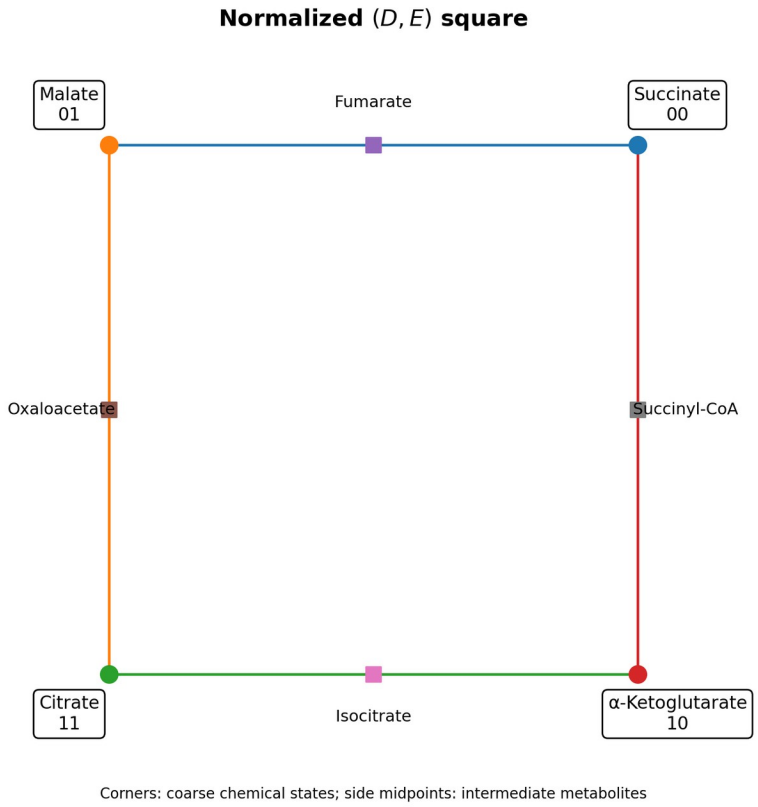
The Krebs Cycle and Bott Periodicity

A combinatorial research hypothesis based on contexts, Clifford involutions, and biochemical symmetry



The proposed common combinatorial skeleton: four corner states and four transition states.

Overview prepared for the Bott Periodicity project
September 2026

Status of the proposal

This document develops a research hypothesis. The biochemical facts and Clifford/Pascal calculations cited here are established or directly derivable. The claim that the Krebs cycle realizes Bott periodicity is not an established result in the literature and is presented as a falsifiable conjectural bridge.

Executive summary

The Krebs (citric-acid or TCA) cycle is conventionally described as an eight-reaction metabolic loop. Real Bott periodicity is an eightfold recurrence in topology and real Clifford algebra. Merely sharing the number eight would mean very little. The interesting question is whether the two systems share a more specific combinatorial mechanism.

The point of view developed here is that Bott periodicity can be read through a two-coordinate signed Pascal recursion. On the Boolean lattice of context subsets, reversion and Clifford conjugation give two canonical involutions. Their traces, denoted here E_n and D_n, obey $E_{n+1}=E_n+D_n$ and $D_{n+1}=D_n-E_n$. After a simple normalization, the pair (D_n,E_n) walks through the four corners and four edge midpoints of a square in eight steps.

Independently, if the Krebs cycle is started at succinate and every second metabolite is selected, the four metabolites succinate, malate, citrate, and alpha-ketoglutarate form a Gray-coded square under two elementary chemical bits: X=whether the carbon skeleton has more than four carbons, and Y=whether a non-carboxyl alcohol OH is present. Their codes are 00, 01, 11, 10. The four intervening metabolites - fumarate, oxaloacetate, isocitrate, and succinyl-CoA - occur exactly between these four corner states in the actual cycle.

A second and deeper biochemical feature concerns information loss. Succinyl-CoA has a chemically distinguished end; succinate is symmetric. Isotope models therefore treat reversed labeling orientations of succinate as equivalent or average them. In a symmetric/antisymmetric decomposition, the symmetrizing projection preserves the symmetric sector and annihilates the antisymmetric orientation distinction. This suggests a combinatorial narrative in which contexts successively create distinctions, a locally organized subsystem emerges, and closure requires forgetting enough information to return to the starting type.

What has been shown is therefore a set of exact mathematical correspondences and exact coarse chemical patterns. What has not been shown is that biochemical transition operators realize the full Clifford representation or that the TCA cycle is topological Bott periodicity in the technical K-theoretic sense. The strongest next tests are atom-resolved transition-operator calculations, uniqueness tests for the chosen chemical bits and phase origin, and a representation-theoretic test of whether the biochemical reset annihilates all nonconstant context characters or only one orientation character.

Core proposal

Read the eightfold clock as a four-state logical square at half-speed: corner, directed side, corner, directed side, and so on. The four corners carry two binary coordinates; the three nontrivial characters of those coordinates are the three sign rhythms ++--, +--+, and +-+-.

Guide to the document

- The viewpoint: context, distinction, and closure.
- The chemistry: all eight Krebs reactions, including stereochemistry and carbon provenance.
- The mathematics: Clifford sign rhythms, D_n and E_n, and the eight-point square.
- The proposed bridge: a Gray-coded chemical square and an eight-position subdivision.
- The reset mechanism: symmetric/antisymmetric decomposition at succinate.
- Partition/equivalence-relation model of an elementary self.
- Established facts, exact derivations, conjectures, and next tests.

1. The point of view: Bott periodicity as a cycle of distinctions

The usual Clifford-algebraic statement of real eightfold periodicity says, in one common convention, that adding eight real Clifford generators returns the same Morita type, with a 16-by-16 real matrix factor. This is standard and powerful, but it can obscure a smaller combinatorial mechanism when one is interested in finite logical or physical systems rather than stabilization itself. The present viewpoint separates multiplicity from type.

$$Cl_{n+8} \cong Cl_n \otimes M_{16}(\mathbb{R}) \qquad \text{(up to signature convention)}$$

The proposed combinatorial question is whether the eightfold return of type can be seen before interpreting the factor 16 as sixteen times as many meaningful physical dimensions. At the level of signed Boolean combinatorics, eight binary refinements rotate a two-coordinate signed trace by a full turn while multiplying its magnitude by 16.

1.1 Contexts and partitions

Let Ω be a set of latent histories. A context is an observable map c: Ω → A. Two histories are equivalent at a given stage when every currently available context gives them the same value. Thus a set of active contexts determines a partition Π of Ω. Adding context refines Π; forgetting context coarsens it.

$$\omega \sim_S \omega' \quad \Longleftrightarrow \quad \omega_i = \omega'_i \text{ for every active context } i \in S$$

An elementary self can then be modeled as a temporary equivalence structure: not a fixed lump of matter, but a system of maintained distinctions.

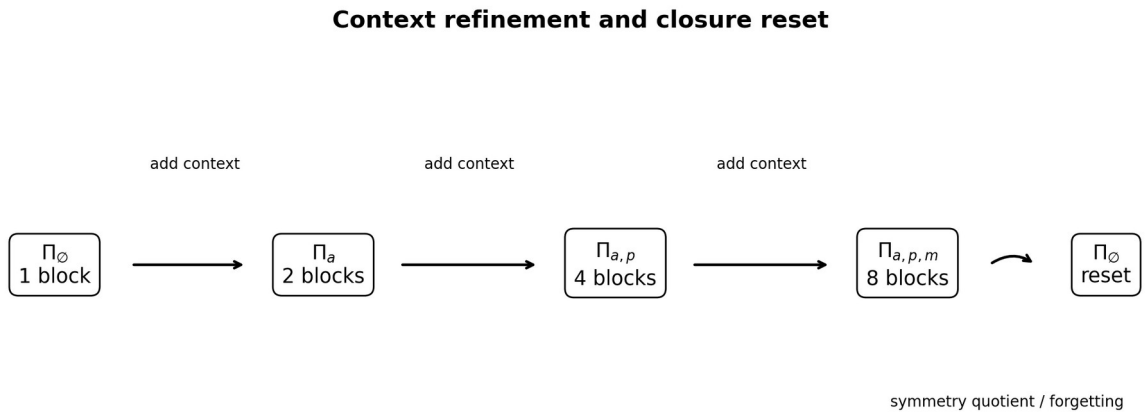


Figure 1. Context addition refines a partition; closure can coarsen it by identifying histories that the final state cannot distinguish.

1.2 Four corners and three nontrivial distinctions

Two independent binary contexts give the four-state set F_2^2. In Gray order: 00 → 01 → 11 → 10 → 00. The three nonzero linear characters are $(-1)^x$, $(-1)^y$, and $(-1)^{x+y}$.

$$\chi_x = (-1)^x, \qquad \chi_y = (-1)^y, \qquad \chi_{x+y} = \chi_x \chi_y$$

$$++\text{--}, \quad +\text{--}+, \quad +\text{-}+\text{-}$$

These are exactly the three sign rhythms that reappear as Clifford grade involution, reversion, and conjugation (up to ordering).

2. The chemistry: the complete eight-step Krebs cycle

The TCA cycle converts the acetyl group of acetyl-CoA into two CO2 molecules while generating reduced cofactors and GTP/ATP. It is conventionally represented as eight enzyme-catalyzed steps, ending with regeneration of oxaloacetate. The cycle is materially open: acetyl-CoA and oxidizing cofactors enter, while CO2, reduced cofactors, and usable chemical energy leave [1,2].

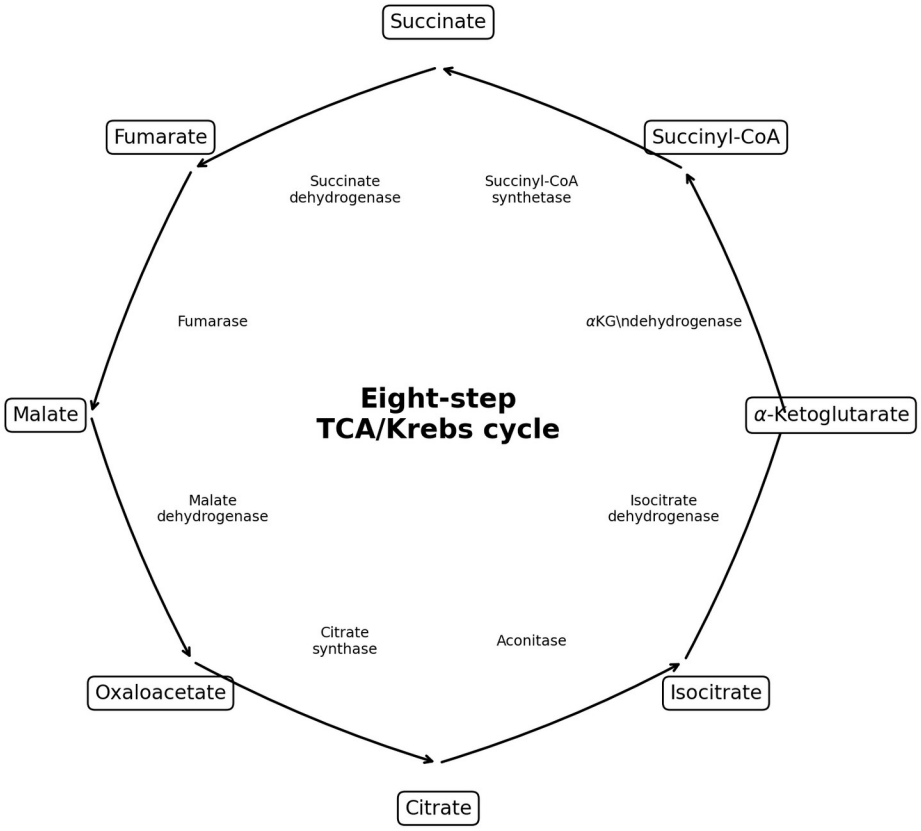


Figure 2. The eight canonical TCA/Krebs reactions, reordered to start at succinate for the combinatorial analysis.

Position	Reaction	Enzyme	Key change
0→1	Succinate → fumarate	Succinate dehydrogenase	Oxidation; reducing equivalents transferred
1→2	Fumarate → malate	Fumarase	Stereospecific hydration to S-malate
2→3	Malate → oxaloacetate	Malate dehydrogenase	Alcohol oxidized to carbonyl; NADH produced
3→4	Oxaloacetate + acetyl-CoA → citrate	Citrate synthase	C-C bond formation; 4C + 2C → 6C
4→5	Citrate ↔ isocitrate	Aconitase	Stereospecific isomerization
5→6	Isocitrate → α-ketoglutarate + CO2	Isocitrate dehydrogenase	Oxidative decarboxylation; NADH
6→7	α-Ketoglutarate → succinyl-CoA + CO2	αKG dehydrogenase	Oxidative decarboxylation; CoA added
7→0	Succinyl-CoA → succinate	Succinyl-CoA synthetase	CoA removed; substrate-level phosphorylation

2.1 Stereochemical information: citrate and fumarase

Citrate is prochiral. Because citrate synthase acts stereospecifically, the pro-S arm of citrate is acetyl-derived and the pro-R arm is oxaloacetate-derived [1]. Aconitase acts stereospecifically on this structure. At the other end of the cycle, fumarase hydrates symmetric fumarate stereospecifically to S-malate [1,7]. Thus the cycle repeatedly moves between symmetric/prochiral and oriented/chiral descriptions.

2.2 Carbon provenance

Atom-transition models used in 13C metabolic-flux analysis give a concrete way to trace carbon provenance. One standard representation writes oxaloacetate abcd plus acetyl-CoA ef as citrate dcbfea; subsequent decarboxylations lead from alpha-ketoglutarate abcde to the four-carbon succinate skeleton bcde [3].

$$OAA\ abcd + AcCoA\ ef \rightarrow citrate\ dcbfea \rightarrow \alpha KG\ abcde \rightarrow succinate\ bcde + CO_2$$

2.3 The special role of succinate symmetry

Succinate and fumarate have C2 symmetry. In isotope-flux models, this symmetry is often handled by averaging a positional labeling pattern with its reversal; one published model explicitly applies a transpose-average operation to account for scrambling caused by succinate symmetry [4]. Labeling experiments also found behavior compatible with molecular rotation during transfer [5]. Other experiments found partial orientation conservation, consistent with substrate channeling, so complete scrambling is not universal [6].

Important qualification

The chemical reset is not necessarily all-or-nothing. A realistic model may contain a memory parameter between complete orientation loss and perfect orientation preservation.

3. The mathematics: Clifford involutions and signed Pascal traces

Let a homogeneous Clifford monomial have degree r. Three canonical involutions act by signs depending only on r modulo 4. The formulas are standard [9-11].

Operation	Sign on degree r	r=0,…,7
Grade involution	$(-1)^r$	+ - + - + - + -
Reversion	$(-1)^{r(r-1)/2}$	+ + - - + + - -
Clifford conjugation	$(-1)^{r(r+1)/2}$	+ - - + + - - +

Conjugation equals grade involution composed with reversion, exactly paralleling the relation among the three nontrivial characters of F_2^2.

$$(-1)^{r(r+1)/2} = (-1)^r\,(-1)^{r(r-1)/2}$$

3.1 Boolean context space

Let V_n have basis e_S indexed by subsets $S \subseteq [n]$. Its dimension 2^n counts all context subsets. For $r=|S|$ define

$$R_n e_S = (-1)^{r(r-1)/2} e_S$$

$$C_n e_S = (-1)^{r(r+1)/2} e_S$$

Their traces are the signed Pascal sums

$$E_n = \mathrm{tr}(R_n) = \sum_{r=0}^{n} \binom{n}{r} (-1)^{r(r-1)/2}$$

$$D_n = \mathrm{tr}(C_n) = \sum_{r=0}^{n} \binom{n}{r} (-1)^{r(r+1)/2}$$

D_n and E_n are signed excesses, not total dimensions. Total context multiplicity is 2^n.

3.2 Adding one context forces the D/E recursion

A new context is either absent or present, so $V_{n+1}=V_n \oplus uV_n$. On the present copy, degree increases by one. This forces

$$R_{n+1} = \mathrm{diag}(R_n, C_n), \qquad C_{n+1} = \mathrm{diag}(C_n, -R_n)$$

Taking traces gives

$$E_{n+1} = E_n + D_n, \qquad D_{n+1} = D_n - E_n$$

$$\begin{pmatrix} D_{n+1} \\ E_{n+1} \end{pmatrix} = \begin{pmatrix} 1 & -1 \\ 1 & 1 \end{pmatrix} \begin{pmatrix} D_n \\ E_n \end{pmatrix}$$

Equivalently, $D_n+iE_n=(1+i)^{n+1}$. One refinement rotates normalized direction by 45 degrees and scales magnitude by $\sqrt{2}$. After eight refinements the direction returns and magnitude is multiplied by 16.

$$D_{n+8} = 16D_n, \qquad E_{n+8} = 16E_n$$

3.3 The square hidden in D_n and E_n

n	D_n	E_n	square-normalized
0	1	1	(+,+)
1	0	2	(0,+)
2	-2	2	(-,+)
3	-4	0	(-,0)
4	-4	-4	(-,-)
5	0	-8	(0,-)
6	8	-8	(+,-)
7	16	0	(+,0)
8	16	16	(+,+)

Dividing by $2^{[n/2]}$ gives the eight points on the boundary of a square, alternating corner and side midpoint. A different normalization, by Euclidean magnitude, gives the unit-circle 45-degree rotation. Both display the same period-eight direction.

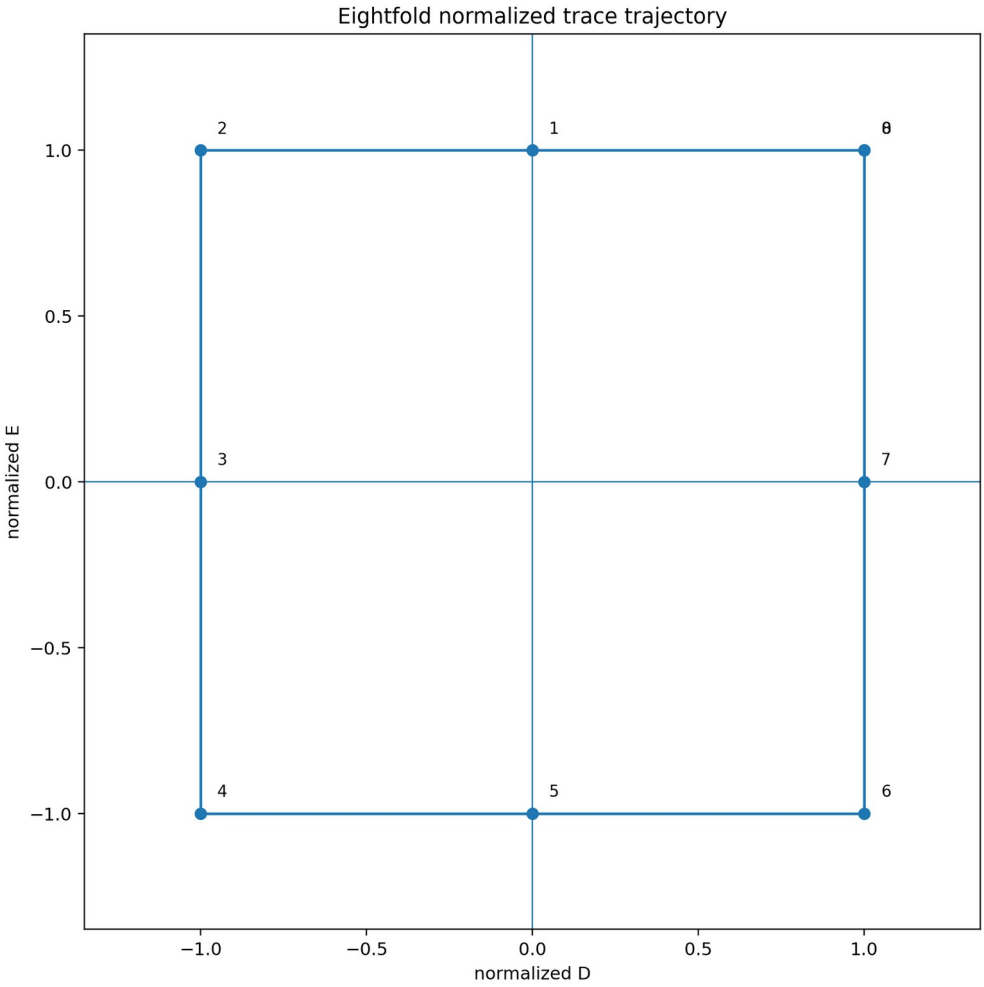


Figure 3. The normalized (D,E) trajectory: four corners and four side midpoints.

4. The proposed bridge: the Krebs cycle realizes the same subdivided square

Choose every second metabolite, beginning at succinate. Define two elementary chemical bits on these four coarse states:

X = 1 if the carbon skeleton has more than 4 carbons; else 0

Y = 1 if a non-carboxyl alcohol OH is present; else 0

Corner	**C atoms**	**Alcohol OH?**	**(X,Y)**	**$((-1)^Y,(-1)^X)$**
Succinate	4	No	00	(+,+)
Malate	4	Yes	01	(-,+)
Citrate	6	Yes	11	(-,-)
α-Ketoglutarate	5	No	10	(+,-)

Succinate 00 → Malate 01 → Citrate 11 → αKG 10 → Succinate 00

This is exactly the Gray-coded square. The four metabolites omitted by taking every second state are precisely the actual intermediates between those corners: fumarate, oxaloacetate, isocitrate, and succinyl-CoA.

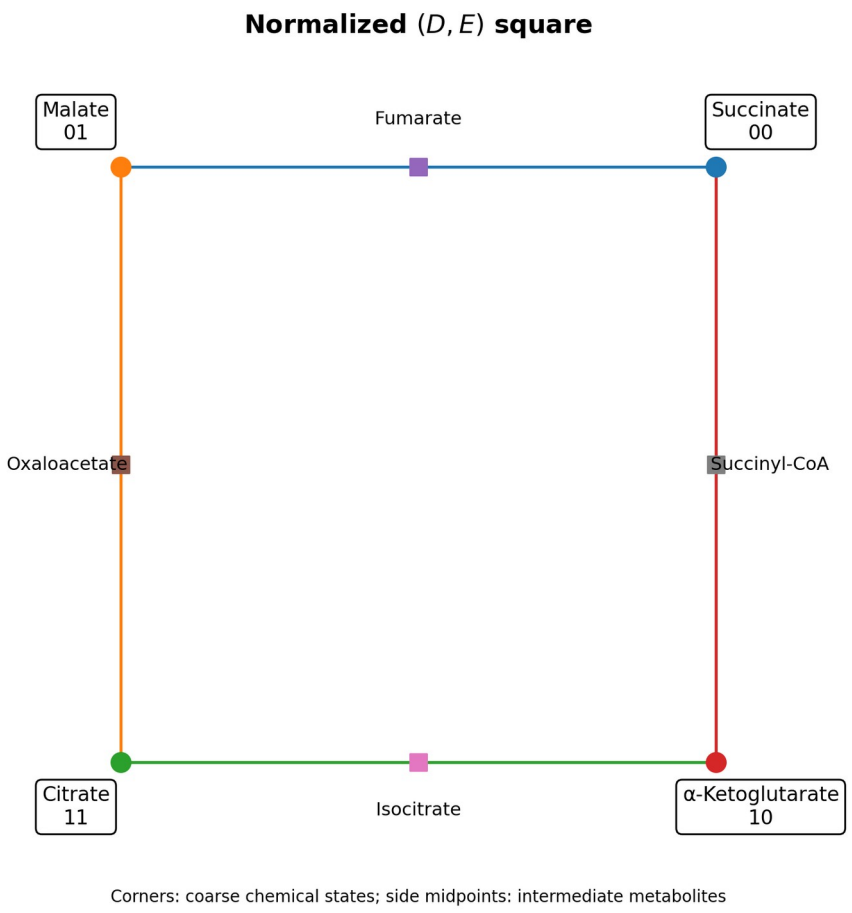


Figure 4. The common square: chemical corner states, chemical transition states, and normalized D/E positions.

This is the strongest exact coarse correspondence found so far. It uses only carbon count, presence of a non-carboxyl alcohol, and the known ordering of the intermediates. A 13C cardiac model independently used citrate, alpha-ketoglutarate, succinate, and malate as four crucial reduced states [8], although it made no Bott-periodicity claim.

4.1 Eight biochemical positions versus eight mathematical positions

n	Metabolite	role	norm. (D,E)	Gray meaning
0	Succinate	corner	(+,+)	00
1	Fumarate	edge	(0,+)	00→01
2	Malate	corner	(-,+)	01
3	Oxaloacetate	edge	(-,0)	01→11
4	Citrate	corner	(-,-)	11
5	Isocitrate	edge	(0,-)	11→10
6	α-Ketoglutarate	corner	(+,-)	10
7	Succinyl-CoA	edge	(+,0)	10→00

5. The fourth side and the reset: symmetric versus antisymmetric information

The fourth macro-side is alpha-ketoglutarate → succinyl-CoA → succinate. An atom-transition model describes the decarboxylation schematically as abcde → bcde + a [3]. Succinyl-CoA has a marked thioester end; succinate is symmetric after CoA is removed.

5.1 Linear orientation space

Let L denote one provenance orientation and R its reversal, with ρL=R and ρR=L. Then

$$v_+ = L + R, \quad \rho v_+ = +v_+; \qquad v_- = L - R, \quad \rho v_- = -v_-$$

Complete observational symmetrization is

$$P_+ = \frac{I + \rho}{2}, \qquad P_+ v_+ = v_+, \qquad P_+ v_- = 0$$

Thus the cycle can erase a distinction without destroying matter: it preserves symmetric content while annihilating the information that says which end was which. This is the linear meaning of the reversal-averaging operations used in isotope models [4].

5.2 Partial memory

$$C_p = (1-p)I + p\rho, \qquad C_p v_- = (1-2p)v_-$$

The coefficient λ=1-2p is an orientation-memory parameter. Experimental evidence for partial orientation conservation [6] means the strict projection model should be treated as a limiting case, not a universal biochemical law.

5.3 Logical reading of the quotient

If L and R represent two values of one internally meaningful distinction, closure at symmetric succinate imposes L~R. On the antisymmetric sector this becomes x=-x, so x=0. The same algebra appears in a signed logical square whose closure relation is inconsistent, although the chemistry reaches it by quotienting rather than by negative holonomy.

$$x = \rho x \ \text{ and } \ \rho x = -x \quad \Longrightarrow \quad x = -x \quad \Longrightarrow \quad x = 0$$

Interpretive lesson

The chemistry supports “closure by forgetting” more directly than “closure by contradiction.” If forgotten opposites are translated into Boolean logic, the distinction and its negation become identified and the nontrivial two-valued logic collapses.

6. A partition/equivalence-relation model of an elementary self

Take a latent history space $\Omega = F_2^3$ with schematic bits a=orientation, p=provenance, and m=marked end. These are not asserted to be literal molecular registers. They index distinctions that can become available under successive chemical contexts.

stage	metabolite	contexts	partition	blocks	interpretation
0	Succinate	none	$\Pi_\varnothing$	1	orientation not distinguished
1	Fumarate	none	$\Pi_\varnothing$	1	symmetric potential state
2	Malate	a	Π_a	2	stereospecific orientation
3	Oxaloacetate	a	Π_a	2	asymmetry retained
4	Citrate	a,p	$\Pi_{a,p}$	4	new acetyl provenance
5	Isocitrate	a,p	$\Pi_{a,p}$	4	distinctions operational
6	α-Ketoglutarate	a,p	$\Pi_{a,p}$	4	history has consequences
7	Succinyl-CoA	a,p,m	$\Pi_{a,p,m}$	8	marked end; maximal articulation
8	Succinate	quotient/reset	coarser Π	1 strong model	endpoint context removed

The strong model takes the final map all the way back to one block: all contexts constitutive of the completed elementary self become unavailable after closure. The weak model asserts only the experimentally supported orientation quotient. These are distinct hypotheses.

6.1 Observable algebra

For a partition Π, let A(Π) be the real functions constant on each block. Refining Π enlarges A(Π). With two active bits a,p,

$$A_{a,p} = \mathrm{span}\{1, \chi_a, \chi_p, \chi_{a+p}\}$$

The three nonconstant characters are the three sign rhythms. A group-averaging reset kills precisely the characters that detect forgotten distinctions. Full averaging over F_2^2 leaves only the constant character; a single reversal quotient leaves more memory.

$$P_G f(\omega) = \frac{1}{|G|} \sum_{g \in G} f(g\omega)$$

7. A possible whole-cycle narrative

The following narrative fits the exact partition mathematics and several established chemical facts, but it is an interpretation rather than a standard biological description.

0. Succinate - indistinction. The relevant two orientations are symmetry-related. Some provenance/orientation information is unavailable.

1. Fumarate - potential distinction. The molecule remains symmetric, but its double bond can be acted on stereospecifically.

2. Malate - symmetry breaking by context. Fumarase selects S-malate. An asymmetric enzyme environment creates an oriented product from a symmetric substrate.

3. Oxaloacetate - internalized asymmetry. The explicit stereocenter disappears, but structural asymmetry remains available for the next stereospecific reaction.

4. Citrate - a new external distinction. Acetyl-CoA enters from the open environment. The six-carbon product carries a new old/new provenance distinction expressed through citrate prochirality.

5. Isocitrate - distinction becomes operational. Aconitase acts selectively on the prochiral structure; the distinction now changes what happens next.

6. α-Ketoglutarate - history accumulates. Oxidative decarboxylation gives consequences to prior provenance.

7. Succinyl-CoA - maximal local articulation. The four-carbon provenance pattern has a chemically distinguished thioester end; “which end is which” is maximally meaningful.

8=0. Succinate - closure by forgetting. CoA is removed and the product is symmetric. The endpoint context disappears and orientation-sensitive information can be averaged away.

> **Compact narrative**
>
> Open system → context creates distinctions → distinctions are combined and made operational → a locally organized subsystem becomes well defined → closure removes a constitutive context → antisymmetric information is erased → the organizational type can begin again.

This fits the biochemical fact that the TCA cycle is closed in the organization of its intermediates but open in matter and energy. What persists most naturally is a pattern of transformations rather than a fixed set of carbon atoms.

8. What has actually been shown

8.1 Established chemistry

- The TCA cycle has the eight canonical enzyme-catalyzed reactions summarized above [1,2].
- Citrate formation and aconitase chemistry are stereospecific; citrate has pro-R/pro-S arms with distinct acetyl/OAA provenance [1].
- Fumarase stereospecifically forms S-malate from fumarate [1,7].

- Atom-transition and isotope-flux models explicitly track carbon provenance through citrate, alpha-ketoglutarate, succinate, and malate [3,8].
- Succinate/fumarate symmetry can scramble positional labeling, and models often average reversed orientations [4,5]. Partial orientation conservation has also been observed [6].

8.2 Exact mathematics derived here

- The three rhythms ++--, +--+, and +-+- are the three nontrivial characters of F_2^2 and also the canonical degree-sign rhythms of Clifford involutions, up to ordering.
- The Boolean-lattice involutions R_n and C_n have traces E_n and D_n equal to the signed Pascal sums above.
- Adding one binary context forces $E_{n+1}=E_n+D_n$ and $D_{n+1}=D_n-E_n$.
- After normalization, (D_n,E_n) alternates through the four corners and four side midpoints of a square and returns after eight steps.
- The coarse Krebs states succinate, malate, citrate, and alpha-ketoglutarate form the same Gray-coded square under fixed chemical bits X and Y.
- The remaining four Krebs metabolites occupy the four intermediate positions in the actual cycle order.

8.3 Conjectural bridge

- That the biochemical eight-position cycle is a physical realization of the same Clifford/Bott clock rather than a structurally suggestive coincidence.
- That biochemical contexts realize the full signed involutions R_n and C_n, rather than only a coarse Gray square.
- That the succinate quotient supplies the biological analogue of a complete logical/Bott reset rather than only erasing one orientation observable.
- That the factor 16 should be interpreted in applications primarily as signed combinatorial multiplicity rather than physical dimensional enlargement.

9. What should be investigated next

1. Uniqueness of the Gray-square coding. Enumerate simple intrinsic binary properties of the eight metabolites and all cyclic phase choices. If many equally simple encodings exist, the match is less significant.

2. Atom-resolved fourth-side operator. Build the exact transition operator on carbon-label histories through alphaKG → succinyl-CoA → succinate → fumarate → malate, including measured orientation retention.

3. Character-survival test. Identify which Walsh characters survive one full biochemical turn. The strong-reset model predicts only the constant character survives; the weak model predicts nonconstant memory.

4. Clifford anticommutation test. Construct operators from biochemical state translations and sign observables and test whether natural pairs anticommute and square to ±1 across all eight stages.

5. D/E trace test. Define stage involutions from actual biochemical symmetries and compute traces without fitting them to the desired sequence.

6. Independent chemical coordinates. Check redox, carbon count, oxygenation, cofactor use, and thermodynamics for a second derivation of the same square or clock.

7. Comparative biology. Test TCA variants, reductive TCA, glyoxylate bypass, and conditions with altered enzyme channeling. A structural principle should predict how the clock changes.

8. Genuine KO/Clifford data. Ask whether the partition/character construction can recover the real/complex/quaternionic sequence, extension classes, or KO groups - not merely the number eight.

9. Isotope experiment. Use position-specific 13C tracers to estimate the antisymmetric memory parameter through the succinate/fumarate span under conditions that alter channeling.

10. Formal theorem. Abstract context refinements plus a closure coequalizer and prove when a four-state logical square, three characters, and an eight-stage corner/edge clock are forced.

10. Perspective

The productive comparison is not “both have eight stages.” It is: what is preserved, what distinctions are created, what information is forgotten, and how can a return of type coexist with nontrivial accumulated history?

On the mathematical side, signed Pascal refinement gives a genuine eightfold return of a two-coordinate type. On the chemical side, the TCA intermediates admit an unexpectedly exact coarse Gray square, and succinate symmetry supplies a concrete operation that can erase antisymmetric provenance information.

This suggests a general principle: periodic organization may require both refinement and forgetting. Contexts create a temporary logic of distinctions; closure identifies states that the closed subsystem can no longer distinguish. The reset allows the same organizational type to recur even though matter, energy, and detailed history have flowed through the system.

Strongest present claim

There is a nontrivial combinatorial correspondence between the signed Boolean/Clifford trace clock and a natural four-state/eight-position coarse-graining of the Krebs cycle. Whether this correspondence is an instance of real Bott periodicity in a substantive mathematical-physical sense remains open.

Appendix A. Compact derivation of the signed Pascal clock

$$R_n(S) = (-1)^{\binom{r}{2}}, \qquad C_n(S) = (-1)^{\binom{r+1}{2}}, \qquad r = |S|$$

Splitting subsets according to whether the new context is absent or present gives the block recursion above. Its trace matrix is

$$T = \begin{pmatrix} 1 & -1 \\ 1 & 1 \end{pmatrix}, \qquad T^8 = 16I$$

The same signs can be written as quadratic forms on the Boolean cube:

$$q_R(x) = \sum_{i<j} x_i x_j, \qquad q_C(x) = q_R(x) + \sum_i x_i \pmod 2$$

$$E_n = \sum_{x \in \mathbb{F}_2^n} (-1)^{q_R(x)}, \qquad D_n = \sum_{x \in \mathbb{F}_2^n} (-1)^{q_C(x)}$$

Thus D_n and E_n are quadratic Gauss sums on the Boolean cube. The quadratic term counts pairwise interactions among active contexts and simultaneously counts the swaps required to reverse a Clifford monomial.

References and source notes

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[4] “Delineation of substrate selection and anaplerosis in the tricarboxylic acid cycle of the heart by 13C NMR spectroscopy and mass spectrometry.” Transpose-average for succinate symmetry. Link

[5] “The mechanism of succinate or fumarate transfer in the tricarboxylic acid cycle allows molecular rotation of the intermediate.” Link

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End of overview