THE LIVING ADDRESS

Mating-Type Regulation in Yeast

The Loaded Address

Stephen Daubney
The Daubney Foundation · thedaubneyfoundation@gmail.com

In which a single cell carries the instructions for two different kinds of self, shows only one at a time, and can change which — not by gaining or losing genes, but by copying a silent stored copy into the one slot it reads — so that identity turns out to be, not what a thing owns, but which address it has loaded.

Tau (T) is the living fabric of time itself — the sole substance of which all physical reality is composed. Every particle, force, wavelength, and conscious experience is a structured configuration of T-flow. There is no gravity, no electromagnetic force, no strong nuclear force as separate entities: all are registers of the single T-field operating across dimensional levels. The conservation law $d\Sigma T=0$ governs all change: T is never created or destroyed, only redistributed.

Introduction — Through the Force of Time

The chapter that follows is, in the conventional telling, the regulation of mating type in yeast — the cassette mechanism by which a cell switches between the a and α states, and the combinatorial logic that specifies its three cell types. Read through the Universal Force of Time, it is differentiation reduced to essentials: identity is the loaded T-address, switched by reversible cassette-loading and named by combinatorial logic.

What makes a cell the kind of cell it is? Not the genes it owns — a liver cell and a skin cell carry the identical genome — but the genes it reads. Yeast makes this visible. A haploid cell carries the information for both mating types, a and α, and expresses only one; the two silent copies sit in stores (HML holds α, HMR holds a), and only the cassette in one active slot, MAT, is read. To switch type, the cell copies a silent store into MAT by gene conversion — overwriting the read-position while leaving the store intact. Nothing is gained or lost; only which coordinate is live changes, and the change is reversible.

Two further things complete the picture. The switch is remembered — a cell stays its new type through many divisions — because the loaded cassette sustains its own expression, the same fixed-point logic that held lambda's sleep. And the whole space of identities is named economically: a few regulators (a1, α1, α2) in different combinations specify all three cell types, with a1 and α2 together — present only in the diploid — shutting off the haploid programmes and licensing meiosis.

Here is the reading this book gives it. Identity is occupancy of an address, not ownership of it: the same genome reading a different T-coordinate becomes a different cell. Switching is reversible address-loading — a coordinate moved into and out of the read-position without loss, the same invertible operation as lambda's integration and excision. Memory of type is the loaded address holding its own gate open. And combinatorial control is address logic — a small basis of couplings spanning many states, the same economy by which {2, 3, 5, π} span the whole lattice. Three identities resolve on the prime 3, and the doubling of the address set (2N ↔ 1N) is gated to the combined diploid state. This is the whole principle of differentiation, small enough to see entire.

Carry this into the chapter: identity is the loaded T-address — which coordinate a cell reads, not which it owns — switched by reversible cassette-loading, held by the loaded coordinate expressing itself, and named by a few regulators combined. Every cell in a body is this writ large: one genome, many selves, each the field reading a different coordinate.

SECTION 16.1

The Loaded Address

The last chapter showed a body scheduling itself from within — keeping its own time, provisioning its own parts. This chapter asks a question that lies just beneath that one, and answers it with unusual clarity: what makes a cell the kind of cell it is? A cell of your liver and a cell of your skin carry the very same genome, letter for letter, and yet they are as different as two creatures. Identity is not written in which genes a cell owns, for they own the same ones. It is written in which genes a cell reads. And there is a humble organism — brewer's yeast, the same single-celled fungus that raises bread and ferments wine — in which this truth is laid so bare that we can watch a cell change what it is by moving one stretch of DNA into the place where it is read.

Yeast comes in kinds, called mating types, the way a species might have two sexes; and a yeast cell can switch from one type to the other within its own lifetime. It does not do this by acquiring new genes. It already carries the information for both types, sitting silent in its genome, and it shows one at a time. To switch, it copies a silent stored version of the other type into a single active slot — and the slot is the only place the cell reads. In the reading of this book, this is the plainest possible statement of what identity is: a cell's kind is the coordinate it currently has loaded and is expressing. The genome is the whole registry of possible selves; the active slot is the read-head; and what a cell is is simply which address the read-head is sitting on. Move the address, and you have changed the cell.

SECTION 16.2

Three Kinds of Yeast

Begin with the kinds themselves, for there are three, and the number will matter. Yeast can live as a single cell with one set of chromosomes — a haploid — and a haploid comes in two mating types, called a and α. Two haploids of opposite type can find each other and fuse, as egg and sperm fuse, to make a cell with two sets of chromosomes: a diploid, of type a/α. So there are three states in all: haploid a, haploid α, and diploid a/α. Each behaves differently. The two haploids seek and mate with their opposite; the diploid does neither — but it, and it alone, can do something the haploids cannot, which is to undergo the special reductive division called meiosis, splitting its double set back into four single-set spores, two of type a and two of type α.

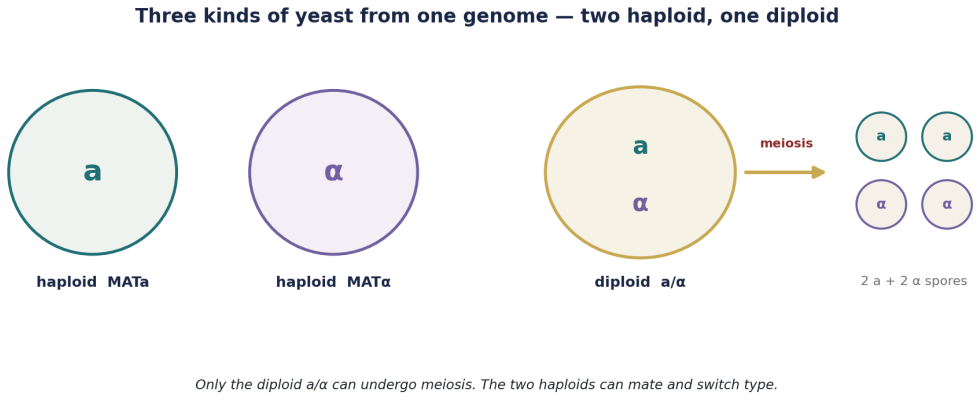

Figure 16.1. Three kinds of yeast from one genome. Haploid a and haploid α can mate; their fusion makes the diploid a/α. Only the diploid can undergo meiosis, dividing its doubled chromosome set back into four spores — two a and two α. Three identities, all from one registry of genes.

Hold on to that shape: three cell types, two of them single and one of them doubled, and only the doubled one able to halve itself again through meiosis. It is a small, closed system of identities — and, as we shall see, the whole of it is governed by a few molecules acting in combination, and the passage between the two haploid types is governed by the moving of a single cassette of DNA. Three states, resolved on the smallest odd prime; a doubled state that alone can run the halving. The lattice is already showing through the biology, and we have barely begun.

SECTION 16.3

Having Both, Showing One

Here is the first surprising fact, and it is the doorway to everything. A haploid yeast cell of type a does not lack the information for type α. It carries it — a complete, silent copy — tucked away in its genome, unread. Likewise a cell of type α carries a silent copy of the a information. Every haploid holds the instructions for both kinds of self and expresses only one. The difference between an a cell and an α cell is therefore not a difference in what genes they possess. It is a difference in which of the two stored sets is being read.

This is worth stating carefully, because it overturns the natural assumption. One might think a cell is a given kind because it has the genes for that kind and lacks the others. Not here. Here the cell has all the genes for all the kinds, and its identity is settled entirely by which set it is expressing. In the reading of this book, this is exactly the picture of the genome as a T-address registry that this whole part of the book has been building toward. The registry holds every coordinate a cell could be. Identity is not ownership of a coordinate but occupancy of it — the field reading one address rather than another. The same genome, reading a different T-address, becomes a different kind of cell. Yeast simply makes the principle visible by keeping the unread copies close at hand, ready.

SECTION 16.4

The Silent Cassettes

Now to the machinery, which is beautifully tidy. On one of its chromosomes the yeast cell carries three locations that all hold mating-type information, but only one of which is ever read. In the middle sits the active slot, called MAT: whatever cassette of information occupies MAT is the cassette the cell expresses, and so MAT’s content is the cell’s type. Flanking it, off to either side, are two silent stores — one, called HML, holding a quiet copy of the α information; the other, called HMR, holding a quiet copy of the a information. These stores are kept forcibly silent, wrapped in a form of the chromosome that the reading machinery cannot open. They are libraries, not broadcasts.

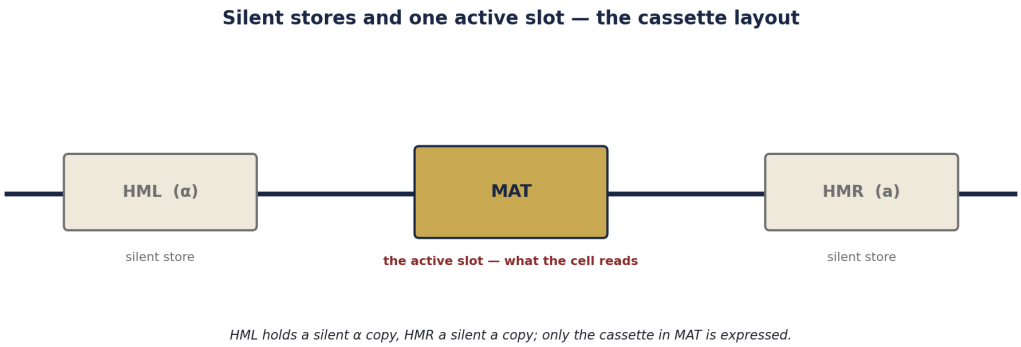

Figure 16.2. The cassette layout. Three locations hold mating-type information, but only the central slot MAT is read — its content is the cell's type. The flanking stores HML (a silent α copy) and HMR (a silent a copy) are held forcibly quiet: libraries kept ready, not expressed.

So the cell is built with its alternatives on the shelf. Whatever sits in MAT it broadcasts; whatever sits in HML and HMR it keeps in reserve, silent and safe. In the reading of this book, this is a registry with a single active read-position and a set of stored, silenced coordinates held ready beside it. The distinction between silent and active is not a difference in the information — the α copy in HML is a faithful copy of what an α cell reads at MAT — but purely a difference in position: in the store, unread; in the slot, read. Identity has been reduced to a matter of which coordinate is loaded, and the cell keeps the other coordinates one step away, waiting to be loaded in its place.

SECTION 16.5

Switching by Copy

Now the switch itself, and it is the crux of the chapter. When a yeast cell changes its mating type — from a to α, say — it does not edit the MAT slot letter by letter, and it does not swap chromosomes. It performs a copy. It takes the silent α information from the HML store and copies it into the MAT slot, overwriting whatever was there. The store is not consumed; it remains, a silent original, ready to be used again. Only the active slot changes. Before the switch, MAT held the a cassette and the cell was type a; after, MAT holds a fresh copy of the α cassette and the cell is type α — and the α store in HML is exactly as it was.

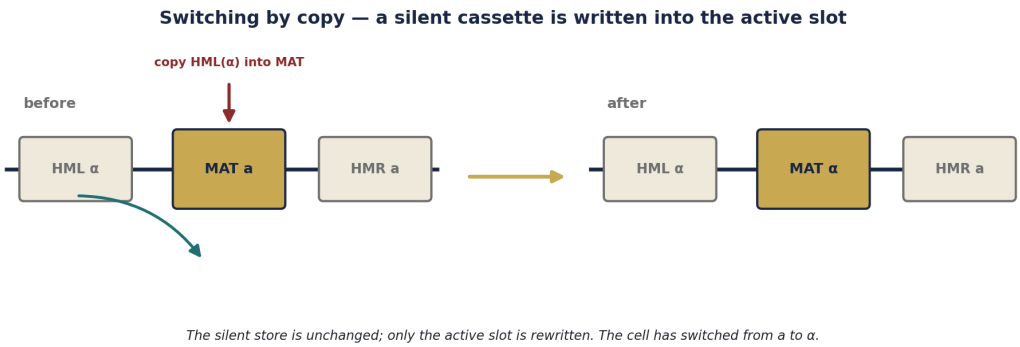

Figure 16.3. Switching by copy. To change type, the cell copies a silent cassette from a store (here HML's α) into the active MAT slot, overwriting the old content. The store is unchanged — only the read-position is rewritten. A cell of type a has become a cell of type α.

The molecular means is a process called gene conversion, in which one stretch of DNA is used as a template to rewrite another — here, the silent store rewriting the active slot. But the meaning, in this book's terms, is what matters. Switching is address-loading: the cell moves a coordinate from the store into the read-position, and the field begins to express the newly loaded address instead of the old. Nothing is created or destroyed — the α information existed all along in HML, and after the switch it exists in two places, store and slot — the change is purely a redistribution of which coordinate occupies the one place that is read. The conservation law is not strained by a change of identity, because a change of identity adds and removes no information; it only moves which information is live.

SECTION 16.6

Reversible Load and Unload

And because the switch is a copy that leaves the store intact, it is fully reversible. A cell that has switched from a to α can switch back, copying the a store from HMR into MAT and becoming a once more; and it can switch again, and again, as its circumstances warrant. The active slot is a socket into which either cassette can be loaded and from which either can be replaced — a read-position that accepts a coordinate, holds it, expresses it, and yields it up for another when the time comes. Load and unload, in and out, with the stores standing by unchanged.

We have seen this flavour of thing before, and it is worth naming the kinship. Lambda's genome, in the last chapter but one, folded into the host chromosome and cut cleanly back out; integration and its reverse, excision, were the two directions of one reversible reaction. Here, at the mating-type locus, a cassette is loaded into the read-slot and can be replaced by its opposite; loading and its reverse are the two directions of one reversible operation. In the reading of this book these are the same theme — a

coordinate moved into and out of an active position without loss — and both are instances of the field's operations being invertible by construction: what is loaded can be unloaded, what is written into the slot can be overwritten, and the registry is never diminished by the traffic.

KEY IDEA

A yeast cell's mating type is set by which cassette occupies one active slot, MAT. The cell carries silent stored copies of both types (HML holds α, HMR holds a) and expresses only the one in MAT. To switch type it copies a silent store into MAT by gene conversion — overwriting the read-position while leaving the store intact, so the change is reversible. And a few regulators (a1, α1, α2) acting in combination specify all three cell types. In this book: identity is the loaded T-address — not which coordinates a cell owns, but which one it currently reads — switched by reversible address-loading and named by combinatorial logic.

SECTION 16.7

The Memory of Type

A cell that has switched to type α stays type α — through division after division — until it switches again. The identity, once loaded, is remembered. And the reason is the same as the reason a lysogen remembers its sleep, met two chapters ago: the loaded cassette sustains its own expression. Whatever sits in MAT is read, and being read, it produces the regulators that maintain the very state it defines. The identity holds because the address in the read-slot keeps asserting itself. Take nothing away, add nothing, and the cell will go on being what it is, copying its type faithfully to its daughters, because the coordinate it has loaded goes on being expressed.

In the reading of this book this is the fixed-point logic we have already named — an address holding its own gate open — now doing the work of identity rather than of a viral switch. Memory of type is not a record kept in some separate ledger; it is the loaded coordinate continually expressing itself, moment to moment, so that the state persists because the state acts to persist. And this is exactly what a cell in a body must do to remain the kind of cell it is: hold its loaded address against the drift of time and the dilution of division. Yeast shows the mechanism naked. A cassette in a slot, read and re-read, is a self, remembered.

SECTION 16.8

A Few Regulators, Many States

There is one more layer, and it explains how three whole cell types — each a distinct programme of behaviour — can be specified without three separate control systems. The mating-type cassettes encode only a small handful of regulatory proteins, with the plain names a1, α1, and α2. These few proteins, acting in different combinations, name all three states. In a haploid a cell, the a1 protein is present and sets the a programme. In a haploid α cell, α1 switches on the α-specific genes while α2 switches off the a-specific ones. And in the diploid, where both cassettes are present, a1 and α2 come together and act as a pair to shut down the genes specific to either haploid state — turning off the mating behaviour and turning on the capacity for meiosis. Three regulators, three combinations, three identities.

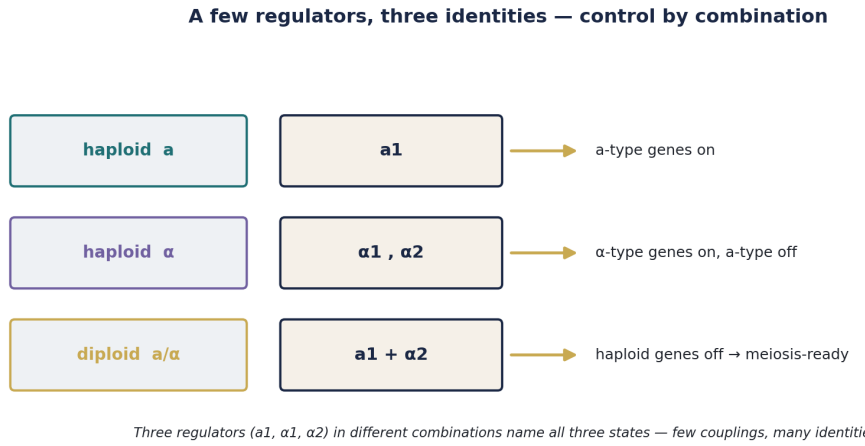

Figure 16.4. A few regulators, three identities. The cassettes encode just a1, α1 and α2. Different combinations name the states: a1 sets the a programme; α1 with α2 sets α; a1 with α2, present together only in the diploid, shuts off the haploid genes and readies meiosis. Few couplings, many selves.

This is combinatorial control, and it is one of the great economies of living things — the reason a genome with a limited set of regulators can specify a body with hundreds of cell types. In the reading of this book it is address logic, and it is deeply familiar. A small set of couplings, combined, spans a large set of distinct states — the same economy by which the four numbers of the lattice, {2, 3, 5, π}, combine to span the whole of the values in nature. The field does not need a separate machine for every identity; it needs a small basis and a rule for combining, and from those it computes many selves. Yeast computes three cell types from three regulators taken in pairs and singly. A developing animal, later in this story, will compute a whole body from not many more.

WORKED EXAMPLE · naming three selves from three regulators

Read the identity off the combination of regulators present. Haploid a: a1 present, no α proteins → a-specific genes ON → type a. Haploid α: α1 turns α-specific genes ON, α2 turns a-specific genes OFF → type α. Diploid a/α: both cassettes read, so a1 and α2 are both present and pair up → they jointly shut OFF the haploid-specific genes and license meiosis → type a/α. One basis of three proteins, combined singly and in pairs, names all three states — and only the combined (diploid) state can run the halving of meiosis.

SECTION 16.9

Three on the Prime, and the Doubled State

Step back and count. The whole system resolves into exactly three identities, and three — the smallest odd prime of the lattice, the number that has recurred through this book from the strong base pair to the codon to the genes that hold lambda's sleep — is the natural size of this smallest complete system of selves. Two of the three are single, the haploids; one is doubled, the diploid. And it is precisely the doubled state, the a/α, that alone can undergo the reductive halving of meiosis, splitting its two chromosome sets back into single ones. The doubling and the halving of the whole address set are gated to the combined identity.

In the reading of this book there is a pleasing rightness to this. Ploidy — the doubling and halving of the entire genome, two sets to one and back — is the coarsest T-operation a cell performs on its own registry, and here it is tied to the combined state, the one in which both haploid coordinates are loaded and read together. Only when the field holds both single-address states at once does it license the halving that returns them to singles. The a1–α2 pair is the molecular sign that both are present; and its presence is exactly the licence for meiosis. Identity, on the smallest odd prime; and the doubling of the address set, gated to the state that combines the primes. The bookkeeping of a yeast's selves is lattice bookkeeping.

SECTION 16.10

One Genome, Many Selves

Gather what the yeast has shown us, because it is a principle far larger than one fungus. Identity is the loaded address. A cell's kind is not fixed by the genes it owns — it owns them all — but by which of them it reads, and reading is a matter of which coordinate occupies the active slot. Change the loaded coordinate, by copying a stored one into the read-position, and you change the cell's kind; and the change is remembered because the loaded coordinate sustains its own expression; and the whole space of kinds is named, economically, by a few regulators combined. A

registry of possible selves, a movable read-slot, a memory that holds, and a combinatorial logic that names: these four are the whole of it.

And these four are the whole of differentiation itself — the process by which one fertilised egg becomes the many kinds of cell in a body. Every cell in you carries your entire genome, every coordinate of every possible self; and each has loaded and locked a particular set of addresses, reads them, remembers them, and so is a liver cell or a nerve cell or a cell of the blood. Yeast, with its two silent cassettes and one read-slot, is that vast process reduced to its irreducible core — small enough to see in full. In the reading of this book it is the field's registry operating at the level of the whole cell's identity: one genome, many selves, each of them the field reading a different coordinate, and each held in being by the reading.

SECTION 16.11

Why This Should Matter to You

You are one genome, worn as thousands of different selves. The cell that beats in your heart and the cell that senses light in your eye descend from the same first cell and carry the same complete set of instructions; they differ only in which of those instructions they have loaded and locked and go on reading. Everything the yeast showed — that identity is occupancy of an address, not ownership of it; that it can be switched by moving a coordinate into the read-position; that it is held by the loaded coordinate expressing itself — is, in richer and more guarded form, the very thing that makes and maintains the differences among your cells. You are a registry of possible selves, most of them silent in every cell, a chosen few loaded and live in each.

This matters most where identity is meant to be changed, or meant not to be. Medicine has learned, in our own age, to do deliberately what yeast does naturally: to reach into a cell and change which addresses it reads — to take a mature cell and load it back toward the unspecialised state of an egg, or to steer a cell from one identity toward another, the beginnings of a medicine that repairs by re-loading. And it matters gravely where identity slips of its own accord. When a cell loses hold of its loaded state — reads addresses it should keep silent, forgets the self it was meant to remember — it can become something it should not be; and a cell that has forgotten which coordinate to hold, and reads instead the coordinates of endless division, is a cell on the road this book will reach at its close. For now, hold this: you are not your genes alone, for every cell has the same ones; you are which of them each cell has chosen to read — a self that is a loaded address, and a body that is a great and orderly library of them.

The Numbers at a Glance

The parts of the system, and the reading the Force of Time gives each. Every biological fact is left exactly as measured.

Part of the system	What it is	The Force of Time reading
Three cell types	haploid a, haploid α, diploid a/α	three identities on the lattice prime 3
MAT (the active slot)	the one location that is read	the read-position — identity = the loaded address
HML and HMR	silent stored α and a copies	coordinates held ready, one step from the slot
Switching	copy a store into MAT (gene conversion)	reversible address-loading — no information gained or lost
Memory of type	the loaded cassette sustains itself	a fixed point — the address holding its own gate open
a1, α1, α2	a few regulators, combined	combinatorial address logic — a small basis spans many states
Diploid alone runs meiosis	2N ↔ 1N, gated to a/α	the doubling of the address set gated to the combined state

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