
NORDITA Discussion
22 February 2008


How I Happen to be Here
(on very short notice)

Late January 2008

Dear Dr McBride

I'm hoping that you might remember me from last year - I was the editor that worked with you on your News & Views article for *Nature*. I'm contacting you because I'm hoping that you might be able to offer me some advice, and, depending on the outcome, maybe write for us again.

Wim Noorduin

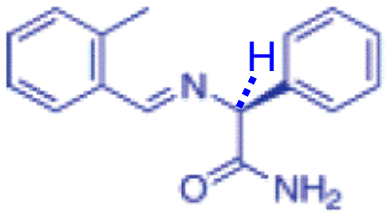
My question concerns a paper by Donna Blackmond and colleagues, "Emergence of a Single Solid Chiral State from a Nearly Racemic Amino Acid Derivative", which appeared recently online in the *Journal of the American Chemical Society.* I've attached a copy to this e-mail.

I understand that you did some of the earlier work in this area (studying similar effects in sodium chlorate), and so I was wondering if you could offer your advice on the following:

1. Do you find these observations convincing?

2. Do you think that this paper is worth reporting in News & Views?

(DBU = Base)

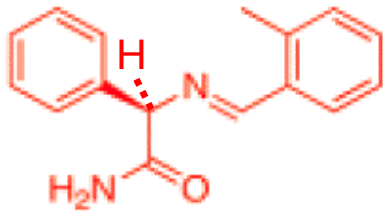


(*S*)-**1**

(*S*)-**1** (solid)

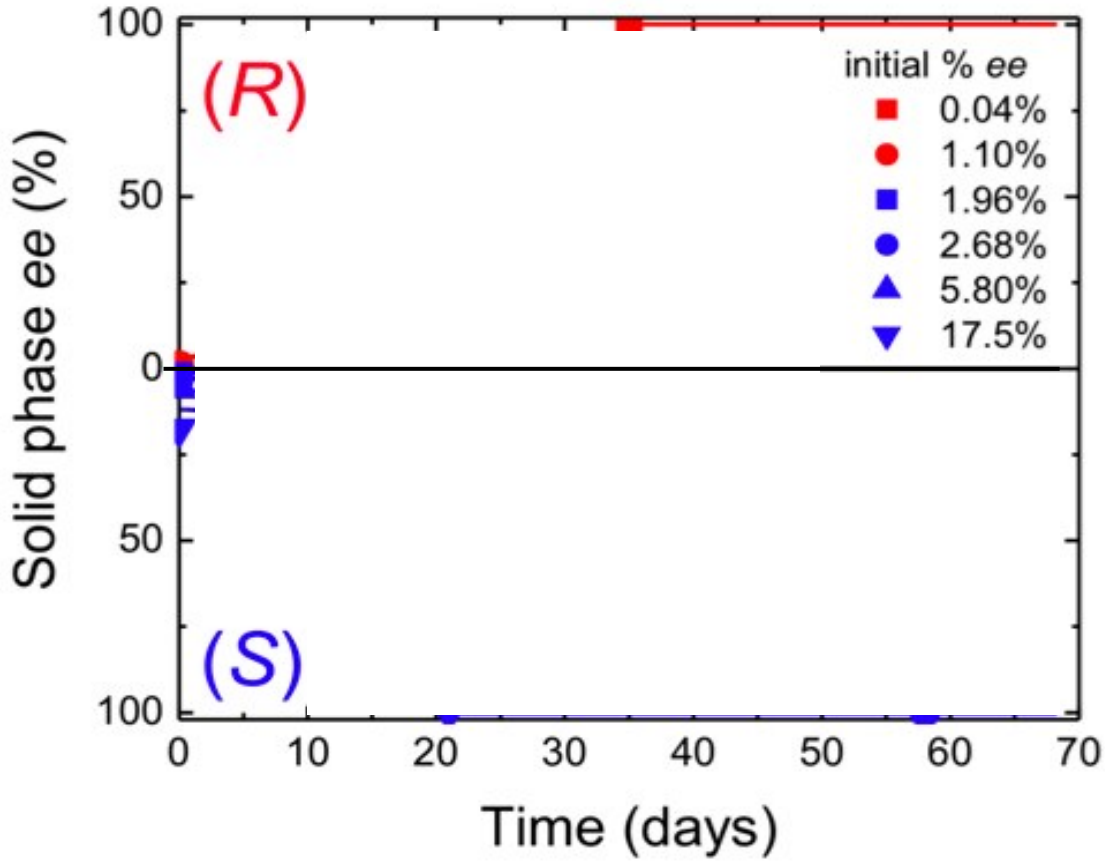
DBU

MeOH or MeCN
25 °C

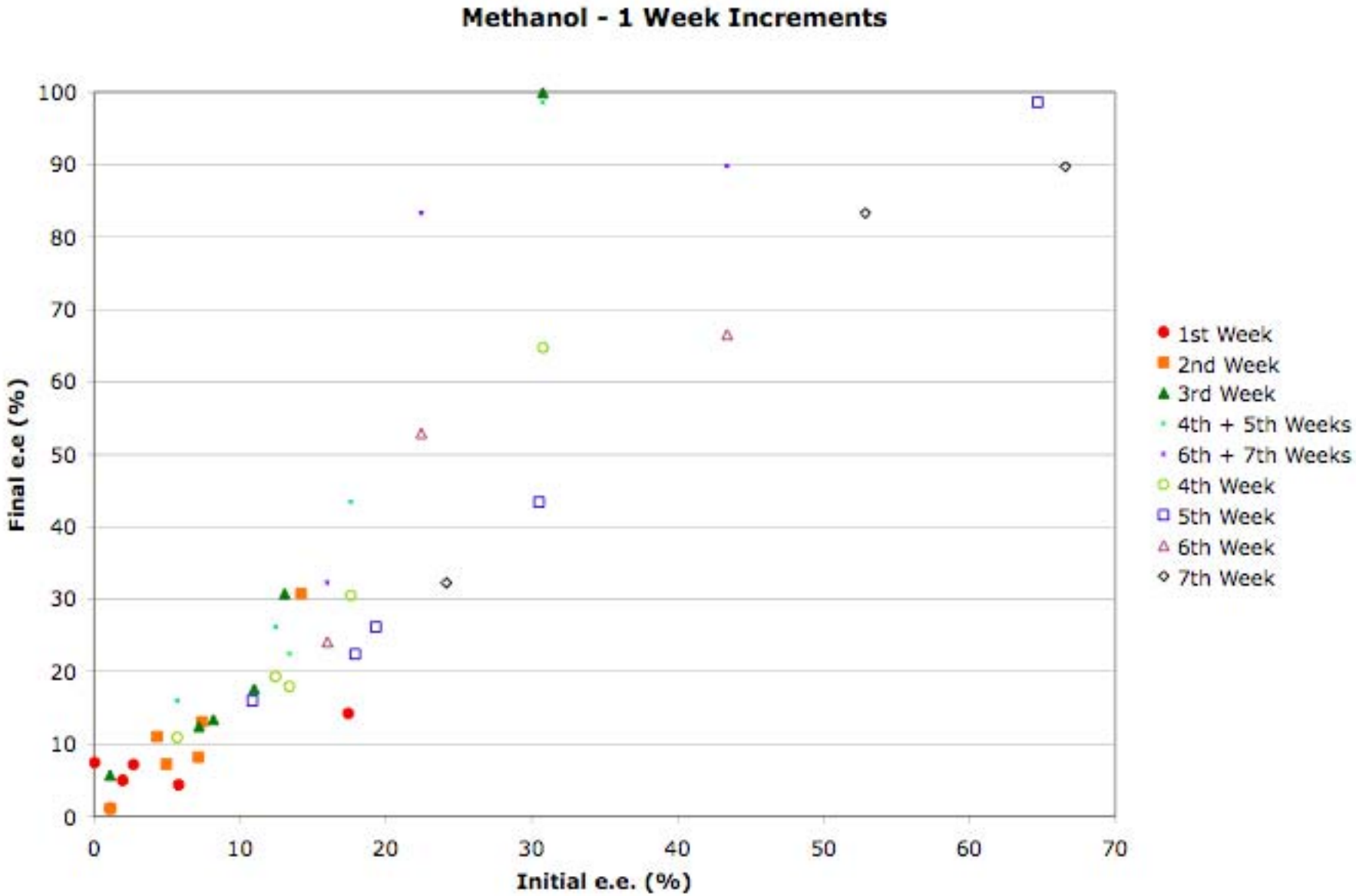


(*R*)-**1**

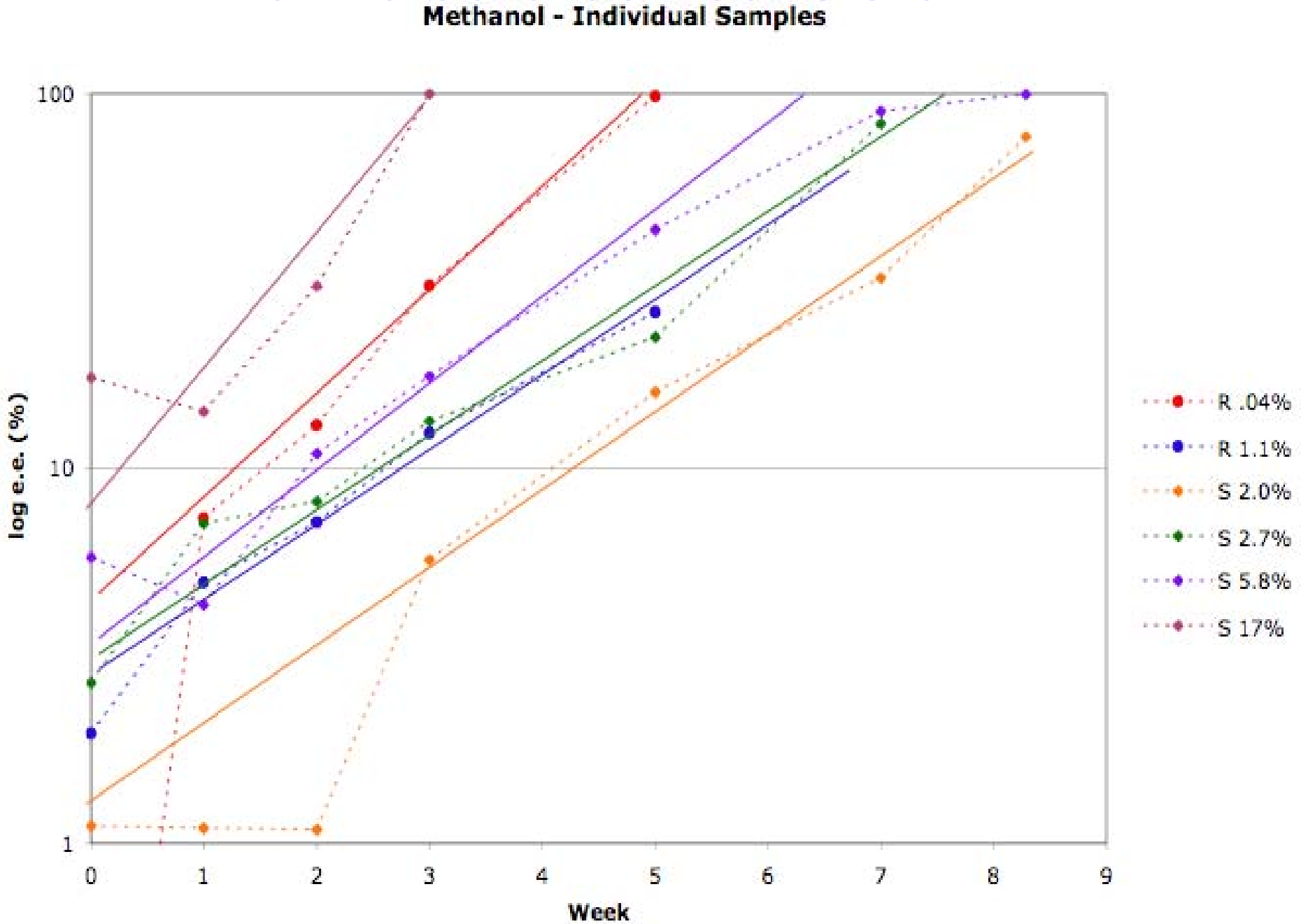
(*R*)-**1** (solid)



Are the data self consistent?



Are the data self consistent?



1. Do you find these observations convincing? √

2. Do you think that this paper is worth reporting in *News & Views*?

How does it work ?

Meir and I have granddaughters.

Mitochondrial Eve?

The matrilineal most recent common ancestor (MRCA) for all currently living humans. Passed down from mothers to offspring for over a hundred thousand years, her mitochondrial DNA (mtDNA) is now found in all living humans: every mtDNA in every living person is derived from hers. Mitochondrial Eve is the female counterpart of Y-chromosomal Adam, the patrilineal most recent common ancestor, although they lived at different times.She is believed to have lived about 140,000 years ago in what is now Ethiopia, Kenya, or Tanzania.

(Wikipedia)

Every other strain died out !

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Research Interests: Probability, stochastic processes, sequential analysis, statistical genetics, evolution, bioinformatics

With my limited intellectual resources I looked explicitly at a much simplified model where a crystal splits into two in each generation and the chance of survival for each descendent is 1/2. Also where crystals split into three with the survival chance of 1/3. Obviously both cases preserve the size of the population.

From this I infer that the chance of progeny survival after N+1 generations of splitting into M pieces is M^(-N).

I'm not sure exactly how to get from this to predicting the number of generations required to make a mixed population uniform, but it doesn't sound completely out of the question if the generation time might be measured in seconds or minutes, so there might be 10^4 generations in an experiment - especially if M is not tiny.

If this sounds interesting to you, I'd be eager to talk more and can provide experimental data (from the papers I've read).

Wright-Fisher Model of Population Genetics

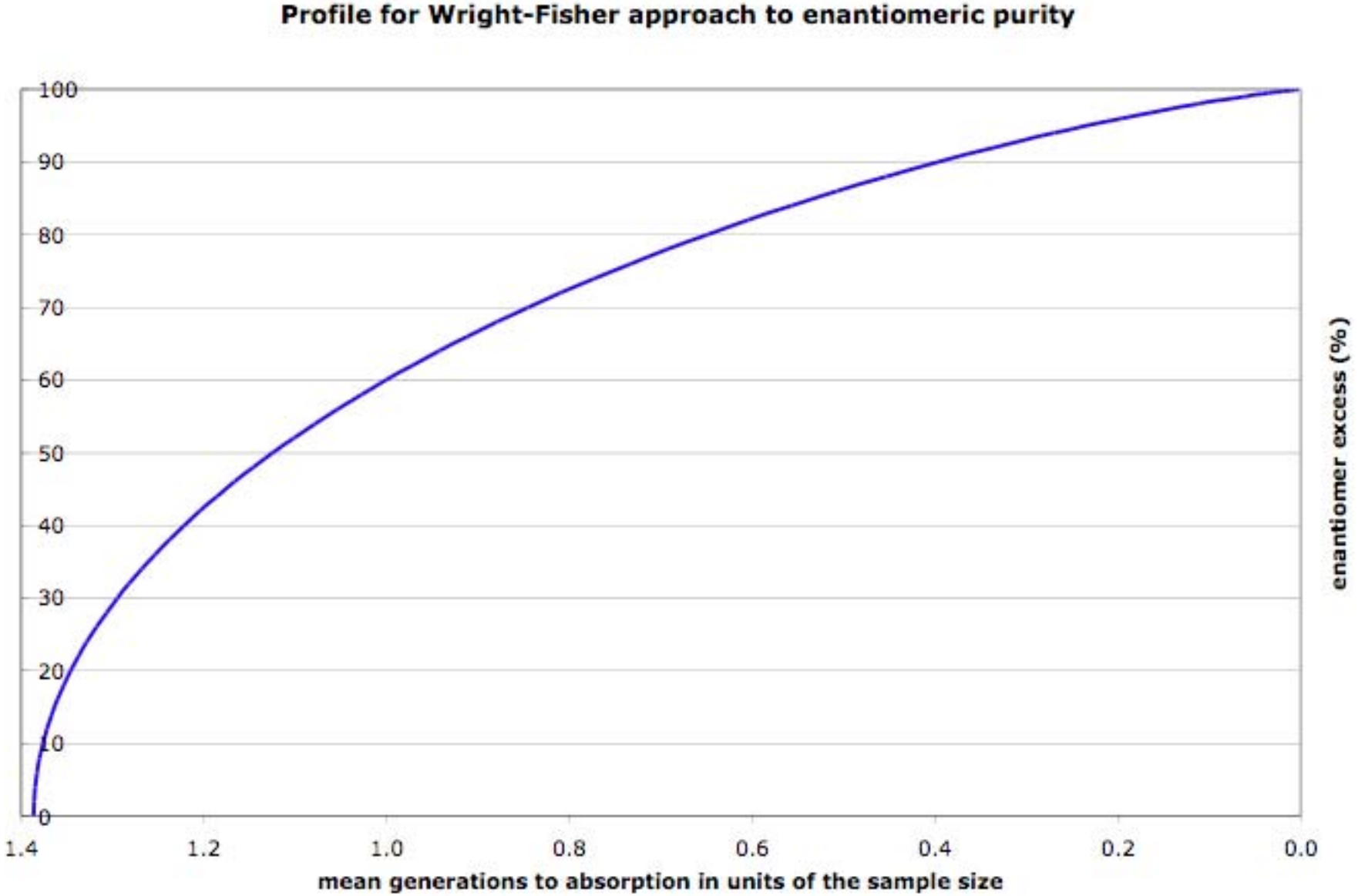
Hi Mike. Here's a bit from the last email:

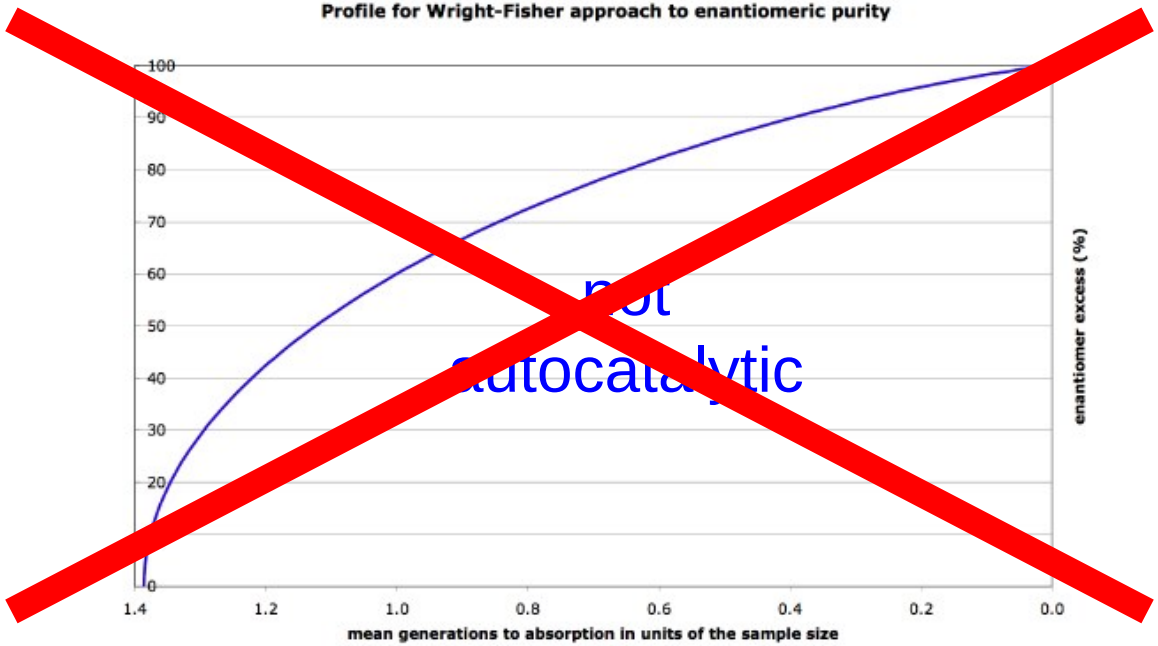
> In this W-F model, we consider an urn with a fixed number (say N) of balls, some white and some black. Say the number of white balls at time t is Wt. The urn at time t+1 is formed by sampling N times with replacement from the urn at time t, so that conditional distribution of the number of white balls at time t+1, given Wt, is Binomial with N trials, each of which has "success" probability Wt/N. In this case, it is as if each individual has a number of offspring that is approximately Poisson distributed with mean 1. Anyway, the number of generations for this model to become "absorbed" at Wt=0 or Wt=N (that is, all balls black or all balls white) is on the order of N generations. (The expected (mean) number would be N times an entropy-like function of W0/N, the initial fraction of white balls)

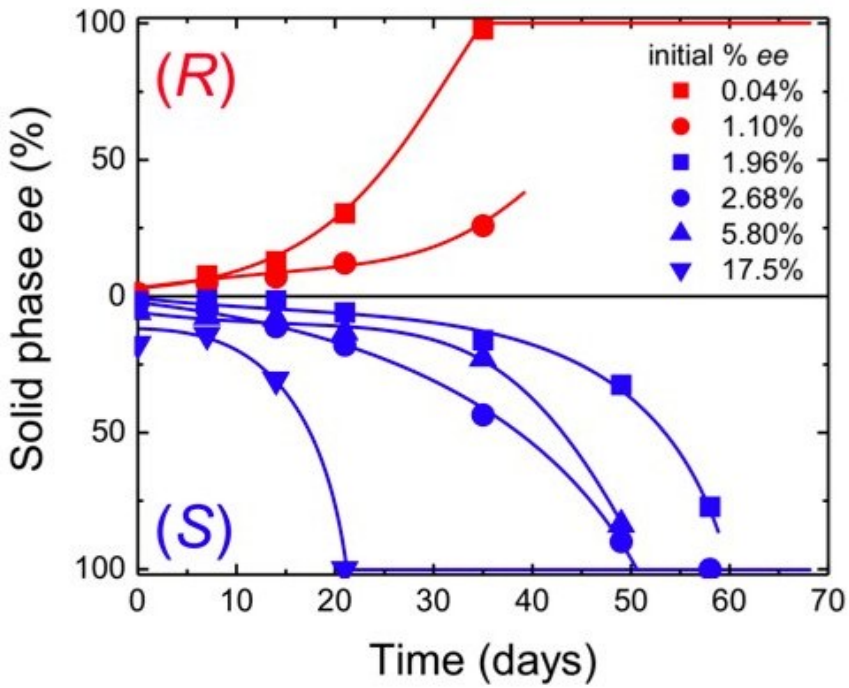
We were using W_t to denote the number of white balls at time t. Let's define X_t to be the fraction of white balls: $X_t = W_t / N$. I was saying that the mean time to absorption of the X process in the state 0 or 1 should scale like N, with a multiplicative factor that depends on the initial state X_0. That is, the expected time should look like $v(X_0) \cdot N$ for some function v. The function v is the solution of the differential equation $v''(x) = \dfrac{-2}{x(1-x)}$ with boundary conditions $v(0) = v(1) = 0$, which is $v(x) = -2[x \log x + (1-x)\log(1-x)]$ where here "log" is the natural log.

Another thing about this process that is intuitive is that if the initial state is x, the probability of being absorbed at the state 1 (all white balls) is also x (and probability $1-x$) for being absorbed in the state all black.

-Joe


Profile for Wright-Fisher approach to enantiomeric purity
100
90
80
70
60
50
40
30
20
10
0
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
mean generations to absorption in units of the sample size
enantiomer excess (%)


Profile for Wright-Fisher approach to enantiomeric purity
enantiomer excess (%)
mean generations to absorption in units of the sample size
not
autocatalytic


(R)
(S)
initial % ee
0.04%
1.10%
1.96%
2.68%
5.80%
17.5%
Solid phase ee (%)
Time (days)

E-mails with Elias Vlieg (and Wim Noorduin)

They kindly sent
their “Ostwald Ripening” preprint,
which Wim will present on Monday.

Makio
Uwaha

Nagoya

Cf.

Saito
&
Hyuga

Keio

Journal of the Physical Society of Japan
Vol. 73, No. 10, October, 2004, pp. 2601–2603

A Model for Complete Chiral Crystallization

Makio UWAHA*

Department of Physics, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8602

(Received July 12, 2004)

A simple reaction-type model that produces complete chiral symmetry breaking in crystallization is proposed. Crystals of homochirality are formed from achiral molecules. The model assumes i) perpetual mixing of the solution and abrasion of the crystals, ii) existence of chiral units smaller than the critical nucleus, iii) all processes have their counterparts, that is, decay of chiral units and crystals also occurs. We show that autocatalysis arises from the reaction of the chiral units so that chiral asymmetry is amplified as crystallization proceeds. Homochirality is achieved via slow relaxation in a later stage of crystallization.

(ii) There is a minimum size cluster that possesses chirality (we call it a chiral unit), and coalescence of the clusters forms a critical nucleus of the chiral crystal. The growth of chiral crystals proceeds via incorporation of the chiral units as well as that of achiral molecules.

Uwaha Model

(Ignores particle discreteness / size distribution)

Growth from Dissolved Material

Growth from Cluster Adsorption

Growth from Cluster Dissociation

Loss to Dissolved Material

Loss by Cluster Ablation

Crystal material

$$\frac{dx}{dt} = k_1 z x + k_u x_u x + k_c x_u^2 - \lambda_1 x - \lambda_u x, \quad (1)$$

$$\frac{dy}{dt} = k_1 z y + k_u y_u y + k_c y_u^2 - \lambda_1 y - \lambda_u y, \quad (2)$$

Cluster material

$$\frac{dx_u}{dt} = k_0 z^2 - k_u x_u x - k_c x_u^2 + \lambda_u x - \lambda_0 x_u, \quad (3)$$

$$\frac{dy_u}{dt} = k_0 z^2 - k_u y_u y - k_c y_u^2 + \lambda_u y - \lambda_0 y_u, \quad (4)$$

Dissolved material

$$\frac{dz}{dt} = -2k_0 z^2 - k_1 z x - k_1 z y + \lambda_1 x + \lambda_1 y + \lambda_0 x_u + \lambda_0 y_u, \quad (5)$$

Primary Nucleation

Cluster Dissolution

Ostwald - Schmostwald

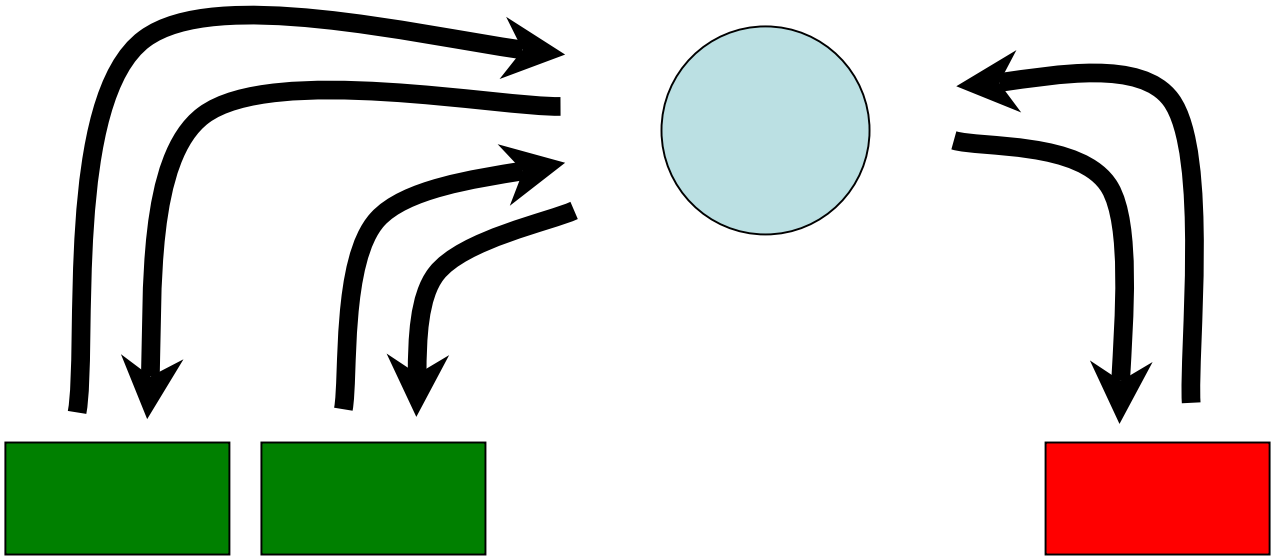
The only connection with Ostwald Ripening theory is that crystals grow, while clusters dissolve, each at a *fixed* rate.

Steady-State Visualization of the Drive to Chiral Purity in an Abraded Polycrystalline Conglomerate

Steady-State Analysis : Achiral Molecules

Static dissolution = crystallization

common solution pool

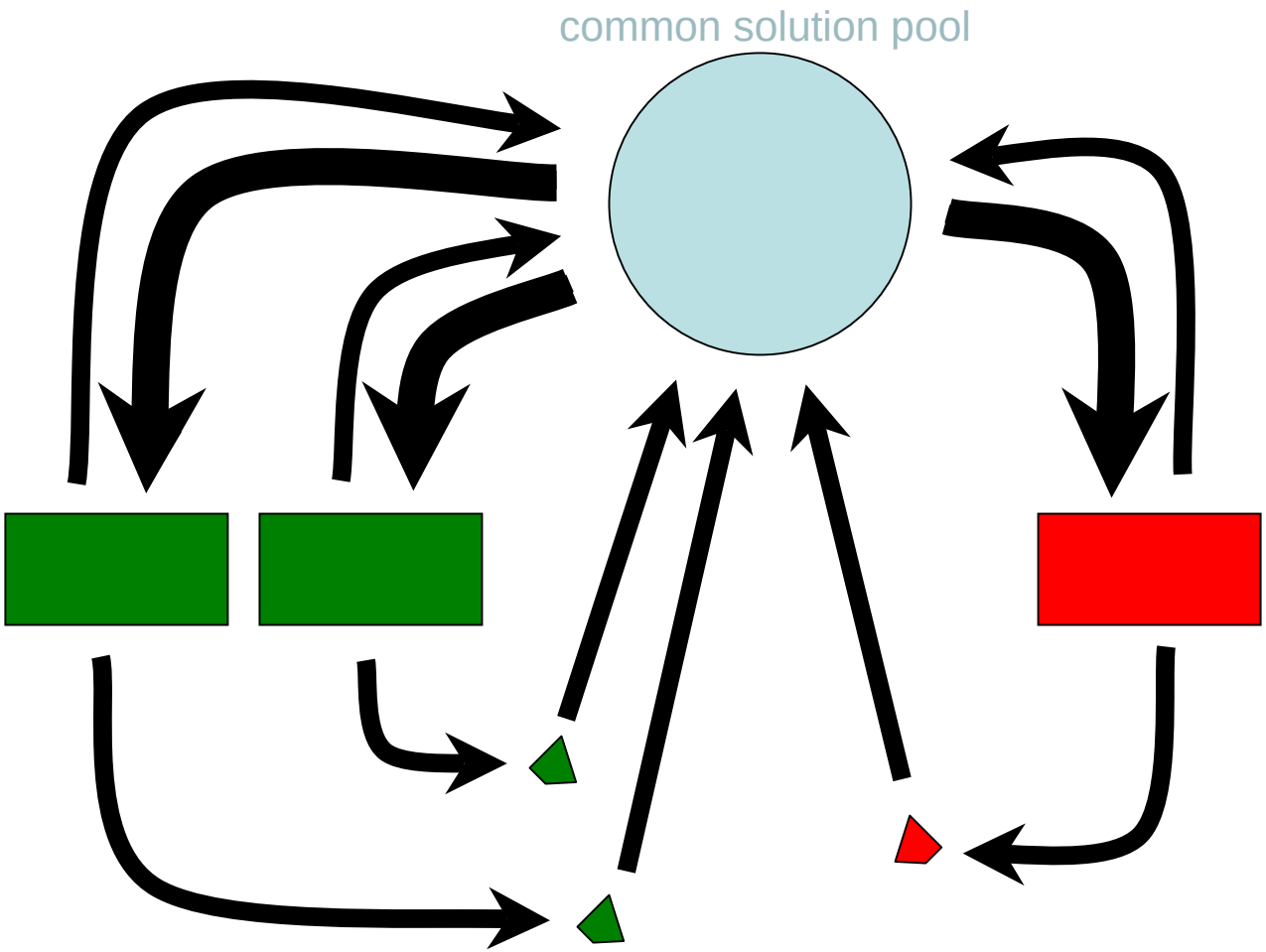


Left Crystals (same size) Right Crystal

Same rates for every crystal - Stable ratio

Steady-State Analysis : Achiral Molecules

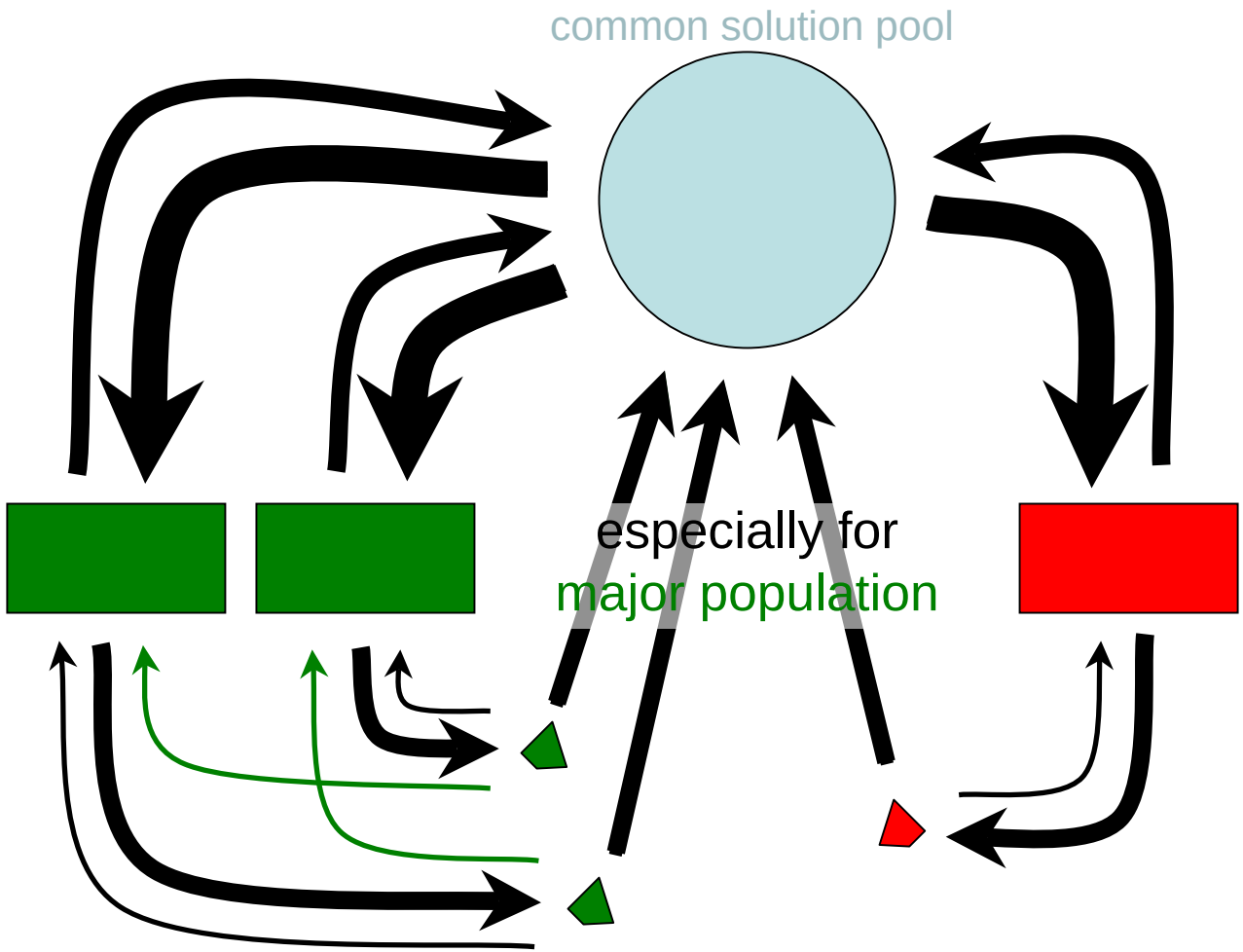
Ablation of subcritical fragments reinforces dissolution.



Same rates for every crystal - Stable ratio

Steady-State Analysis : Achiral Molecules

Reincorporation of subcritical fragments slows forced dissolution,



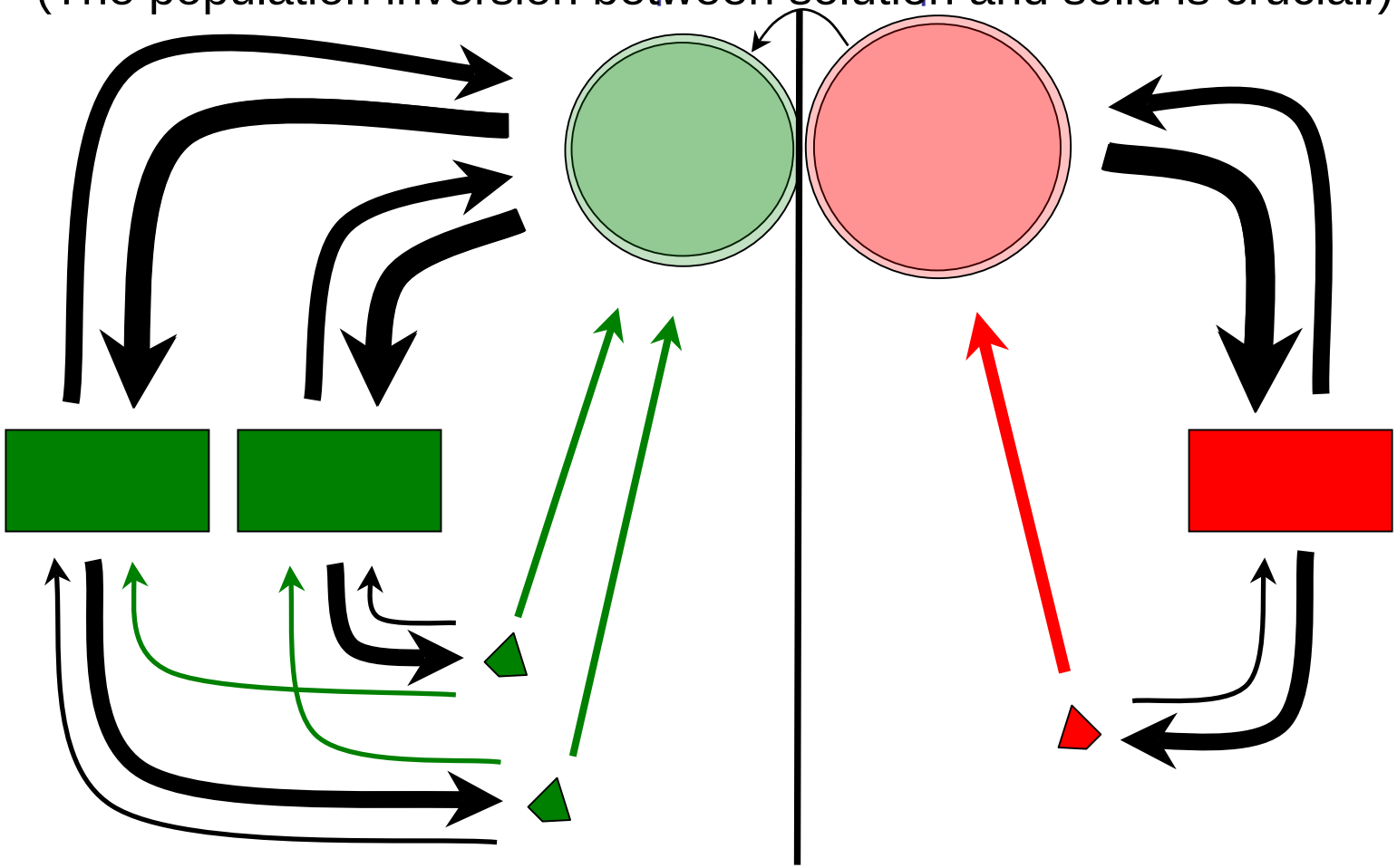
Faster dissolution of minor population feeds major population.

Conversion accelerates as the populations diverge.

Steady-State Analysis : *Chiral* Molecules

Base-catalysis drives major toward minor *in solution.*

(The population inversion between solution and solid is crucial.)

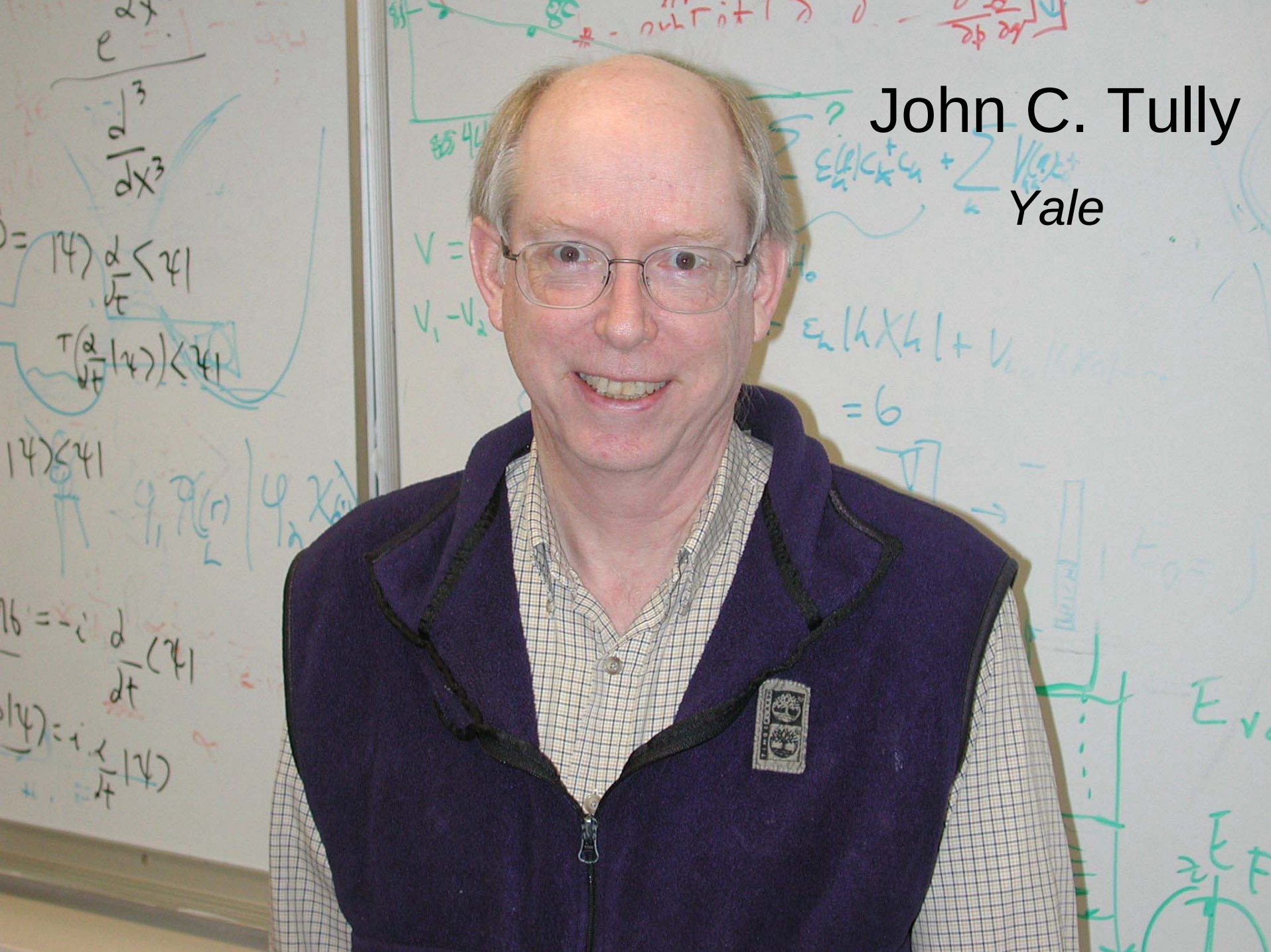


again

Faster dissolution of minor population feeds major population.

Whether the molecules in solution be chiral or achiral, retardation of dissolution by reincorporation of Uwaha's subcritical, chiral, abraded clusters drives the solid to chiral purity.

Note that nucleation need not enter this scheme, and that Ostwald ripening is neither necessary nor, in the absence of this reincorporation, sufficient to create a drive toward chiral purity in a polycrystalline sample.


John C. Tully
Yale

Uwaha Equations: M. Uwaha, *J. Phys. Soc. Jpn*. **73**,2601 (2004)

Species:

B^+ = # in big crystals (right handed)

S^+ = # in small crystals (right handed)

B^- = # in big crystals (left handed)

S^- = # in small crystals (left handed)

M = # of monomers (achiral)

T = total # of molecules = Σ *above*

Processes (Rate Constants):

Ablation of large Xtal (***A***)

Small-Large ***C***oalesce (***C***)

Small Xtals ***D***issolution (***D***)

Growth of large Xtals (***G***)

~~Small Xtal Nucleation (***F***)~~

$$dB^+/dt = -AB^+ + GB^+M + CB^+S^+$$

$$dS^+/dt = +AB^+ - DS^+ - CB^+S^+ + FM^n$$

$$dB^-/dt = -AB^- + GB^-M + CB^-S^-$$

$$dS^-/dt = +AB^- - DS^- - CB^-S^- + FM^n$$

$$dM/dt = -GB^+M - GB^-M + DS^+ + DS^- + 2FM^n$$

Uwaha Equations: M. Uwaha, *J. Phys. Soc. Jpn*. **73**,2601 (2004)

Species:

B^+ = # in big crystals (right handed)

S^+ = # in small crystals (right handed)

B^- = # in big crystals (left handed)

S^- = # in small crystals (left handed)

M = # of monomers (achiral)

T = total # of molecules = Σ *above*

Processes (Rate Constants):

Ablation of large Xtal (***A***)

Small-Large ***C***oalesce (***C***)

Small Xtals ***D***issolution (***D***)

Growth of large Xtals (***G***)

~~Small Xtal Nucleation (***F***)~~

Steady-State:

$$dB^+/dt = dS^+/dt = dB^-/dt = dS^-/dt = dM/dt = 0$$

Trivial solution:

$$B^+ = S^+ = B^- = S^- = 0\,, \qquad M = T$$

Uwaha Equations: M. Uwaha, *J. Phys. Soc. Jpn*. **73**,2601 (2004)

Species:

B^+ = # in big crystals (right handed)

S^+ = # in small crystals (right handed)

B^- = # in big crystals (left handed)

S^- = # in small crystals (left handed)

M = # of monomers (achiral)

T = total # of molecules = Σ *above*

Processes (Rate Constants):

Ablation of large Xtal (***A***)

Small-Large ***C***oalesce (***C***)

Small Xtals ***D***issolution (***D***)

Growth of large Xtals (***G***)

~~Small Xtal Nucleation (***F***)~~

Steady-State:

$$dB^+/dt = dS^+/dt = dB^-/dt = dS^-/dt = dM/dt = 0$$

Non-Trivial Solution:

$$B^- = S^- = 0$$

$$B^+ = \tfrac{1}{2}(T - D/C - A/C) \pm \tfrac{1}{2}\sqrt{(T - D/C - A/C)^2 - 4(AD/CG - TD/C)}$$

$$S^+ = AB^+/(CB^+ + D) \qquad M = AD/G(CB^+ + D)$$

Uwaha Equations: M. Uwaha, *J. Phys. Soc. Jpn*. **73**,2601 (2004)

Species:

B^+ = # in big crystals (right handed)

S^+ = # in small crystals (right handed)

B^- = # in big crystals (left handed)

S^- = # in small crystals (left handed)

M = # of monomers (achiral)

T = total # of molecules = Σ *above*

Processes (Rate Constants):

Ablation of large Xtal (***A***)

Small-Large ***C***oalesce (***C***)

Small Xtals ***D***issolution (***D***)

Growth of large Xtals (***G***)

~~Small Xtal Nucleation (***F***)~~

for physical solution:
quantity in square root must be > 0

Non-Trivial Solution:

$$B^- = S^- = 0$$

$$B^+ = \tfrac{1}{2}(T - D/C - A/C) \pm \tfrac{1}{2}\sqrt{(T - D/C - A/C)^2 - 4(AD/CG - TD/C)}$$

$$\Rightarrow \quad G > \frac{4AD}{(A+D)^2/C + T(C+2D-2A)}$$

"critical parameter value"

Excel Simulation