

# Plastics – Kind to the Environment

Plastics are practical – not least because they last. But when they find their way into the environment, this is precisely what becomes a problem. The amount of plastic waste in the environment is constantly increasing. A team headed by **Frederik Wurm** at the **Max Planck Institute for Polymer Research** in Mainz is therefore developing polymers that can be broken down by microorganisms once they have served their purpose. The researchers are applying what they've learned from their work on biodegradable polymers for medical use.

TEXT **KARL HÜBNER**

Every year, 380 million tons of plastic enter the material cycle. If it were to be loaded into 40-ton trucks, the line would encircle the Earth nearly four times. This figure includes plastics for bags, food packaging and cosmetic bottles, toothpaste tubes and tights, as well as plastics for computer monitors and smartphones, CDs, linoleum and laminate flooring. Similarly, car and aircraft manufacturers are continuously increasing the proportion of plastics in their products – to reduce weight and thus lower fuel consumption.

The reason plastics are so omnipresent is quite simply because they offer so many advantages. Not only are they lightweight and strong, they are also versatile and long-lasting. The key chemical characteristic of plastics is that they are made by joining basic building blocks – monomers – to form enormous chains, sometimes thousands of monomers long. Chemists use different types of monomers to modify the properties of a plastic, such as hardness, ductility, tensile strength, thermal stability and much more.

Once synthesized, most polymers are virtually indestructible. Even exposing them to weathering and light causes no more than slight discoloration. And microorganisms that use many other materials as food sources are at a loss when it comes to dealing with most plastics. Depending on the type of polymer and the conditions it is exposed to, it can take decades or even centuries before the giant molecules are fully broken down into carbon dioxide, water and other residues. Until then, they continue to represent a potential hazard to fish, seabirds and many other animals.

## 4.9 BILLION TONS OF PLASTIC WASTE

For many applications, the longevity of plastics is one of their major advantages, but today it is also considered to be one of their greatest disadvantages. About a year ago, a team of researchers in the US published some shocking figures on the fate of plastics. According to their calculations, between 1950 and 2015, 8.3 billion tons of plastic were manufactured worldwide, of which 6.3

Easy pickings for microbes: These phosphate-based plastic plates can be broken down by microorganisms – plastics like these wouldn't accumulate in the environment.





Almost indestructible: Plastic waste can endure for hundreds of years. Finding its way into a landfill, as here in the Maldives, must be considered a good outcome, as particularly in countries without a functioning waste collection system, colossal volumes of plastic end up directly in the environment.

billion tons have already become waste. Of that amount, just over a fifth has been recycled or incinerated. The remaining 4.9 billion tons have ended up as waste either in landfills or directly in the environment. The corresponding line of trucks would encircle the Earth almost 50 times.

Although some plastics are readily biodegradable, they currently make up only a very small proportion of total plastics. Polylactic acid, for example, is used in bags for compostable waste and plastic tableware for street festivals. However, if they are to actually decompose after use, the material must be correctly disposed of. "Little is gained when polylactic acid beer cups end up in normal household waste or in the recycling container," explains Frederik Wurm, Research Group Leader in Katharina Landfester's department at the Max Planck Institute for Polymer Research in Mainz. Only when disposed of in the organic waste bin or composter will polylactic acid come into

contact with the microorganisms required to break it down.

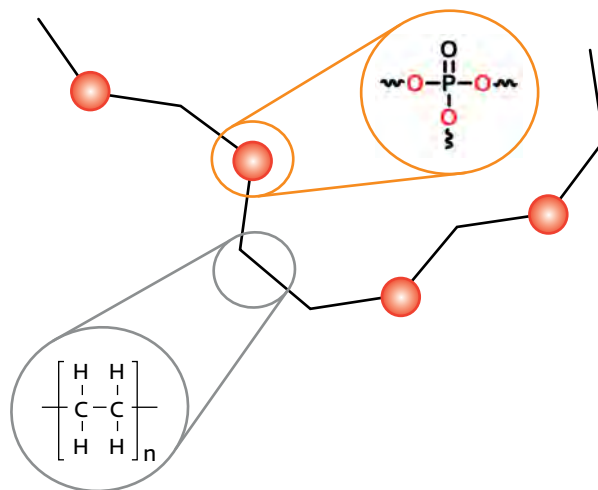
Frederik Wurm and his colleagues develop polymers with customized properties, one of which is biodegradability. "This needn't necessarily involve the use of renewables," explains Wurm, clearing up a popular misconception: "Firstly, not everything that's based on biological materials is automatically biodegradable," says Wurm. "And secondly, not everything that's biodegradable is necessarily of biological origin." His group is doing a lot of work with phosphates and phosphonates, for instance, and although these substances are geological in origin, polymers produced from them are fully biodegradable.

#### **PE MOLECULES WITH BUILT-IN CLEAVAGE SITES**

"The idea is actually very simple," Wurm says in reference to one of his current projects. "We make normal PE molecules, but we incorporate a few phosphate groups into them as cleavage sites." PE stands for polyethylene, one of the most widely used plastics in the world. It's used for making plastic films for the food industry and agriculture, as well as for shopping bags and containers for shampoo, cleaning agents and cosmetics.

Phosphate groups in the PE chain whet the appetite of certain microorganisms, giving them something to sink their metaphorical teeth into. A PE molecule with phosphate groups incorporated into it would therefore be readily broken down in the environment. All that would remain are the many small PE sections between each pair of phosphate groups. In contrast to the giant chains in normal polyethylene, if these sections are short enough, they, too, says Wurm, are readily biodegradable.

But does incorporating phosphate alter polyethylene's other properties? "Our aim is to make materials that can be used like PE, but are also biodegradable," explains Wurm. The mechanical properties are decisive here, and the key to these is how the polymer chains line up with each other. In pure PE, for example, it is known that the long molecules are folded like an accordion. The chemists in Mainz therefore wondered whether the polymer would behave in the same way with the added phosphate groups. With respect to biodegradability, there was another important point to consider: "To be accessible to microorganisms and their enzymes, the phosphate sections need to be on the outside of the kinks in the chain," explains Wurm.



**Above** Standard polyethylene consists of thousands of repeat units consisting of only carbon (C) and hydrogen (H). To make the plastic biodegradable, the chemists in Mainz add phosphate groups, consisting of phosphorus (P) and oxygen (O), at the kinks in the polymer.

**Below** Hisachi Tee, a member of Frederik Wurm's (right) research group, is using phosphorus chemistry to develop new polymers. The researchers are also trying to reproduce properties of common plastic films.

The researchers used transmission electron microscopy to confirm that both of these requirements are met. They found that their polymers folded in exactly the same way as pure polyethylene, and that the phosphate groups were located, as they had hoped, at the kinks in the chains.

The team isn't yet completely satisfied, though. "Our molecular weight

isn't yet high enough for most practical applications," admits Wurm. In other words, the molecular chains the chemists produce in the laboratory aren't as long as standard PE chains. This is because, in order to incorporate the phosphate groups, they use a different technique to manufacture their polymer than that used to produce industrial polyethylene.

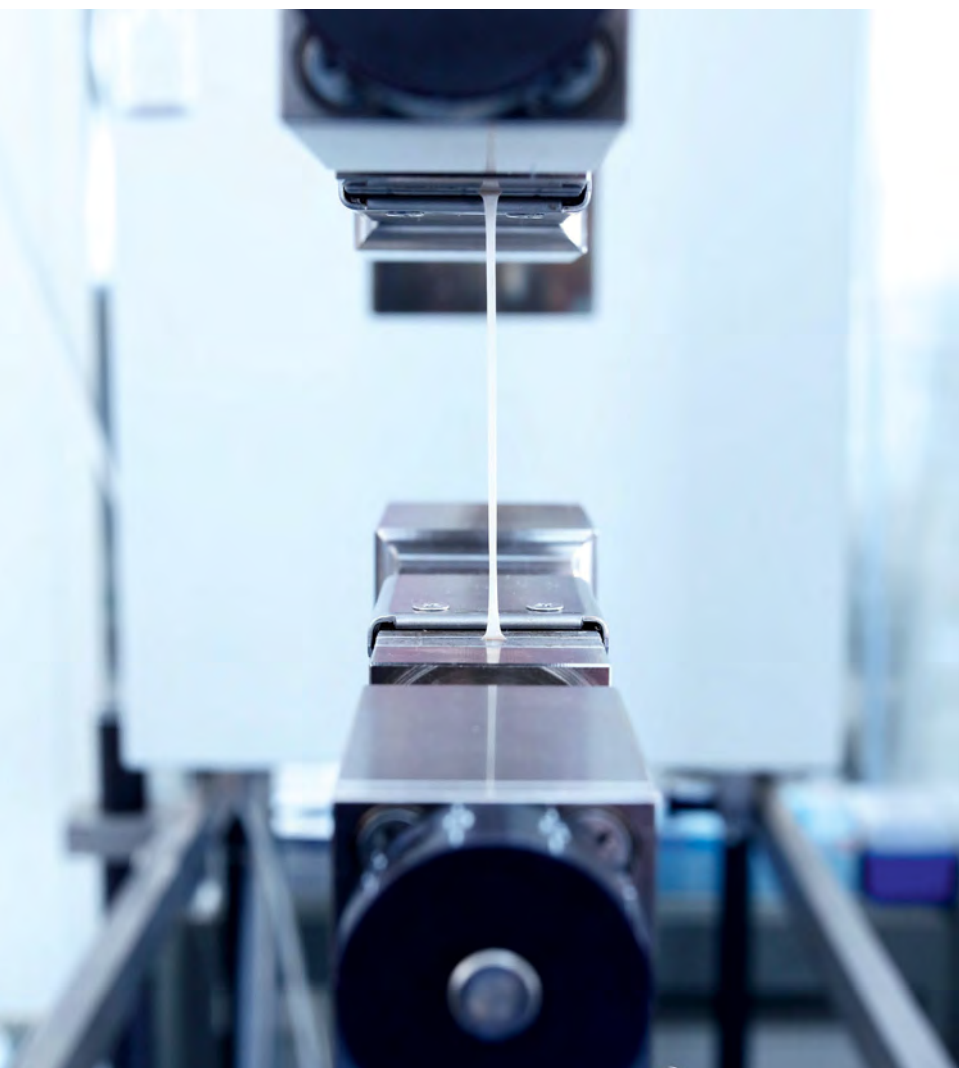
### PAYING A BIT MORE FOR A BETTER ENVIRONMENT

Nevertheless, the team in Mainz now has a general approach to producing biodegradable PE. Frederik Wurm is, of course, well aware that not all PE users will immediately switch over to the PE-phosphate polymer. After all, the low cost of pure PE is currently unrivalled. Few manufacturers can afford to pass on the extra costs to their customers, especially when it comes to bulk products like packaging materials. But Frederik Wurm can imagine that some customers might be prepared to pay a little more for the environmental benefits – customers who shop in organic grocery stores or other relevant chains, for example.

In medical applications, in contrast, material costs are almost completely irrelevant, and it is precisely for the



Graphic: MPI for Polymer Research; photo: Thomas Hartmann

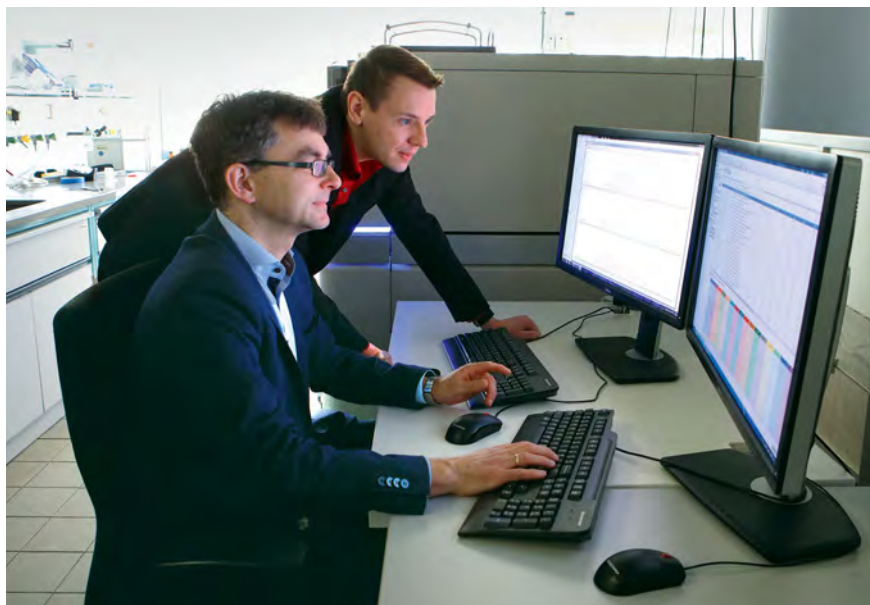


medical sector that Wurm's team developed the first phosphate-based biodegradable polymers. Their success in doing so is what gave the chemists the idea of incorporating phosphate groups into other common plastics, such as PE.

For medical applications, the primary focus is on polymer-drug conjugates. This involves embedding drugs, such as anti-cancer drugs, in nanoparticles. The particles, or sometimes the drugs themselves, are then coated in innumerable polyethylene glycol (PEG) chains, which flutter about the conjugate like fringes. These PEG chains act to hide the nanoparticles from the body's immune defenses, preventing them from being broken down prematurely. As a result, the conjugates circulate much longer in the blood than the drug alone, which also increases the duration of action. In addition, most conjugates are chemically programmed to deliver the drug to specific cells. This enhances the desirable effects while reducing side-effects.

"The market for such conjugates is already worth billions," notes Frederik Wurm. To date, however, the long-term fate of the PEG units remains unclear. Within the body, they are believed to be nondegradable; this, Wurm notes, is a good thing, as the monomer, ethylene glycol, is harmful to health. "If the PEG chains are short enough, they are excreted via the kidneys," explains Wurm. For longer chains, however, it

Polymers for testing: Max Planck researchers polymerize monomers, added via the turquoise syringe (top), in a reaction vessel heated in a water bath. They test the elasticity of their polymers using tension experiments (bottom).



Stealth effect uncovered: By analyzing mass spectrometry data, Volker Mailänder (left), Katharina Landfester (not pictured) and Frederik Wurm discovered that endogenous proteins attach themselves to their tiny drug delivery vectors. As a result, the body's immune defenses fail to recognize the payload as a foreign body.

to achieve this. One of the researchers' current goals is to develop vectors for delivering a drug to immune cells. The substance is designed to reprogram the immune cells to attack melanoma cells.

But before PEEP can be used in actual medical practice, there are a number of questions that Wurm and Mailänder still need to answer. For example, whether polymers such as PEEP can achieve the same stealth effect, allowing the polymer-drug conjugate to reach its target undetected. For test purposes, the researchers created stand-in nanotransporters for the drug payload, and then attached their PEEP fringes to these tiny particles. "We were able to show that these also circulate in the blood for a long time, proving that they aren't attacked by immune cells," says Wurm.

With the help of a special type of mass spectrometry, the researchers in Mainz have since also determined how the stealth effect actually works. "The polymer chains, whether PEG or PEEP, recruit from the blood specific proteins that attach to the conjugate," explains Mailänder. This shell, made up of the body's own proteins, gives the conjugates a sort of free pass, allowing them to circulate unhindered.

In and of itself, the long dwelling time in the blood is of no great benefit, medically speaking. The key thing is the

should be assumed that they accumulate in the body, which could pose a problem in the case of drugs for chronic conditions. It's conceivable, for example, that PEG chains could form crystals at certain sites in the body.

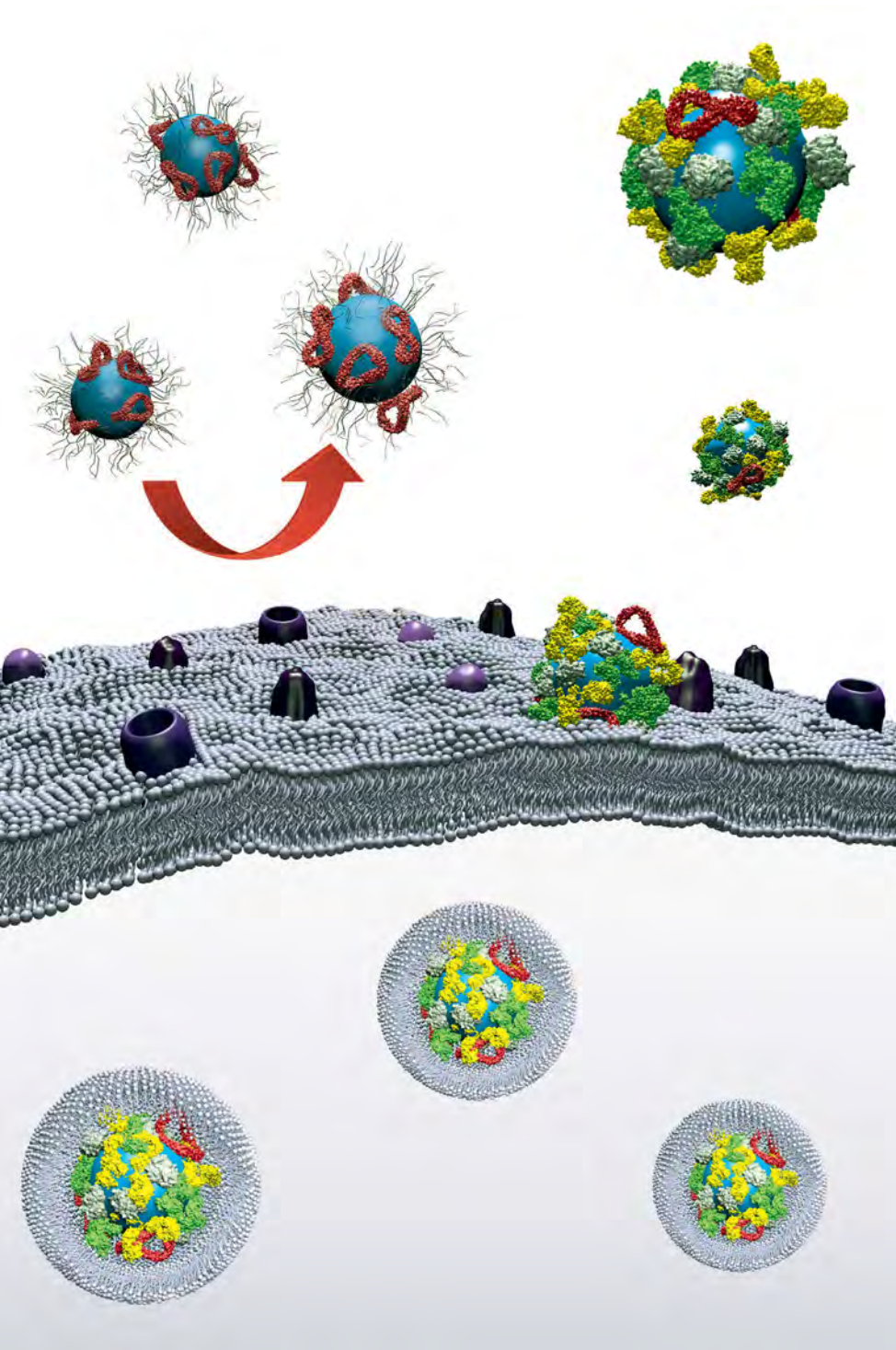
### POLYPHOSPHATES ARE BROKEN DOWN IN THE BODY

In collaboration with the University Medical Center Mainz, Wurm is currently investigating whether his phosphorus-based polymers could be used as an alternative to polyethylene glycol. In contrast to the above-mentioned PE, in which the chemists incorporate only isolated phosphate groups into the PE chains, here they use polymers constructed almost exclusively from phosphate groups. But what makes these substances particularly suitable for use as medical polymers? "We know for certain that polyphosphates can be broken down into phosphate within the body, which is then entirely harmless," explains Wurm. One polyphosphate that has proven particularly suitable in terms of water and thus blood

solubility, as well as biodegradability, is poly(ethyl ethylene phosphate), or PEEP for short. Frederik Wurm's Group has already developed a clever technique for synthesizing the polymer.

In contrast to polyethylene, in which the ethylene monomers form an endless chain, in PEEP each ethylene monomer is sandwiched between one phosphorus and one oxygen atom, making it much easier for enzymes to break these bonds as compared with pure PE. So, once the drug delivery vector has delivered its payload to the target, the enzymes cleave one ethyl ethylene phosphate monomer after another from the PEEP chain. "These small phosphate molecules are easily excreted via the kidneys," explains Wurm.

"The degradability in the organism and even in individual cells is very important and makes these polymers of great interest for further development," emphasizes his collaboration partner Volker Mailänder from the University Medical Center Mainz. The physician is currently researching ways to replace PEG with readily degradable polymers and is collaborating with Frederik Wurm



It's all in the mix: When a variety of endogenous proteins attach to particles camouflaged with polymer fringes, the potential drug delivery vectors are absorbed by the cells and, enclosed in membranes, transported into the interior of the cell, as shown on the right in this image. If, in contrast, the particles attract only one type of protein, they remain unable to enter the cell.

ing a kind of bone cement such as surgeons use for minor bone repairs, for instance. At present, the main types of adhesives used in this area are acrylic acid polymers. An adhesive that would disappear without a trace after a certain time would be a big plus.

### PHOSPHORUS CHEMISTRY YIELDS NEW FLAME RETARDANTS

Of course, for that kind of application, the material needs to exhibit a certain robustness. "The first materials we made were as brittle as cold candle wax," Wurm recalls with a smile. To refine their phosphate polymer bone cement, the chemists once again had to reach for their box of chemistry tricks. "On the one hand, we needed to increase the molecular weight," explains Wurm. The chains needed to be made much longer than the fringes for the drug vector, the maximum length of which was a little over a hundred phosphate groups. On the other hand, to make the cement both more elastic and harder, the chemists needed to tinker with the design of the side chains.

The possibilities for this kind of tinkering are exactly what Frederik Wurm loves about phosphorus chemistry. Owing to their nature, phosphorus atoms are able to form one more bond than carbon – the backbone of traditional polymers. This gives synthetic chemists like Wurm more leeway. With poly-

address label that the PEEP-nanotransporter conjugate uses to reach its intended target. In the cooperative project with the University Medical Center Mainz and other researchers in Landfester's department, sugar groups serve as address labels, as they stick to very specific immune cells. But there are still a few details to be fine-tuned. Accord-

ing to Wurm, it isn't all that easy, for example, "to strike the right balance between adequate camouflaging and sufficient pinpoint accuracy."

Because phosphate-based polymers are so readily biodegradable, the researchers in Mainz want to use them in other areas, too. In one project with a commercial partner, they are develop-

phosphates, for example, chemists can attach one more chemical group to the phosphorus atoms than they would be able to with the carbon atoms in analogous carbon-based polymers. “We can design this group any way we need to in order to achieve a particular property, such as stickiness,” gushes Wurm, describing the possibilities this opens up as an “enormous playground.”

The Max Planck researchers in Mainz also want to use their expertise in phosphorus chemistry to develop new flame retardants. Phosphorus compounds are already used as flame retardant additives, as they release flame retardant substances upon burning, while they themselves merely carbonize. Until now, these additives have generally simply been mixed with existing plastics. “We are working on incorporating such phosphorus groups directly into other polymers to make them flame resistant,” says Wurm.

The chemist admits, however, that for the time being this solution isn’t going to be used in areas where the emphasis is on price, simply because such plastics are too expensive. But epoxy resins and epoxy adhesives used for gluing floors, for instance, are a different matter. Here, the plastics being produced in Wurm’s laboratory could well have a role to play. “We are currently looking at whether we can improve flame retardancy in such products,” says Wurm. A further side effect would be that it would remove the need to use bisphenol A. This is currently an important starting material for the production of epoxy resins, but it is controversial, as it can be harmful to health.

As even the work of flame retardant products will one day be done, and they too will end up as waste, it would of course be good if they were readily biodegradable under normal environ-

mental conditions. Existing flame retardants tend not to be, and may even be toxic. Against this backdrop, new solutions based on phosphates or related phosphorous compounds have a certain attraction.

### MANY ALTERNATIVES TO LONG-LASTING PLASTICS

The researchers are testing how quickly their compounds really break down using the types of enzymes microorganisms release in the environment. These include lipases, proteases and depolymerases, as well as phosphatases and phosphodiesterases, which specifically target phosphorus groups. “We

perform tests both with individual enzymes and with mixtures,” says Wurm. The team also uses real-life fluids, such as blood plasma and sewage sludge.

Frederik Wurm is aware that the approaches his group is taking aren’t going to revolutionize the world of plastics on their own. But they do offer a few possibilities among many others that, together, could ensure that plastics will one day no longer be a problem for the environment. “There’s not going to be just a single solution,” says Frederik Wurm. The problem of long-lasting plastics in the environment will require a range of alternative materials. His group, for its part, is working on a few of them. ◀

#### TO THE POINT

- **More than 8.3 billion tons of plastics have been produced since 1950. Of these, 4.9 billion tons have ended up in landfill or elsewhere in the environment. The majority of these plastics are not readily biodegradable.**
- **Scientists at the Max Planck Institute for Polymer Research are developing biodegradable polymers. To achieve this, they incorporate phosphate groups into polyethylene (PE). These groups can be attacked by enzymes present in the environment, cleaving the polymer molecules.**
- **In addition, the researchers in Mainz are producing polyphosphate polymers for medical use. They are also working on biodegradable polymers with flame retardant, adhesive and other properties.**

#### GLOSSARY

**Mass spectrometry:** A technique for identifying unknown substances. Large molecules such as polymers are split into often characteristic fractions. An electric charge is applied to these fractions and they are then sorted according to their mass-to-charge ratio by deflecting them in an electric field. This produces a characteristic spectrum.

**Polymer:** A molecule consisting of chains of a basic building block (monomer), often thousands of monomers long. Polyethylene (PE) consists of long chains of ethylene molecules, whereas poly(ethyl ethylene phosphate) (PEEP) consists of long chains of ethyl ethylene phosphate monomers.

**Polymer-drug conjugate:** A conjugate in which a drug – generally embedded in a nanoparticle – is coated with polyethylene glycol (PEG) or poly(ethyl ethylene phosphate) to hide it from the immune system. These conjugates remain in the body longer and can have chemical address labels attached to send them to specific cells.