximately +0.75 pH units. The predicted and required pH changes are therefore opposite in sign.

8. An additional acidifying mechanism must therefore operate if the reported oxygen-affinity effects are correct. Donnan-induced alkalisation alone cannot account for the observed right-shift of the oxygen-equilibrium curve.
9. The osmotic consequences of high extracellular ITPP concentrations are predicted to be severe. Assuming complete extracellular retention of ITPP, RBCs would retain only about 44%, 34%, and 20% of their original cell water at 78, 120, and 240 mM ITPP, respectively.
10. The incubation conditions used in the present work are essentially isotonic. Addition of 0.9 mM ITPP increases medium osmolality by only ~1.5%, giving a predicted relative cell-water volume of 0.986.
11. The Donnan effect is sufficient to explain only modest intracellular pH changes at low-millimolar ITPP concentrations. At concentrations employed in the present study and by Koj et al. [6] predicted pH shifts are small but measurable.
12. The combination of Donnan and osmotic calculations provides a quantitative benchmark against which proposed ITPP transport or intracellular actions can be evaluated. Any interpretation of high-concentration ITPP experiments must simultaneously satisfy the observed pH changes, oxygen-affinity changes, and osmotic constraints.

Summary of the Output

These 12 points move in sequence from validation → calibration → predictions → comparison with experiments → physiological implications.

References

1. Mathematica, *Wolfram 14.3 for DeskTop*. 2025, Wolfram Research Inc.: Champaign, IL, USA.
2. Donnan, F.G., *Theorie der membrangleichgewichte und membranpotentiale bei vorhandensein von nicht dialysierenden elektrolyten. Ein beitrag zur physikalisch-chemischen physiologie*. Zeitschrift für Elektrochemie und angewandte physikalische Chemie, 1911. **17**: p. 572-581.
3. Kirk, K., P.W. Kuchel, and R.J. Labotka, *Hypophosphite ion as a ³¹P nuclear magnetic resonance probe of membrane potential in erythrocyte suspensions*. Biophysical Journal, 1988. **54**(2): p. 241-247.
4. Schneider, M.A., et al., *Phase 1b dose-escalation study of the hypoxia-modifier Myo-inositol trispyrophosphate in patients with hepatopancreatobiliary tumors*. Nature Communications, 2021. **12**: p. 3807:1-12.
5. Duarte, C.D., et al., *myo-inositol trispyrophosphate: a novel allosteric effector of hemoglobin with high permeation selectivity across the red blood cell plasma membrane*. ChemBioChem, 2010. **11**: p. 2543-2548.

6. Koj, S., et al., *Modulation of the oxygenation state and intracellular pH of erythrocytes by inositol-trispyrophosphate investigated by ^{31}P NMR study of 2,3-DPG*. Journal of Cellular and Molecular Medicine, 2025. **29:e70343**: p. 1-12.

Quantitative Donnan analysis...ITPP in RBCs

HOW TO RUN

Open this file in *Mathematica* (File > Open), or copy the sections into a new Notebook

Evaluate top to bottom with Shift+Enter

Section 7 writes the figure as a PDF next to this file

Every section prints its result. Expected values are given in the comments so you can confirm the port is faithful

```
In[1]:= ClearAll["Global`*"];
```

1. Define parameters and their values

```
In[2]:=
```

```
RTF    = 25.69;      (* RT/F in mV at 298 K *)
zITPP  = 6.;         (* anionic charge on the ITPP hexa-anion *)
mwITPP = 737.8;      (* g/mol, hexasodium salt *)
bohr   = -0.48;      (* d log P50 / d pH, human whole blood *)

teal   = RGBColor[29/255, 158/255, 117/255];
purple = RGBColor[83/255, 74/255, 183/255];
coral  = RGBColor[216/255, 90/255, 48/255];
grey   = RGBColor[136/255, 135/255, 128/255];
red    = RGBColor[163/255, 45/255, 45/255];
blue   = RGBColor[24/255, 95/255, 165/255];
band   = RGBColor[192/255, 221/255, 151/255];

labStyle = Directive[FontFamily -> "Helvetica", FontSize -> 10];
```

2. Kirk, Kuchel & Labotka 1988, Biophys J 54:241–247, Table I Extracellular NaCl replaced iso-osmotically with Na₃-citrate

```
In[17]:= citrate = {0., 25., 51., 76.}; (* mM, extracellular *)
pHi  = {6.97, 7.13, 7.24, 7.41}; (* measured, electrode + NMR*)
pHo  = {7.11, 7.19, 7.22, 7.21};
rHPA = {0.65, 0.79, 1.00, 1.59}; (* hypophosphite ratio, Table I *)

Zout = 3.citrate; (* extracellular impermeant anionic charge *)
logr = pHi - pHo; (* = Log10[r] by the Donnan relation *)
rH = 10.^logr;
Em = RTF Log[rH]; (* membrane potential, mV *)

Print[Style["1. Kirk et al. 1988 Table I -- internal consistency", Bold]];
Print[Grid[
  Prepend[
    Transpose[{citrate, Zout, pHi, pHo,
      Round[rH, 0.01], rHPA,
      Round[logr, 0.001], Round[Em, 0.1]}],
    {"citrate/mM", "Zo/mEq", "pHi", "pHo", "r(H+)", "r(HPA)",
      "log r", "Em/mV"}],
  Frame → All, Alignment → Right, Spacings → {1.4, 0.8}]];

Print["mean |r(H+) - r(hypophosphite)| = ",
  Round[Mean[Abs[rH - rHPA]], 0.001],
  " -> the Donnan relation r(Cl) = r(permeant anion) holds"];
Print["Em spans ", Round[First[Em], 0.1], " to ", Round[Last[Em], 0.1],
  " mV (Kirk reported -11 to +12 mV)"];

(* EXPECTED
  r(H+)  0.72  0.87  1.05  1.58
  log r  -0.140 -0.060 0.020 0.200
  Em/mV  -8.3  -3.5  1.2  11.8
  mean |r(H+) - r(HPA)| = 0.052
*)
```

1. Kirk et al. 1988 Table I -- internal consistency

citrate/mM	Zo/mEq	pHi	pHo	r(H+)	r(HPA)	log r	Em/mV
0.	0.	6.97	7.11	0.72	0.65	-0.14	-8.3
25.	75.	7.13	7.19	0.87	0.79	-0.06	-3.5
51.	153.	7.24	7.22	1.05	1.	0.02	1.2
76.	228.	7.41	7.21	1.58	1.59	0.2	11.8

```
mean |r(H+) - r(hypophosphite)| = 0.052
-> the Donnan relation r(Cl) = r(permeant anion) holds
Em spans -8.3 to 11.8 mV (Kirk reported -11 to +12 mV)
```

3. Calibration: $d(\text{pHi}) / d(\text{Zout})$

```
In[29]:= segSlopes = Differences[logr]/Differences[Zout];

sel      = {1, 2, 3};                                (* Zout <= 153 mEq/L *)
fitData = Transpose[{Zout[[sel]], logr[[sel]]}];
lm       = LinearModelFit[fitData, z, z];
{cLin, kLin} = lm["BestFitParameters"];

Print[Style["\n2. Calibration of the Donnan response", Bold]];
Do[Print["  Zout ", Round[Zout[[i]]], " -> ", Round[Zout[[i + 1]]],
      " mEq/L : d(log r)/dZ = ",
      Round[1000 segSlopes[[i]], 0.001], " x10^-3 per mEq/L",
  {i, 3}];
Print["  linear coefficient over Zout = 0-153 mEq/L:"];
Print["      kLin = ", Round[1000 kLin, 0.001],
      " x10^-3 pH units per mEq/L"];
Print["      = ", Round[100 kLin, 0.001],
      " pH units per 100 mEq/L, at clamped pHo"];
Print["  NOTE the response accelerates above ~150 mEq/L as [Cl]o becomes"];
Print["  small, so kLin is a LOWER BOUND at high charge loading."];

(* EXPECTED
   segment slopes  1.067, 1.026, 2.400  x10^-3
   kLin = 1.046 x10^-3  ->  0.105 pH units per 100 mEq/L
   cLin = -0.139
*)
```

2. Calibration of the Donnan response

```
Zout 0 -> 75 mEq/L : d(log r)/dZ = 1.067 x10^-3 per mEq/L
Zout 75 -> 153 mEq/L : d(log r)/dZ = 1.026 x10^-3 per mEq/L
Zout 153 -> 228 mEq/L : d(log r)/dZ = 2.4 x10^-3 per mEq/L
linear coefficient over Zout = 0-153 mEq/L:
      kLin = 1.046 x10^-3 pH units per mEq/L
           = 0.105 pH units per 100 mEq/L, at clamped pHo
NOTE the response accelerates above ~150 mEq/L as [Cl]o becomes
small, so kLin is a LOWER BOUND at high charge loading.
```

4. Prediction for the published ITPP protocols

```
In[45]:= cKoj = 3.0/mwITPP*1000.;      (* Koj 3 mg/mL -> mM *)

protocols = {
  {"Kuchel (this work)",    0.9},
  {"Koj 2025 in vitro",    cKoj},
  {"Okninska 2020 loading", 78.},
  {"Duarte 2010 OEC",      120.},
  {"Duarte 2010 stock",    240.}};

predTable = Table[
  {p[[1]], Round[p[[2]], 0.01], Round[zITPP p[[2]], 1],
   Round[kLin zITPP p[[2]], 0.001]},
  {p, protocols}];

Print[Style["\n3. Predicted intracellular alkalinisation, no permeation",
  Bold]];
Print[Grid[Prepend[predTable,
  {"protocol", "[ITPP]/mM", "Zo/mEq", "dpHi predicted"}],
  Frame -> All, Alignment -> {{Left, Right, Right, Right}},
  Spacings -> {1.4, 0.8}]];

(* EXPECTED dpHi = 0.006, 0.026, 0.489, 0.753, 1.506 *)
```

3. Predicted intracellular alkalinisation, no permeation

protocol	[ITPP]/mM	Zo/mEq	dpHi predicted
Kuchel (this work)	0.9	5	0.006
Koj 2025 in vitro	4.07	24	0.026
Okninska 2020 loading	78.	468	0.489
Duarte 2010 OEC	120.	720	0.753
Duarte 2010 stock	240.	1440	1.506

5. Koj 2025 in vitro: predicted vs observed

```
In[55]:= ZKoj      = zITPP cKoj;
dpHpred   = kLin ZKoj;

(* 2,3-DPG 31P chemical shift vs pH, from Koj's own reported values:
   intact RBC 3-P at nominal pH 6.8 -> 3.20 ppm; at pH 7.0 -> 3.32 ppm *)
slopePPM  = (3.32 - 3.20)/(7.0 - 6.8);
dShiftObs = 0.05;                               (* ppm, downfield, Koj Fig 2 *)
dpHobs    = dShiftObs/slopePPM;
dpHobsLo  = dShiftObs/0.9;                       (* slope range 0.5 - 0.9 ppm/pH *)
dpHobsHi  = dShiftObs/0.5;

Print[Style["\n4. Koj 2025 in vitro -- predicted vs observed", Bold]];
Print[" [ITPP] = ", Round[cKoj, 0.01], " mM -> Zo = ",
      Round[ZKoj, 0.1], " mEq/L"];
Print[" PREDICTED dpHi (lower bound) = +", Round[dpHpred, 0.001]];
Print[" 2,3-DPG shift/pH slope      = ", slopePPM, " ppm per pH unit"];
Print[" OBSERVED dpHi                = +", Round[dpHobs, 0.001],
      " (range +", Round[dpHobsLo, 0.001],
      " to +", Round[dpHobsHi, 0.001], ")"];
Print[" ratio observed/predicted    = ", Round[dpHobs/dpHpred, 0.1], "x"];
Print[" SIGN AGREES; magnitude within a factor of 2-4."];
Print[" The prediction is a lower bound because (i) their HEPES buffer"];
Print[" clamps pHo, and (ii) ITPP was added, not iso-osmotically"];
Print[" substituted, so the cells also shrink."];

(* EXPECTED dpHpred = 0.026 ; dpHobs = 0.083 (range 0.056 - 0.100) *)
```

4. Koj 2025 in vitro -- predicted vs observed

```
[ITPP] = 4.07 mM -> Zo = 24.4 mEq/L

PREDICTED dpHi (lower bound) = +0.026

2,3-DPG shift/pH slope      = 0.6 ppm per pH unit

OBSERVED dpHi                = +0.083 (range +0.056 to +0.1)

ratio observed/predicted    = 3.3x

SIGN AGREES; magnitude within a factor of 2-4.

The prediction is a lower bound because (i) their HEPES buffer
clamps pHo, and (ii) ITPP was added, not iso-osmotically
substituted, so the cells also shrink.
```

6. Duarte 2010: the 34% P50 right-shift needs ACIDIFICATION

```
Out[*]=
-ACIDIFICATION needs shift + 34 Null P50 right the
```

```

In[77]:= p50ctrl = 24.25; (* Torr, Duarte Fig 1A control *)
p50itpp = 32.47; (* Torr, Duarte Fig 1A + ITPP *)
dlogP50 = Log10[p50itpp / p50ctrl];
dpHreq = dlogP50 / bohr;

Print[Style["\n5. Duarte 2010 -- the P50 right-shift", Bold]];
Print[" P50 ratio = ", Round[p50itpp / p50ctrl, 0.001],
      " (", Round[100 (p50itpp / p50ctrl - 1)], "% rise)"];
Print[" d log P50 = +", Round[dlogP50, 0.001]];
Print[" Bohr coefficient = ", bohr];
Print[" => required dpHi = ", Round[dpHreq, 0.001],
      " i.e. ACIDIFICATION"];
Print[" Donnan at 120 mM predicts ALKALINISATION of +",
      Round[kLin zITPP 120., 0.01], " -> a LEFT shift."];
Print[" Donnan therefore cannot explain the right-shift; an independent"];
Print[" acidifying mechanism is needed (ITPP acid strength)."];
Print[" Bohr range -0.40 to -0.60 gives required dpHi ",
      Round[dlogP50 / -0.4, 0.01], " to ", Round[dlogP50 / -0.6, 0.01],
      " -- sign robust."];

(* EXPECTED dlogP50 = 0.127 ; dpHreq = -0.264 *)

```

5. Duarte 2010 -- the P50 right-shift

```

P50 ratio = 1.339 (34% rise)
d log P50 = +0.127
Bohr coefficient = -0.48
=> required dpHi = -0.264 i.e. ACIDIFICATION
Donnan at 120 mM predicts ALKALINISATION of +0.75 -> a LEFT shift.
Donnan therefore cannot explain the right-shift; an independent
acidifying mechanism is needed (ITPP acid strength).
Bohr range -0.40 to -0.60 gives required dpHi -0.32 to -0.21 -- sign robust.

```

7. Tonicity of the published incubations

In[90]:=

```
phi    = 0.70;      (* osmotic coefficient, polyvalent electrolyte *)
npart  = 7.;        (* ITPP(6-) + 6 Na+ *)
osmIso = 300.;

vrel[c_] := osmIso/(osmIso + phi npart c);

tonTable = Table[
  {Round[c, 0.01], Round[phi npart c], Round[osmIso + phi npart c],
   Round[vrel[c], 0.001], Round[1/vrel[c], 0.01]},
  {c, {0.9, cKoj, 78., 120., 240.}}];

Print[Style["\n6. Osmotic consequence of the added ITPP", Bold]];
Print[Grid[Prepend[tonTable,
  {"[ITPP]/mM", "osmol added", "total/mOsm", "rel cell water",
   "[Hb] rise"}],
  Frame -> All, Alignment -> Right, Spacings -> {1.4, 0.8}]];
Print[" Duarte's 120 mM incubation was ",
  Round[(osmIso + phi npart 120.)/osmIso, 0.01],
  "x isotonic; cells lose ",
  Round[100 (1 - vrel[120.])], "% of their water."];
Print[" This work at 0.9 mM is ",
  Round[100 ((osmIso + phi npart 0.9)/osmIso - 1), 0.1],
  "% hypertonic -- physiologically innocuous."];

(* EXPECTED rel cell water 0.986, 0.938, 0.440, 0.338, 0.203 *)
```

6. Osmotic consequence of the added ITPP

[ITPP]/mM	osmol added	total/mOsm	rel cell water	[Hb] rise
0.9	4	304	0.986	1.01
4.07	20	320	0.938	1.07
78.	382	682	0.44	2.27
120.	588	888	0.338	2.96
240.	1176	1476	0.203	4.92

Duarte's 120 mM incubation was 2.96x isotonic; cells lose 66% of their water.

This work at 0.9 mM is 1.5% hypertonic -- physiologically innocuous.

8. Figure -- three panels

In[105]:=

```
(* -- Panel A: calibration, with a second axis in mV ----- *)

rightTicks = Table[{v/(RTF Log[10]), v},
  {v, {-7.5, -5, -2.5, 0, 2.5, 5, 7.5, 10, 12.5}}];

panelA = Show[
  Plot[kLin z + cLin, {z, 0, 230},
    PlotStyle -> Directive[purple, Thickness[0.006]]],
```

```

ListPlot[Transpose[{Zout, logr}],
  PlotStyle -> Directive[teal, PointSize[0.03]],
  Frame -> True,
  FrameLabel -> {
    {"log r      ( = pHi - pHo )", "Em (mV)"},
    {"Extracellular Impermeant Charge Zo (mEq/L)", None}},
  FrameTicks -> {{Automatic, rightTicks}, {Automatic, None}},
  PlotRange -> {{-8, 240}, {-0.17, 0.225}},
  GridLines -> {None, {{0, Directive[Gray, Dotted]}}},
  PlotLabel -> Style["A      Donnan Calibration (Kirk et al. 1988)",
    Bold, 14],
  LabelStyle -> labStyle, ImageSize -> 380, AspectRatio -> 0.85];

(* -- Panel B: predicted dpHi vs [ITPP] ----- *)

markConc = {{0.9, "This Work", teal}, {cKoj, "Koj 2025", coral},
  {78., "Okninska 2020", grey}, {120., "Duarte 2010", red}};

vlinesB = Table[
  ListLogLinearPlot[{{m[[1]], -0.05}, {m[[1]], 1.0}}, Joined -> True,
    PlotStyle -> Directive[m[[3]], Thickness[0.004],
      Dashing[{0.02, 0.015}]]],
  {m, markConc}];

errBarKoj = ListLogLinearPlot[{{cKoj, dpHobsLo}, {cKoj, dpHobsHi}},
  Joined -> True, PlotStyle -> Directive[coral, Thickness[0.008]]];

panelB = Show[
  LogLinearPlot[kLin zITPP c, {c, 0.1, 250},
    PlotStyle -> Directive[purple, Thickness[0.006]],
    Sequence @@ vlinesB,
    errBarKoj,
    ListLogLinearPlot[{{cKoj, dpHobs}},
      PlotStyle -> Directive[coral, PointSize[0.035]],
      Frame -> True,
      FrameLabel -> {"Predicted dpHi (Alkalinisation)", None},
        {"[ITPP] Added to Medium (mM)", None}},
      PlotRange -> {{Log[0.1], Log[250]}, {-0.05, 1.0}},
      PlotLabel -> Style["B      ITPP with no Permeation", Bold, 14],
      Epilog -> Table[
        Text[Style[m[[2]], m[[3]], 8], {Log[m[[1]]], 0.95}, {-1, 0}, {0, 1}],
        {m, markConc}],
      LabelStyle -> labStyle, ImageSize -> 380, AspectRatio -> 0.85];

(* -- Panel C: osmotic consequence ----- *)

vlinesC = Table[
  ListLogLinearPlot[{{m[[1]], 0.15}, {m[[1]], 1.12}}, Joined -> True,
    PlotStyle -> Directive[m[[3]], Thickness[0.004],
      Dashing[{0.02, 0.015}]]],
  {m, markConc}];

panelC = Show[
  LogLinearPlot[vrel[c], {c, 0.1, 250},
    PlotStyle -> Directive[blue, Thickness[0.006]],

```

```

Sequence @@ vlinesC,
Frame -> True,
FrameLabel -> {"Relative Cell Water Volume", None},
            {"[ITPP] added to Medium (mM)", None}},
PlotRange -> {{Log[0.1], Log[250]}, {0.15, 1.12}},
GridLines -> {None, {{1.0, Directive[Gray, Dotted]}}},
Prolog -> {band, Opacity[0.45],
            Rectangle[{Log[0.1], 0.9}, {Log[250], 1.1}]},
Epilog -> {Text[Style["Physiological", Darker[Green], 14],
                {Log[0.13], 0.945}, {-1, 0}]},
PlotLabel -> Style["C      Osmotic Consequence", Bold, 14],
LabelStyle -> labStyle, ImageSize -> 380, AspectRatio -> 0.85];

(* -- assemble and export ----- *)

figure = GraphicsColumn[{panelA, panelB, panelC}, ImageSize -> 700, Spacings -> 25]

outDir = Quiet@Check[NotebookDirectory[], Directory[]];
Export[FileNameJoin[{outDir, "donnan_figure_Mathematica.pdf"}], figure];
Print[Style["\nFigure written to ", Bold],
      FileNameJoin[{outDir, "donnan_figure_Mathematica.pdf"}]];

figure

```

Figure written to

/Users/pkuc2216/Sydney Uni Dropbox/Philip Kuchel/_MISCELLANY/RBC-ITPP
 260702/ITPP PAPER/_ITPP NATURE COMMUNICATIONS/donnan_figure_Mathematica.pdf

Out[136]=



