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How does bleach bleach?

[Heidi Ledford](#)

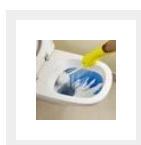
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The ubiquitous disinfectant may kill bacteria by unfolding their proteins.

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Bleach kills
bugs by
unfolding
their
proteins.

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It is the gold standard of sanitation, and a single drop is often all it takes to render a litre of water bacteria-free and safe to drink. Yet the molecular tricks behind bleach's fearsome bacteria-fighting power have not been fully worked out.

Now, researchers have found that bleach can kill bacteria by attacking proteins, quickly destroying their delicate shape. Furthermore, the model bacterium *Escherichia coli* even produces a protein that is activated by bleach and rescues injured proteins before the damage becomes permanent.

It has long been recognized that bleach, which is a solution of the chemical sodium hypochlorite, can wreak havoc with proteins. Bleach rapidly dissociates to form the highly reactive hypochlorous acid, which can attack the amino acids that make up proteins and so alter a protein's three-dimensional structure.

A protein's structure is critical to its function, and when important proteins lose their shape cells can no longer survive. But most studies have looked at how bleach reacts with proteins and membranes in test tubes rather than in living organisms.

The unfolding

Biochemist Ursula Jakob of the University of Michigan, Ann Arbor, and her colleagues became interested in bleach while studying a protein called Hsp33, which acts as a molecular 'chaperone', helping other proteins to achieve and maintain their proper shape.

They found that *E. coli* genetically engineered to lack Hsp33 became much more sensitive to bleach. When the researchers looked more closely at the effects of bleach on proteins in living cells, they found that treatment with bleach caused many proteins to clump together. Their results are published today in *Cell*¹.

One possibility is that the proteins are damaged and begin to unfold, exposing 'sticky' amino acids that were once buried deep inside the protein. When those molecules become exposed, they interact with similar amino acids on other damaged proteins, eventually forming intractable, non-functional globules.

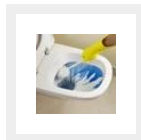
Jakob likens the process to boiling an egg: heat from the boiling water causes protein in the gooey egg whites to unfold and aggregate, gradually becoming solid. "In the same way that you cannot unboil an egg, cells have a very difficult time resolving these aggregates," she says. Instead, cells use Hsp33 to prevent the aggregation from occurring by refolding proteins before they clump together.

An unlikely 'on' switch

In fact, Hsp33 becomes more active when cells are exposed to hypochlorous acid. When bleach reacts with some of this protein's amino acids, Hsp33 partly unfolds and assumes an active structure. This is unusual: unfolding renders most proteins non-functional, yet for Hsp33 the process acts as switch to turn the protein on. Another bacterial chaperone protein called HdeA is also activated by partly falling apart under very acidic conditions², and Jakob expects that researchers may find more examples of this counterintuitive stress response in the future.

But why would *E. coli* bother to develop a warning system for a disinfectant invented by humans? The answer to that question could be that hypochlorous acid occurs naturally as well. Immune cells called neutrophils, for example, produce the acid to kill bacteria that they have engulfed. However, this does not quite account for *E. coli*'s behaviour, says microbiologist James Imlay of the University of Illinois at Urbana-Champaign. "*E. coli* does not make a living around neutrophils, he says. Jakob notes that one study suggests the acid may limit the growth of bacteria in insect guts³, and says that there could be other naturally occurring sources that have not yet been identified.

Meanwhile, the study does not rule out the possibility that bleach could have other modes of action. It is known, for instance, that bleach can react with the molecules that make up membranes. If this occurs in living cells, it could cause the membranes to rupture, killing the cell. But protein unfolding and aggregation seem to be an important part of the picture, filling in details that have long been missing. "Everyone knew that bleached worked, and that was enough," says Jakob. "Few really cared how it worked."



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