Chapter 4

Marcel Proust

The Method of Memory

Even a bureau crammed with souvenirs,
Old bills, love letters, photographs, receipts,
Court depositions, locks of hair in plaits,
Hides fewer secrets than my brain could yield.
It's like a tomb, a corpse-filled Potter's field,
A pyramid where the dead lie down by scores.
I am a graveyard that the moon abhors.

—Charles Baudelaire, LXXVI

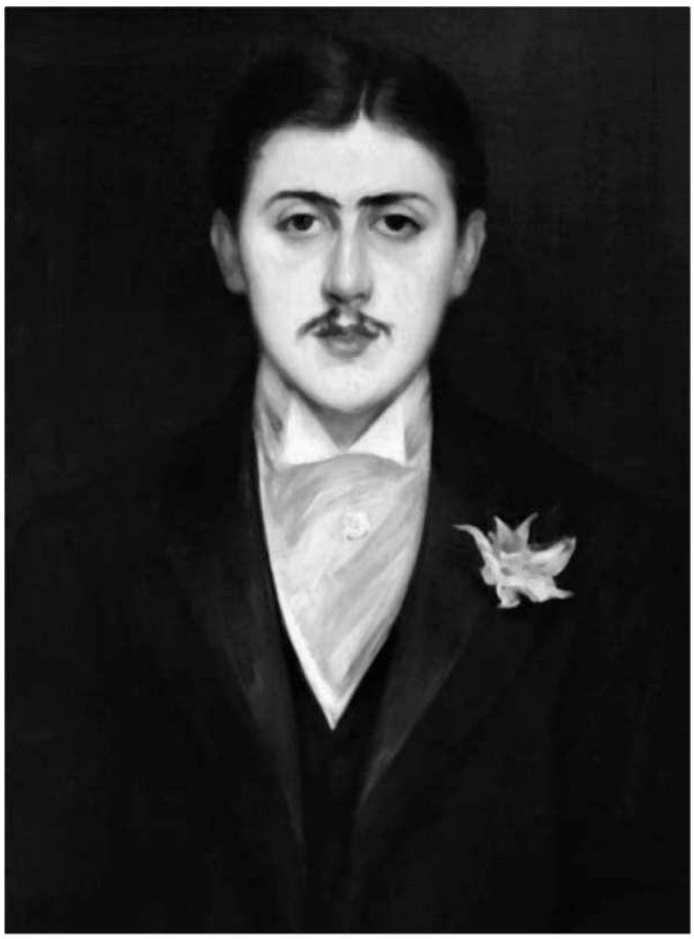
Proust's novel *In Search of Lost Time* is literal. In his fiction, Proust was searching for the hidden space where time stops. Obsessed with "the incurable imperfection in the very essence of the present moment," Proust felt the hours flowing over him like cold water. Everything was ebbing away. A sickly thirty-something, Proust had done nothing with his life so far except accumulate symptoms and send self-pitying letters to his mother. He wasn't ready to die.

And so, seeking a taste of immortality, Proust became a novelist. Deprived of a real life—his asthma confined him to his bedroom—Proust made art out of the only thing he had: his memory. Nostalgia became his balm, "for if our life is vagabond, our memory is sedentary." Proust knew that every time he lost himself in a recollection he also lost track of time, the tick-tock of the clock drowned out by the echoey murmurs of his mind. It was there, in his own memory, that he would live forever. His past would become a masterpiece.

Emboldened by this revelation, Proust began writing. And writing. And

writing. He disappeared into his drafts, emerging only, he said, "when I need help remembering." Proust used his intuition, his slavish devotion to himself and his art, to refine his faith in memory into an entire treatise. In the stuffy silence of his Parisian studio, he listened so intently to his sentimental brain that he discovered how it operated.

What sort of truth did Proust discover? It's a cliché to say that he described a very real milieu, a snapshot of Parisian society during the glory days of glamour. Other literary scholars focus on the style of his sentences, their rapturous roll and lulling cadences as he describes yet another dinner party. Proust covers vast distances within the space of periods (one sentence is 356 words long), and often begins with the obscure detail (the texture of a napkin or



A portrait of Marcel Proust by Jacques Emile Blanche, completed in 1892

the noise of water in the pipes) and ends with an inductive meditation on all things. Henry James, no slouch at verbosity himself, defined Proust's style as "an inconceivable boredom associated with the most extreme ecstasy which it is possible to imagine."

But all those beliefs in Proust's panache and artistic skill, while true, ignore the seriousness of his thoughts on memory. Although he had a weak spot for subclauses and patisserie, somehow, by sheer force of adjectives and loneliness, he intuited some of modern neuroscience's most basic tenets. As scientists dissect our remembrances into a list of molecules and brain regions, they fail to realize that they are channeling a reclusive French novelist. Proust may not have lived forever, but his theory of memory endures.

Intuitions

Proust wouldn't be surprised by his prophetic powers. He believed that while art and science both dealt in facts ("The impression is for the writer what experimentation is for the scientist"), only the artist was able to describe reality as it was actually experienced. Proust was confident that every reader who read his novel would "recognize in his own self what the book says ... This will be the proof of its veracity."

Proust learned to believe in the strange power of art from the philosopher Henri Bergson. When Proust began writing the Search, Bergson was becoming a celebrity. The metaphysician sold out opera halls, the intellectual tourists listening with rapt attention to his discussions of Élan-vital, comedy, and "creative evolution." The essence of Bergson's philosophy was a fierce resistance to a mechanistic view of the universe. The laws of science were fine for inert matter, Bergson said, for discerning the relationships between atoms and cells, but us? We had a consciousness, a memory, a being. According to Bergson, this reality—the reality of our self-consciousness—could not be reduced or experimentally dissected. He believed that we could only understand ourselves

through intuition, a process that required lots of introspection, lazy days contemplating our inner connections. Basically, it was bourgeois meditation.

Proust was one of the first artists to internalize Bergson's philosophy. His literature became a celebration of intuition, of all the truths we can know just by lying in bed and quietly thinking. And while Bergson's influence was not without its anxiety for Proust—"I have enough to do," he wrote in a letter, "without trying to turn the philosophy of M. Bergson into a novel!"—Proust still couldn't resist Bergsonian themes. In fact, Proust's thorough absorption of Bergson's philosophy led him to conclude that the nineteenth- century novel, with its privileging of things over thoughts, had everything exactly backward. "The kind of literature which contents itself with 'describing things,'" Proust wrote, "with giving them merely a miserable abstract of lines and surfaces, is in fact, though it calls itself realist, the furthest removed from reality." As Bergson insisted, reality is best understood subjectively, its truths accessed intuitively.

But how could a work of fiction demonstrate the power of intuition? How could a novel prove that reality was, as Bergson put it, "ultimately spiritual, and not physical"? Proust's solution arrived in the unexpected form of a buttery cookie flavored with lemon zest and shaped like a seashell. Here was a bit of matter that revealed "the structure of his spirit," a dessert that could be "reduced back into its psychological elements." This is how the Search begins: with the famous madeleine, out of which an entire mind unfolds:

> No sooner had the warm liquid mixed with the crumbs touched my palate than a shudder ran through me and I stopped, intent upon the extraordinary thing that was happening to me. An exquisite pleasure had invaded my senses, something isolated, detached, with no suggestion of its origin. And at once the vicissitudes of life had become indifferent to me, its disasters innocuous, its brevity illusory; it was me. I had ceased to feel mediocre, contingent, mortal. Whence could it have come to me, this all-powerful joy? I sensed that it was connected with the taste of the tea and the cake, but that

> it infinitely transcended those savours, could not, indeed, be of the same nature. Whence did it come? What did it mean? How could I seize it and apprehend it?
>
> I drank a second mouthful, in which I find nothing more than in the first, then a third, which gives me rather less than the second. It is time to stop; the potion is losing its magic. It is plain that the truth I am seeking lies not in the cup but in myself.

This gorgeous paragraph captures the essence of Proust's art, the truth wafting up like steam from a limpid cup of tea. And while the madeleine was the trigger for Proust's epiphany, this passage isn't about the madeleine. The cookie is merely a convenient excuse for Proust to explore his favorite subject: himself.

What did Proust learn from these prophetic crumbs of sugar, flour, and butter? He actually intuited a lot about the structure of our brain. In 1911, the year of the madeleine, physiologists had no idea how the senses connected inside the skull. One of Proust's deep insights was that our senses of smell and taste bear a unique burden of memory:

> When from a long distant past nothing subsists, after the people are dead, after the things are broken and scattered, taste and smell alone, more fragile but enduring, more unsubstantial, more persistent, more faithful, remain poised a long time, like souls, remembering, waiting, hoping, amid the ruins of all the rest; and bear unflinchingly, in the tiny and almost impalpable drop of their essence, the vast structure of recollection.

Neuroscience now knows that Proust was right. Rachel Herz, a psychologist at Brown, has shown—in a science paper wittily entitled "Testing the Proustian Hypothesis"—that our senses of smell and taste are uniquely sentimental. This is because smell and taste are the only senses that connect directly to the hippocampus, the center of the brain's long-term memory. Their mark is indelible. All our other senses (sight, touch, and hearing) are first processed by

the thalamus, the source of language and the front door to consciousness. As a result, these senses are much less efficient at summoning up our past.

Proust intuited this anatomy. He used the taste of the madeleine and the smell of the tea to channel his childhood. Just looking at the scalloped cookie brought back nothing. Proust even goes so far as to blame his sense of sight for obscuring his childhood memories in the first place. "Perhaps because I had so often seen such madeleines without tasting them," Proust writes, "their image had disassociated itself from those Combray days." Luckily for literature, Proust decided to put the cookie in his mouth.

Of course, once Proust began to remember his past, he lost all interest in the taste of the madeleine. Instead, he became obsessed with how he felt about the cookie, with what the cookie meant to him. What else would these crumbs teach him about his past? What other memories could emerge from these magic mouthfuls of flour and butter?

In this Proustian vision, the cookie is worthy of philosophy because in the mind, everything is connected. As a result, a madeleine can easily become a revelation. And while some of Proust's ensuing mental associations are logical (for example, the taste of the madeleine and the memory of Combray), others feel oddly random. Why does the cookie also bring to his mind "the game wherein the Japanese amuse themselves by filling a porcelain bowl with water and steeping in it little pieces of paper"? And whydoes a starchy napkin remind him of the Atlantic Ocean, which "swells in blue and bosomy undulations"? An honest chronicler of his own brain, Proust embraced such strange associations precisely because he couldn't explain them. He understood that idiosyncrasy was the essence of personality. Only by meticulously retracing the loom of our neural connections—however nonsensical those connections may be—can we understand ourselves, for we are our loom. Proust gleaned all of this wisdom from an afternoon tea.

The Lie of Yesterday

So there is time, and there is memory. Proust's fiction, which is mostly nonfiction, explores how time mutates memory. Just before Marcel takes a sip of his lime-flower tea, he issues a bleak warning to his reader: "It is a labor in vain to attempt to recapture memory: all the efforts of our intellect must prove futile..." Why does Proust think the past is so elusive? Why is the act of remembering a "labor in vain"?

These questions cut to the core of Proust's theory of memory. Simply put, he believed that our recollections were phony. Although they felt real, they were actually elaborate fabrications. Take the madeleine. Proust realized that the moment we finish eating the cookie, leaving behind a collection of crumbs on a porcelain plate, we begin warping the memory of the cookie to fit our own personal narrative. We bend the facts to suit our story, as "our intelligence reworks the experience." Proust warns us to treat the reality of our memories carefully, and with a degree of skepticism.

Even within the text itself, the Proustian narrator is constantly altering his remembered descriptions of things and people, particularly his lover Albertine. Over the course of the novel, Albertine's beauty mark migrates from her chin to her lip to a bit of cheekbone just below her eye. In any other novel, such sloppiness would be considered a mistake. But in the Search, the instability and inaccuracy of memory is the moral. Proust wants us to know that we will never know where Albertine's beauty mark really is. "I am obliged to depict errors," Proust wrote in a letter to Jacques Rivière, "without feeling compelled to say that I consider them to be errors." Because every memory is full of errors, there's no need to keep track.

The strange twist in the story is that science is discovering the molecular truth behind these Proustian theories. Memory is fallible. Our remembrance of things past is imperfect.

The dishonesty of memory was first scientifically documented by Freud, by accident. In the course of his psychotherapy, he dealt with a staggering number of women who traced their nervous hysterias back to sexual abuse in their childhood. To explain their confessions, Freud was forced to confront two equally dismaying scenarios. Either the women were lying, or sexual molestation was disturbingly common in bourgeois Vienna. In the end, Freud realized that the real answer was beyond the reach of his clinic. The psychotherapist would never discover what really happened, for the moment the women "remembered" their sexual abuse, they also created sincere memories. Even if their tales of abuse were fabrications, the women weren't technically lying, since they believed every word of it. Our recollections are cynical things, designed by the brain to always feel true, regardless of whether or not they actually occurred.

For most of the twentieth century, neuroscience followed Freud's pose of indifference. It wasn't interested in investigating the fictionality of memory, or how the act of remembering might alter a memory. Scientists assumed that memories are just shelved away in the brain, like dusty old books in a library. But this naive approach eventually exhausted itself. In order to investigate the reality of our past, in order to understand memory as we actually experience it, scientists needed to confront the specter of memory's lie.

Every memory begins as a changed connection between two neurons. This fact was first intuited by Santiago Ramon y Cajal, who won the Nobel Prize for Medicine in 1906. Cajal's scientific process was simple: he stared at thin slices of brain under a microscope and let his imagination run wild. (Cajal called his science a "speculative cavort.")—At the time, scientists assumed

that the human brain's neurons were connected in a seamless reticular web, like electrical wires linked in a circuit. Cajal, however, believed that every neuron was actually an island, entirely bounded by its own membrane (an idea that wasn't confirmed until electron microscopy studies in the 1950s). But if neurons don't touch, then how do they form memories and exchange information? Cajal hypothesized that the vacant gaps between cells—what we now call synaptic clefts—were the secret sites of communication. What Joseph Conrad said about maps is also true of the brain: the most interesting places are the empty spaces, for they are what will change.

Cajal was right. Our memories exist as subtle shifts in the strength of synapses, which make it easier for neurons to communicate with one another. The end result is that when Proust tastes a madeleine, the neurons downstream of the cookie's taste, the ones that code for Combray and Aunt Leonie, light up. The cells have become inextricably entwined; a memory has been made. While neuroscientists still don't know how this happens,* they do know that the memory-making process needs new proteins. This makes sense: proteins are the bricks and mortar of life, and a remembrance requires some cellular construction. The moment in time is incorporated into the architecture of the brain.

But in a set of extraordinary experiments done at NYU in 2000 by Karim Nader, Glenn Shafe, and Joseph LeDoux, scientists demonstrated that the act of remembering also changes you. They proved this by conditioning rats to associate a loud noise with a mild electrical shock. (When it comes to pain, the mind is a quick learner.) As predicted, injecting a chemical that stops new proteins from being created also prevented the rats from creating a fearful memory. Since their brains were unable to connect their context to the electrical shock, the shock was always shocking.

But Nader, LeDoux, and Shafe took this simple experiment one step

further. First, they made sure that the rats had a strong memory associating the shock with the noise. They wanted rodents that would cower in fear whenever the sound was played. After letting this memory solidify for up to forty-five days, they re-exposed the rats to the scary noise and injected a protein inhibitor into their brains. But what made their experiment different was its timing. Instead of interrupting the process of making a memory, they interrupted the process of remembering a memory, injecting the noxious chemical at the exact moment the rats were recalling what the noise meant. According to the dogma of remembrance, nothing much should have happened. The long-term memory should exist independently of its recall, filed away in one of the brain's protected file cabinets. After the poison is flushed out of their cells, the rats should remember their fear. The noise should still remind them of the shock.

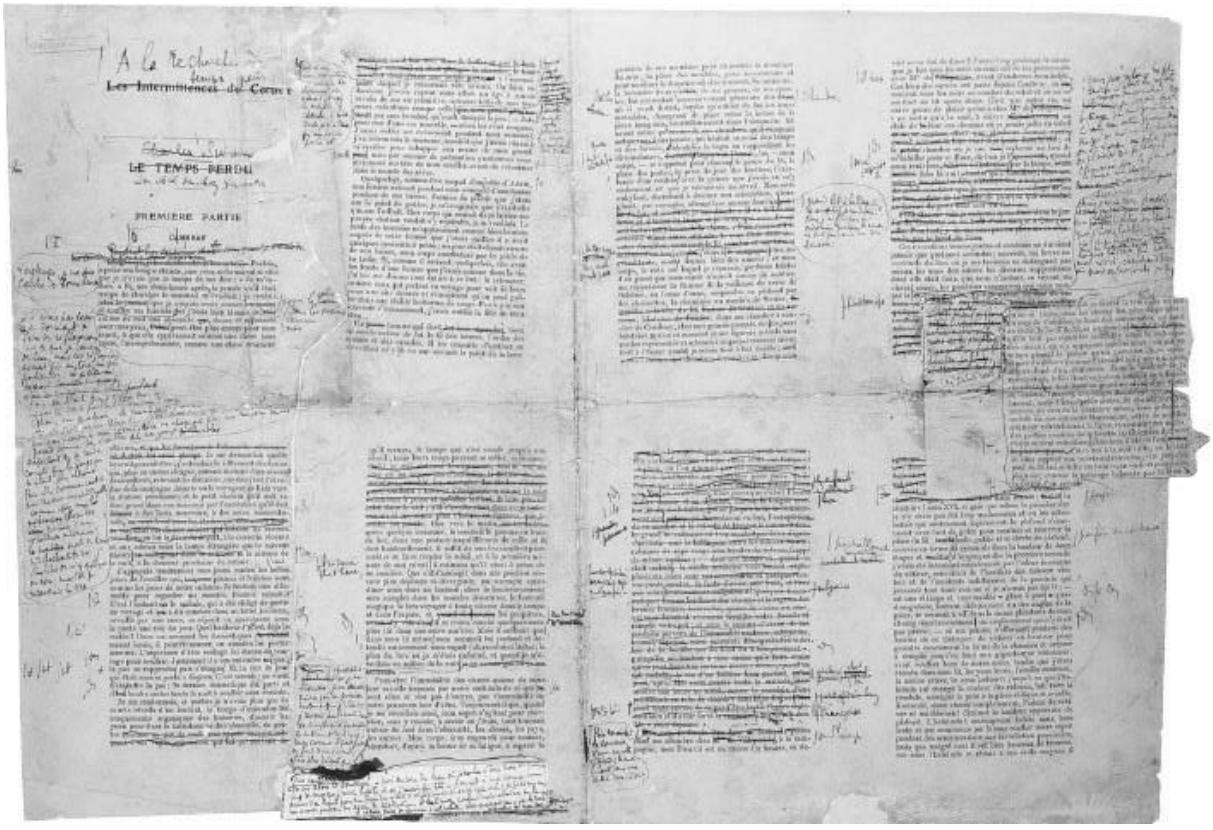
But this isn't what happened. When Nader and his group blocked the rats from remembering their fearful memory, the original memory trace also disappeared. After only a single interruption of the recollection process, their fear was erased. The rats became amnesiacs.

At first glance, this experimental observation seems incongruous. After all, we like to think of our memories as being immutable impressions, somehow separate from the act of remembering them. But they aren't. A memory is only as real as the last time you remembered it. The more you remember something, the less accurate the memory becomes.

The Nader experiment, simple as it seems, requires science to completely re-imagine its theories of remembering. It reveals memory as a ceaseless process, not a repository of inert information. It shows us that every time we remember anything, the neuronal structure of the memory is delicately transformed, a process called reconsolidation. (Freud called this process Nachtraglichkeit, or "retroactivity.") The memory is altered in the absence of

the original stimulus, becoming less about what you remember and more about you. So the purely objective memory, the one "true" to the original taste of the madeleine, is the one memory you will never know. The moment you remember the cookie's taste is the same moment you forget what it really tasted like.

Proust presciently anticipated the discovery of memory reconsolidation. For him, memories were like sentences: they were things you never stopped changing. As a result, Proust was not only an avid sentimentalist, he was also an insufferable rewriter. He scribbled in the margins of his drafts and then, when the margins over flowed, he supplemented his pages with paperoles, little cut pieces of paper that he would paste onto his original manuscript. Nothing he wrote was ever permanent. It was not uncommon for him to stop the printing presses at his own expense.



Page proof for the Search. The book had already been sent to the printer, but Proust insisted on making extensive changes.

Clearly, Proust believed in the writing process. He never outlined his stories first. He thought that the novel, like the memories it unfaithfully described, must unfurl naturally. While the Search began as an essay against the literary critic Charles Augustin Sainte-Beuve—Proust argued that literature cannot be interpreted in terms of the literal life of the artist—it quickly swelled into an epic about childhood, love, jealousy, homosexuality, and time. Then World War I intervened, the printing presses were turned into tanks, and Proust's novel, having no commercial outlet, metastasized from a formidable half a million words into a Talmudic 4 million words. At the same time, the love of Proust's life, Alfred Agnostelli, tragically crashed his plane into the sea. Proust lavished his grief on a whole new plot line in which the character Albertine, Alfred's doppelganger in the novel, also dies.

For a novel about memory, the plasticity of the novel's narrative was one of its most realistic elements. Proust was always refining his fictional sentences in light of new knowledge, altering his past words to reflect his present circumstances. On the last night of his life, as he lay prostrate in bed, weakened by his diet of ice cream, beer, and barbiturates, he summoned Celeste, his beloved maid, to take a little dictation. He wanted to change a section in his novel that described the slow death of a character, since he now knew a little bit more about what dying was like.

The uncomfortable reality is that we remember in the same way that Proust wrote. As long as we have memories to recall, the margins of those memories are being modified to fit what we know now. Synapses are crossed out, dendrites are tweaked, and the memorized moment that feels so honest is thoroughly revised. In his own lifetime, Proust never saw the complete Search printed. For him, the work would always remain malleable, just like a memory.

Before Nader created his forgetful rats in 2002, neuroscientists had avoided the murky area of remembrance and reconsolidation. Instead, scientists focused on meticulously outlining the molecules responsible for storing a memory. They

assumed that a memory was like a photograph, a fixed snapshot of a moment, so it didn't really matter how the memory was actually remembered. If only they had read Proust.

One of the morals of the Search is that every memory is inseparable from the moment of its recollection. This is why Proust devoted fifty-eight tedious pages to the mental state of the narrator before he ate a single madeleine. He wanted to show how his current condition distorted his sense of the past. After all, when Marcel was actually a child in Combray, eating madeleines to his heart's content, all he wanted was to escape his small town. But once he escaped, Marcel incessantly dreamed of recovering the precious childhood that he had so wantonly squandered. This is the irony of Proustian nostalgia: it remembers things as being far better than they actually were. But Proust, at least, was acutely aware of his own fraudulence. He knew that the Combray he yearned for was not the Combray that was. (As Proust put it, "The only paradise is paradise lost.") This wasn't his fault: there simply is no way to describe the past without lying. Our memories are not like fiction. They are fiction.

Proust's novels tantalizingly toy with the fictionality of memory in a very postmodern way: the narrator, who identifies himself as Marcel only once in three thousand pages, begins sentences with I. Like Proust, the narrator has translated Ruskin, dabbled in high society's parlors, and is now a sickly recluse writing In Search of Lost Time. And some characters, though Proust denied it to the bitter end, are thinly veiled acquaintances. In his books, fiction and reality are hopelessly intertwined. But Proust, always coy, denied this verisimilitude:

> In this book, in which every fact is fictional and in which not a single character has been based on a living person, in which everything has been invented by me according to the needs of my demonstration, I must state to the credit of my country that only Francoise's millionaire relatives, who interrupted their retirement in order to help their needy niece, are real people, existing in the world.

This passage comes toward the end of Time Regained, the last book of the Search. It is not a denial of the novel's mirroring of reality so much as an attempt to explode any investigation of it. Proust gives a sarcastic point of intersection (Francoise's millionaire relatives) as the sole meeting place of reality and literature, truth and memory. Proust here is being more than a little disingenuous. The novel and the life, the journalist and the fabulist, are really hopelessly blurred together. Proust likes it that way because that's how memory actually is. As he warned at the end of Swann's Way, "How paradoxical it is to seek in reality for the pictures that are stored in one's memory ... The memory of a particular image is but regret for a particular moment; and houses, roads, avenues are as fugitive, alas, as the years."

In this Proustian paradigm, memories do not directly represent reality. Instead, they are imperfect copies of what actually happened, a Xerox of a Xerox of a mimeograph of the original photograph. Proust intuitively knew that our memories required this transformative process. If you prevent the memory from changing, it ceases to exist. Combray is lost. This is Proust's guilty secret: we have to misremember something in order to remember it.

Sentimental Proteins

Some memories exist outside time, like magic carpets folded delicately in our mind. Unconscious recollection is at the heart of Proust's model of memory because even as our memories define us, they seem to exist without us. When Swanns Way begins, Proust has forgotten all about the sugary pastries of his childhood. Com-bray is just another Parisian suburb. But then, when he eats the madeleine that reminds him of Aunt Leonie, and the scent of the tea conspires with the texture of the napkin, the memory returns to haunt him, like a ghost. Lost time is found. Proust worshipped these sudden epiphanies of the

past because they seemed more truthful, less corrupted by the lies of the remembering process. Marcel is like the boy described by Freud who liked to lose his toys because he so loved to find them.

But how do these unconscious memories persist? And how do we remember them after they have already been forgotten? How does an entire novel, or six of them, just hide away in the brain, waiting patiently for a madeleine?

Until a few years ago, neuroscience had no explanation for Proust's *moments bienheureux* ("fortunate moments"), those shattering epiphanies when recollection appears like an apparition. The standard scientific model for memory revolved around enzymes and genes that required lots of reinforcement in order to be activated. The poor animals used for these experiments had to be trained again and again, their neurons bullied into altering their synaptic connections. Senseless repetition seemed to be the secret of memory.

Unfortunately for neuroscience, this isn't the way most memories are made. Life only happens once. When Proust remembers the madeleine in Swanns Way, it wasn't because he'd eaten lots of madeleines. In fact, the opposite was true. Proust's memory is hauntingly specific and completely unexpected. His memory of Combray, cued by some chance crumbs, interrupts his life, intruding for no logical reason, "with no suggestion of its origin." Proust is shocked by his past.

These literary memories are precisely the sort of remembrances that the old scientific models couldn't explain. Those models don't seem to encapsulate the randomness and weirdness of the memory we live in. They don't describe its totality, the way memories appear and disappear, the way they change and float, sink and swell. Our memories obsess us precisely because they disobey every logic, because we never know what we will retain and what we will forget. But what makes science so wonderful is its propensity to fix itself. Like Proust,

who was perfecting sentences until the printer set his type, scientists are never satisfied with their current version of things. In the latest draft of the science of memory, the theorizing has undergone a remarkable plot twist. Scientific rumors are emerging that may unlock the molecular details of how our memories endure even when we've forgotten all about them.

This theory, published in 2003 in the journal Cell, remains controversial. Nevertheless, the elegance of its logic is tantalizing. Dr. Kausik Si, a former postdoc in the lab of Nobel laureate Eric Kandel, believes he has found the "synaptic mark" of memory, the potent grain that persists in the far electrical reaches of neurons. The molecule he and Dr. Kandel have discovered could very well be the solution to Proust's search for the origin of the past.

Si began his scientific search by trying to answer the question posed by the madeleine. How do memories last? How do they escape the withering acids of time? After all, the cells of the brain, like all cells, are in constant flux. The average half-life of a brain protein is only fourteen days. A small subset of our hippocampal neurons dies and is reborn; the mind is in a constant state of reincarnation. And yet Si knew that the past feels immutable. Si concluded that our memories must be made of a very strong material, something sturdier even than our cells.

But a neuronal memory cannot simply be strong: it must also be specific. While each neuron has only a single nucleus, it has a teeming mass of dendritic branches. These twigs wander off in every direction, connecting to other neurons at dendritic synapses (imagine two trees whose branches touch in a dense forest). It is at these tiny crossings that our memories are made: not in the trunk of the neuronal tree, but in its sprawling canopy.

How does a cell alter a remote part of itself? Si realized that none of the conventional models of memory could explain such a phenomenon. There must be something else, some unknown ingredient, which marked a specific branch

as a memory. The million dollar-question was, what molecule did the marking? What molecular secret lurked in our dendritic densities, silently waiting for a cookie?

Si began his search by thinking through the problem. He knew that any synaptic marker would have to be able to turn on messenger RNA (mRNA), since mRNA helps make proteins, and new memories need new proteins. Furthermore, because mRNA is regulated where memories are regulated—in the dendrites—activating mRNA would allow a neuron to selectively modify its details. This insight led Si to frog eggs. He had heard of a molecule that was able to activate specific scraps of mRNA during the egg's development. This same molecule also happened to be present in the hippocampus, the brain's memory center. Its ignominious name was CPEB, for cyptoplasmic polyadenylation element binding protein.

To see if CPEB was actually important for memory (and not just for frog zygotes), Si began by searching for it in purple sea slugs, a favorite experimental animal among neuroscientists. To his pleasant surprise, CPEB was present in the slug's neurons.
Furthermore, CPEB was present precisely where a synaptic marker should be, silently skulking in the dendritic branches.

Si and Kandel were intrigued. They now tried to understand CPEB by blocking it. If CPEB was removed, could the neuron make a memory? Could the cell still mark a synapse? Though they hardly believed the data, the answer was clear: without CPEB, the slug's neurons were unable to remember anything.

But he still couldn't figure out how CPEB worked. How did this molecule exist outside time? What made it so strong? How did it survive the merciless climate of the brain? Si's first clue arrived when he decoded the protein's amino

acid sequence. Most proteins read like a random list of letters, their structures a healthy mix of different amino acids. CPEB however, looked completely different. One end of the protein had a weird series of amino acid repetitions, as if its DNA had had a stuttering fit (Q stands for the amino acid glutamine):

QQQLQQQQQQBQLQQQQ

Immediately, Si began looking for other molecules with similar odd repetitions. In the process, he stumbled into one of the most controversial areas of biology. He found what looked like a prion.

Prions were once regarded as the nasty pathogens of a tribe of the worst diseases on earth: mad cow disease, fatal familial insomnia (whose victims lose the ability to sleep, and after three months die of sleep deprivation), and a host of other neurodegenerative diseases. Prions are still guilty of causing these horrific deaths. But biologists are also beginning to realize that prions are everywhere. Prions are roughly defined as a class of proteins that can exist in two functionally distinct states (every other protein has only one natural state). One of these states is active and one is inactive. Furthermore, prions can switch states (turn themselves on and off) without any guidance from above; they change proteomic structure without changing DNA. And once a prion is turned on, it can transmit its new, infectious structure to neighboring cells with no actual transfer of genetic material.

In other words, prions violate most of biology's sacred rules. They are one of those annoying reminders of how much we don't know. Nevertheless, prions in the brain probably hold the key to changing our scientific view of memory. Not only is the CPEB protein sturdy enough to resist the effects of the clock—prions are famous for being virtually indestructible—but it displays an astonishing amount of plasticity. Free from a genetic substrate, CPEB prions are able to change their shapes with relative ease, creating or erasing a memory.

Stimulation with serotonin or dopamine, two neurotransmitters that are released by neurons when you think, changes the very structure of CPEB, switching the protein into its active state.

After CPEB is activated, it marks a specific dendritic branch as a memory. In its new conformation, it can recruit the requisite mRNA needed to maintain long-term remembrance. No further stimulation or genetic alteration is required. The protein will patiently wait, quietly loitering in your synapses. One could never eat another madeleine, and Combray would still be there, lost in time. It is only when the cookie is dipped in the tea, when the memory is summoned to the shimmering surface, that CPEB comes alive again. The taste of the cookie triggers a rush of new neurotransmitters to the neurons representing Combray, and, if a certain tipping point is reached, the activated CPEB infects its neighboring dendrites. From this cellular shudder, the memory is born.

But memories, as Proust insisted, don't just stoically endure: they also invariably change. CPEB supports Proust's hypothesis. Every time we conjure up our pasts, the branches of our recollections become malleable again. While the prions that mark our memories are virtually immortal, their dendritic details are always being altered, shuttling between the poles of remembering and forgetting. The past is at once perpetual and ephemeral.

This rough draft of a theory has profound implications for the neuroscience of memory. First of all, it's proof that prions are not some strange biological apocrypha. In reality, prions are an essential ingredient of life and have all sorts of intriguing functions. Swiss scientists, following up on the research of Si and Kandel, have even discovered a link between the prion gene that causes mad cow disease and increased long-term memory. Essentially, the more likely your neurons are to form misfolded prions, the better your memory is. Other experiments have linked a lack of CPEB in the mouse hippocampus to specific

deficits in long-term memory. Though the details remain mostly obscure, there seems to be a deep connection between prions and remembrance.

But the CPEB model also requires that we transform our metaphors for memory. No longer can we imagine memory as a perfect mirror of life. As Proust insisted, the remembrance of things past is not necessarily the remembrance of things as they were. Prions reflect this fact, since they have an element of randomness built into their structure. They don't mind fibbing. While CPEB can switch to an active state under a given set of experimental circumstances (like a few puffs of serotonin), Si's experiments also show that the protein can become active for no real reason, since its transformation is largely dictated by the inscrutable laws of protein folding and stoichiometry. Like memory itself, CPEB delights in its contingency.

This indeterminacy is part of CPEB's design. For a protein, prions are uniquely liberated. They are able to ignore everything from the instructions of our DNA to the life cycles of our cells. Though they exist inside us, they are ultimately apart from us, obeying rules of their own making. As Proust said, "The past is hidden … in some material object of which we have no inkling."

And though our memory remains inscrutable, the CPEB molecule (if the theory is true) is the synaptic detail that persists outside time. Dr. Si's idea is the first hypothesis that begins to explain how sentimental ideas endure. It is why Combray can exist silently below the surface, just behind the curtain of consciousness. It is also why Marcel remembers Combray on, and not on. It is a molecular theory of explicit memory that feels true. Why? Because it embraces our essential randomness, because prions are by definition unpredictable and unstable, because memory obeys nothing but itself. This is what Proust knew: the past is never past. As long as we are alive, our memories remain wonderfully volatile. In their mercurial mirror, we see ourselves.