The Gömböc Pill, Continuing …

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The world is beginning to reopen after two long years in lockdown. Children are returning to school and adults are returning to work. In 2021, the Lasker Foundation awarded biochemist Katalin Karikó and immunologist Drew Weissman its Clinical Medical Prize for their decades of research on messenger RNA (mRNA) and the rapid development of an injectable vaccine for Covid-19 [15].

But the pandemic isn't over yet. Though over five billion people have been vaccinated with at least one dose, another 2.8 billion have not, for a complicated mix of economic, logistical, medical, and psychological reasons. An oral vaccine would redress many of those concerns. "It doesn't take much imagination to understand how much advantage oral vaccines have over vaccines injected into the muscle," says Karikó [18]. "There would be no need to go to the doctor. Everyone can take it themselves. People would much rather swallow anything than allow themselves to be stung. There is also much less resistance to the vaccine in oral cases." Thus the recent announcement of progress toward an oral vaccine for Covid-19 by an MIT–Harvard team of biomedical engineers is welcome news indeed [1]; see also [4].

The key to the pill is the gömböc, a remarkable shape whose adventures the readers of this journal have been following for years [19].

Its history begins millennia ago, with the first loaded dice [7] and roly-poly toys. But let us fast-forward to 1966, when John H. Conway and Richard Guy posed questions about the stability of polyhedra [5]. Is there, they asked, "an example of a homogeneous convex polyhedron which will rest in a stable position when lying on only one of its faces?" In technical terms, is there a monostatic polyhedron? In 1969, they answered their own question [6] with the monostatic 19-hedron shown in Figure 1.

In addition to its single stable face, the Conway–Guy 19-hedron can also balance on four of its vertices, but only for a split millisecond. Then it rolls over. Those vertices are positions of unstable equilibria. Together with Péter Várkonyi and Gábor Domokos, we say that a body with j stable and k unstable equilibria is of class $\{j, k\}$ [20]. Those of classes $\{1, k\}$ and $\{j, 1\}$ are called monostable and mono-unstable, respectively, and the two families of classes are jointly referred to as monostatic. The Conway–Guy 19-hedron is the first known homogeneous monostable polyhedron in class $\{1, 4\}$ [12]. This idea not only sparked research to find monostable polyhedra with fewer faces [2, 16], but also initiated a search for mono-unstable polyhedra with a minimal number of vertices [3].

If $j = k = 1$, the body is called mono-monostatic. There are no homogeneous mono-monostatic bodies in two dimensions, because every convex homogeneous planar disk has at least two stable and two unstable equilibrium points
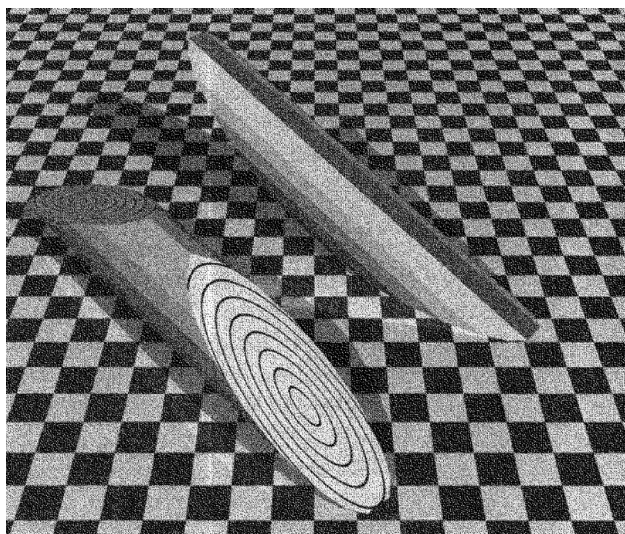
Figure 1. This monostatic 19-hedron, due to John Conway and Richard Guy, is an irregular 17-sided cylinder. From [7].

Figure 2. József Zalavári's gömböc statue in the Corvin Quarter in Budapest, 2017. (Reproduced under license from Creative Commons Attribution-Share Alike 4.0 International.)

Figure 3. The *Mathematical Intelligencer*, fall 2006, showing the gömböc and a gömböc-approximative turtle.

Figure 4. An MIT-led research team has developed a gömböc-inspired drug capsule. (Courtesy of Felice Frankel.)

[13]. But as Vladimir Arnold suggested to Gábor Domokos in 1995, convex homogeneous mono-monostatic bodies might exist in three-space [9]. He was right! By 2006, Domokos and Várkonyi had found a continuum of them. One is the now well known gömböc shape, with curved surfaces joined at sharp edges. A mono-monostatic polyhedron with 21 point masses at its vertices and also having 21 faces has been described recently [11].

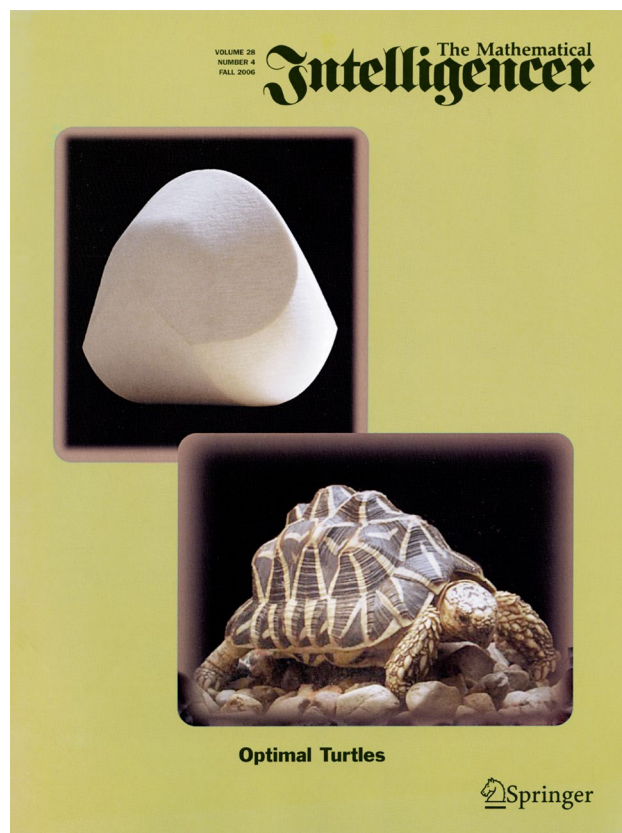Despite the difficulty[1] in pronouncing its name, the gömböc has inspired the imaginations of people interested in mathematics, art, biology, and medicine. Its fans are an international, interdisciplinary community.[2] It has even been immortalized in a work of public art (Figure 2).

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[1]For non-Hungarian speakers. For English speakers, "gum-buts" is close.
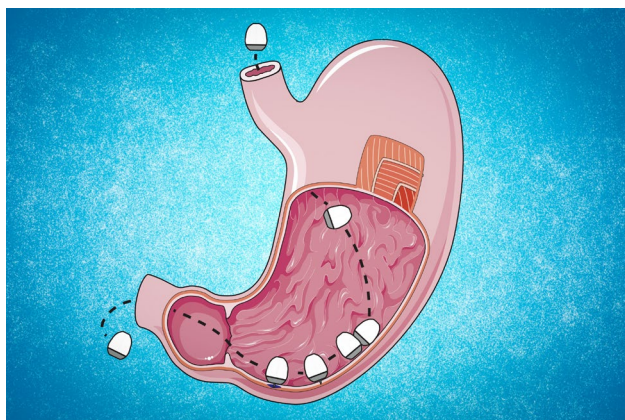[2]See https://gomboc.eu/en/inspiration/.

Figure 5. MIT researchers have designed an ingestible capsule that after being swallowed, can attach itself to the lining of the stomach and inject its cargo of antigen-encoding mRNA. (Courtesy of the researchers, edited by MIT News.)

As the cover of the fall 2006 issue of this journal (Figure 3) suggests, the gömböc resembles the shells of certain turtles that can right themselves if they happen to find themselves on their backs. Domokos and Várkonyi showed that such shells are close to optimal for self-righting [14]. "Evolution solved a far-from-trivial geometrical problem and equipped some turtles with monostatic shells: beautiful forms which rarely appear in nature otherwise."

The gömböc also drew the attention of an MIT–Harvard team of biomedical engineers, led by Giovanni Traverso and Robert Langer, who were researching new methods of drug delivery. The traditional methods, injection and ingestion, are often hindered by patient needle-phobia for the former and poor regimen compliance for the latter. In many cases, pills are ineffective because their contents are destroyed by stomach acid. But then the researchers learned about the gömböc (see, e.g., [8]). Before Covid-19 had emerged from the market stalls in Wuhan, they had designed a gömböc-inspired insulin pill for type 1 diabetes [10, 17]; see Figure 4.

When a gömböc pill is swallowed, it lands on its "feet," so to speak, like a roly-poly toy, with its stable base aligned with the stomach lining. A microneedle—made of compressed insulin in this case—is extruded, which injects its contents directly into the bloodstream, and then the capsule is excreted. The stomach has few pain receptors, and so the recipient doesn't feel the pinprick. Which brings us full circle: this team is creating gömböc capsules for Covid-19 vaccines. Figure 5 shows how they will work.

Katalin Karikó, Robert Langer, and Drew Weissman will share the 2022 Spanish BBVA Frontiers of Science Award "for their contributions to messenger RNA (mRNA) therapeutics and delivery technology that enable our own cells to produce proteins for disease protection and treatment." Says Dr. Karikó:

Science is built on the knowledge of researchers. We are constantly drawing ideas from the work of others. In biology, we look for analogous processes, we look for precedents for different things. That is why it is good to read as much as possible about different areas of science. All this knowledge is valuable for hypothesis-driven research.[3]

Exercise 1. Explain Figure 5 to the next person you see!

It is a pleasure to thank Gábor Domokos and Katalin Karikó for their comments and suggestions on earlier drafts of this note.

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