Nanoparticle Bombs

DOI: 10.1002/anie.200900121

Nanoparticle Missiles from Exploding Polyelectrolyte Capsules

*Lars Dähne**

hydrogels · layer-by-layer technology · nanoparticles · polyelectrolyte capsules

There are numerous examples in nature of the explosive opening of capsule vessels for the widest possible distribution of seeds and defensive materials into the local environment. A well-known example in the case of flora is the ornamental jewelweed Himalayan balsam (*Impatiens glandulifera*), which at the slightest touch projects ripe seeds up to seven meters.[1] During ripening the internal cell pressure rises considerably so that even a light touch is sufficient to "detonate" the capsule. Amongst fauna the bombardier beetle (*Brachininae*), for example, uses an explosion initiated by a catalytic reaction with hydrogen peroxide to project poison at its enemies, in fact up to a distance equal to 15 times its body length.[2]

Recently De Geest et al. have succeeded in developing microscopically small capsules that can project nanoparticles into the local environment at high speed using a comparable mechanism.[3] As the authors have indicated, these tiny projectiles could be used to introduce poorly soluble drugs into a tumor or into organs with a broader distribution than was previously possible and in this way achieve a more uniform action. De Geest et al. filled micrometer-sized capsules with a readily decomposable polymer network and nanoparticles; the capsule walls were then stabilized mechanically by cross-linking and made impervious to larger molecules, while OH^- ions could still pass (Figure 1). A change in pH led to a rapid decomposition of the polymer network with the formation of many smaller and in part highly charged fragments which cannot penetrate the wall; consequently, the osmotic pressure increased and caused the capsule to explode within a few seconds. The 200 nm sized particles from the interior were projected up to 400 µm into the local environment. The average speed of the nanoprojectiles was about 800 times faster than normal Brownian diffusion, which indicates a far higher initial speed.

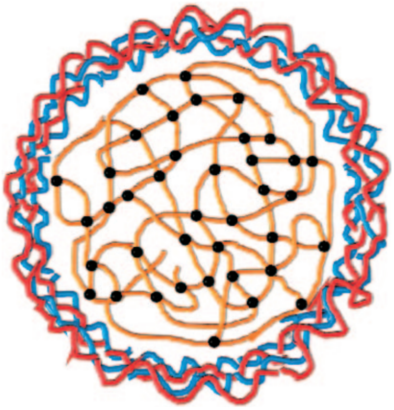

Figure 1. Construction of an exploding capsule: a pH-sensitive hydrogel (orange) and the nanoparticles (black) are located within; the jacket consists of layer-by-layer polyelectrolyte layers that are also covalently cross-linked.[3]

The explosive capsules were prepared by the layer-by-layer (LbL) technique developed by Hong and Decher in 1991.[4] Here polycations and polyanions are deposited alternately onto surfaces connected with a charge reversal after each layer (Figure 2). The thickness of the layer is limited by the charge. For simple polyelectrolytes showing linear growth behavior, the thickness lies within the range of 1–3 nm per layer.[5] Although the polymers are held together only by electrostatic interactions, the high number of charges per polymer leads to exceptionally robust films that are stable even at high ion strengths and over a broad pH range.[4] A remarkable extension of this technique was achieved by Donath et al. in 1998: they realized LbL deposition onto colloidal particles with subsequent dissolution of the template and formation of hollow capsules.[6] The technique led to a

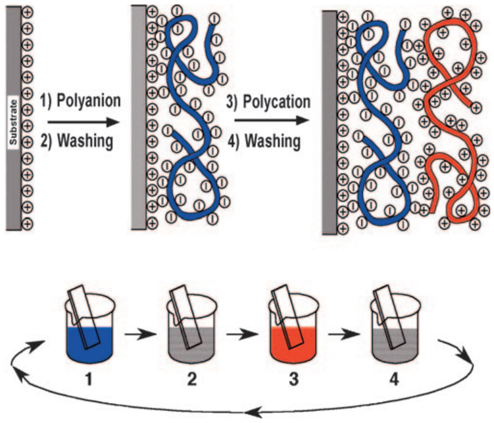

Figure 2. Scheme of the layer-by-layer technology.[4]

---

[*] Dr. habil L. Dähne
Surflay Nanotec GmbH
Schwarzschildstrasse 8, 12489 Berlin (Germany)
E-mail: l.daehne@surflay.com
Homepage: http://www.surflay.com

series of interesting developments in the encapsulation of active substances and the delayed or triggered release of drugs or other materials.[7] Milestones in this area include the delayed release of low-molecular-mass substances through an increase in the number of layers,[7,8] the control of capsule permeability by ion strength [9] or pH,[10] and the a reduction in capsule permeability either through heating above 60 °C[11] or by cross-linking the wall material.[12] A triggered release of the encapsulated materials could be achieved by selective energy input into the capsule wall by laser excitation and two-photon absorption of gold nanoparticles.[13] Also worthy of mention is the work in which the capsules were made to explode by means of high-energy laser irradiation.[14] Also routes for filling LbL capsules with macromolecules have been developed by a “controlled precipitation” of the macromolecules on the template before LbL deposition,[15] or “ship-in-the-bottle” polymerization in the capsules,[16] or through mesoporous materials[17] as well as loading with nanoparticles.[18]

However, the walls of LbL layers are too flexible to achieve the explosion described here. Thus capsules filled with polystyrene sulfonate (PSS) showed considerable swelling up to four times their original diameter in water owing to the osmotic pressure,[16] which is attributable to the exceptional expansibility of the electrostatically cross-linked polymers. Systematic investigations on the viscoelastic behavior of LbL films[19] showed purely plastic behavior with high expansion potential of the layers. However, significantly more rigid walls with elastic behavior could be achieved by cross-linking the polymers.[12,19]

De Geest et al. exploited these findings for the exploding capsules. They synthesized 150 μm sized spheres (usual LbL capsule templates range in size from 200 nm to 10 μm) of a readily hydrolyzable microgel with dextran molecules, which were cross-linked through ester bonds with polymethacrylate. In addition, cationic dimethylaminoethyl groups were attached to the gel both to fix fluorescein-labeled polystyrene nanoparticles with a diameter of 200 nm and to facilitate LbL coating with negatively charged PSS. These templates were encased with an LbL capsule of PSS and a cationic polydiazonium salt. The LbL film was cross-linked through the polydiazonium salt by UV irradiation,[12] by which rigidity was increased and the permeability reduced.

The explosion-like release of the nanoparticle was achieved by adjusting the pH to 13–14 by the addition of 1M NaOH solution. The template is hydrolyzed very rapidly at this pH; a large number of dextran molecules with a molecular mass of 20 kD and a highly charged polymethacrylate polymer are formed (Figure 3). Both types of fragments lead to high osmotic pressure, whereby the dextran acts through the high number of molecules and the polymethacrylate through the high number of counterions. Although, according to the authors, although the dextran is important for the generation of the explosion pressure, the polymethacrylate contributes twice as much.

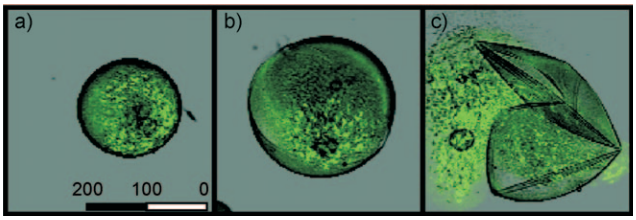

Figure 3. Exploding capsule a) before and b) immediately after a change in the pH; c) 10 s later.[3] The cloud of ejected fluorescing nanoparticles is clearly recognizable.

An exploitation of the explosion capsule for the indicated pharmaceutical areas have already been proposed by the authors. However, there is still a long way to go to acheive the first in vivo application. Problems with pharmaceutical approval must be overcome and the core destruction has to take place at physiological pH. Unfortunately the authors have given no clue as to whether a similar explosion takes place upon slow hydrolysis at pH 7.4 over a longer period, or whether with a slow rise in the pressure the molecules escape from the capsule or whether the LbL layer expands more extensively—both would impede an explosion.

However, the principle of exploding polyelectrolyte capsules can also play an important role in nonpharmaceutical applications; for example, for the efficient dispersion of components in mixing processes, such as curing agents in monomeric materials, catalysts in viscous media, or active substances (fertilizers, herbicides, pesticides) in plants, soil, etc. However, the required process should not be based on the basic hydrolysis of ester groups. The preparation of templates based on hydrogen bonds would be feasible, for example from polymethacrylic acid and polyvinylpyrrolidone or polyvinylcaprolactam at pH 2, which then decompose instantaneously at pH > 6 with the generation of a similar osmotic pressure.[20] A further possibility is provided by ampholytes (e.g. proteins) that form insoluble particles at the isoelectric point and could generate high osmotic pressures by protonation/deprotonation.[21] Regardless, a series of further interesting applications in nanotechnology can be anticipated for these capsules in the near future.

---

[1] M. Zimmermann, *Naturlexikon* **2008**, in http://www.natur-lexikon.com; I. Kowarik in *Biologische Invasionen. Neophyten und Neozoen in Mitteleuropa*, Ulmer, Stuttgart, **2003**, ISBN 3-8001-3924-3.

[2] H. Schildknecht, *Angew. Chem.* **1961**, *73*, 1 – 7; A. McIntosh, N. Beheshti, *Phys. World* **2008**, *22/4*, 29 – 31.

[3] B. G. De Geest, M. J. McShane, J. Demeester, S. C. De Smedt, W. E. Hennink, *J. Am. Chem. Soc.* **2008**, *130*, 14480 – 14482.

[4] G. Decher, J. D. Hong, *Thin Solid Films* **1992**, *210*, 831 – 835; G. Decher, *Science* **1997**, *277*, 1232 – 1237.

[5] J. M. Garza, P. Schaaf, S. Muller, V. Ball, J.-F. Stoltz, J.-C. Voegel, P. Lavalle, *Langmuir* **2004**, *20*, 7298 – 7302.

[6] E. Donath, G. B. Sukhorukov, F. Caruso, S. A. Davis, H. Möhwald, *Angew. Chem.* **1998**, *110*, 2323 – 2327; *Angew. Chem. Int. Ed.* **1998**, *37*, 2201 – 2205.

[7] C. S. Peyratout, L. Dähne, *Angew. Chem.* **2004**, *116*, 3850 – 3872; *Angew. Chem. Int. Ed.* **2004**, *43*, 3762 – 3783.

[8] A. A. Antipov, G. B. Sukhorukov, E. Donath, H. Möhwald, *J. Phys. Chem. B* **2001**, *105*, 2281 – 2284.

[9] G. Ibarz, L. Dähne, E. Donath, H. Möhwald, *Adv. Mater.* **2001**, *13*, 1324 – 1327.

[10] A. A. Antipov, G. B. Sukhorukov, S. Leporatti, I. L. Radtchenko, E. Donath, H. Möhwald, *Colloids Surf. A* **2002**, *198*, 535–541.

[11] a) G. Ibarz, L. Dähne, E. Donath, H. Möhwald, *Chem. Mater.* **2002**, *14*, 4059–4062; b) C. Déjugnat, K. Köhler, M. Dubois, G. B. Sukhorukov, H. Möhwald, T. Zemb, P. Guttmann, *Adv. Mater.* **2007**, *19*, 1331–1336.

[12] H. G. Zhu, M. J. McShane, *Langmuir* **2005**, *21*, 424–430.

[13] B. Radt,, T. Smith, F. Caruso, *Adv. Mater.* **2004**, *16*, 2184–2189.

[14] A. G. Skirtach, J. A. Muñoz, O. Kreft, K. Köhler, A. Piera Alberola, H. Möhwald, W. J. Parak, G. B. Sukhorukov, *Angew. Chem.* **2006**, *118*, 4728–4733; *Angew. Chem. Int. Ed.* **2006**, *45*, 4612–4617.

[15] I. L. Radtchenko, G. B. Sukhorukov, S. Leporatti, G. B. Khomutov, E. Donath, H. Möhwald, *J. Colloid Interface Sci.* **2000**, *230*, 272–280.

[16] L. Dähne, S. Leporatti, E. Donath, H. Möhwald, *J. Am. Chem. Soc.* **2001**, *123*, 5431–5436.

[17] Y. J. Wang, F. Caruso, *Chem. Commun.* **2004**, 1528–1534; L. Dähne, B. Baude, DE102004013637A1, **2004**.

[18] N. Gaponik, I. L. Radtchenko, G. B. Sukhorukov, H. Weller, A. L. Rogach, *Adv. Mater.* **2002**, *14*, 879–882.

[19] F. Dubreuil, N. Elsner, A. Fery, *Eur. Phys. J. E* **2003**, *12*, 215–221.

[20] V. Kozlovskaya, S. Ok, A. Sousa, M. Libera, S. A. Sukhishvili, *Macromolecules* **2003**, *36*, 8590–8592.

[21] F. Caruso, D. Trau, H. Möhwald, R. Renneberg, *Langmuir* **2000**, *16*, 1485–1489.