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Miguel Mota (1922–2016)—the kinetochore engine(er)

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One thing I learned from my mentors, and hopefully inherited, was the importance of knowing the literature in my field. But what I never expected was that this passion could bring together scientists that were more than 50 years apart in age. It was 2008 and I had been invited by the Gulbenkian Foundation to talk about cell division to a broad audience of high-school kids, teachers, and any lay public that would show up. I talked about microscopy, chromosomes, and pulling forces, so that at the end of a division cycle, each cell gives rise to two genetically identical sisters ("omnis cellula e cellula"!). At the end of the talk, and after answering many questions from the audience, there was a rough male voice in the back of the room that assertively approached me (in Portuguese) to say that already back in 1957 he had proposed an explanation for anaphase chromosome movement, which was by all means similar to what I had just told people during my talk. My embarrassment lasted only a few fractions of seconds, because I immediately realized that he could be only one person—Miguel Mota—whose name I knew from digging (with permission!) the archives of my post-doc mentor Conly Rieder (whom, like me, is a library rat) and from Daniel Mazia's mitosis chapter (Mazia 1961). Instantly, it all made sense, as if I had been waiting years to establish this connection, and could not hide my secret joy that another Portuguese, 50 years before me, shared the same interest about the problems that cause me sleepless nights and made me want to be a scientist.

Miguel Mota was trained as an Agronomy Engineer and was a pioneer in, by then, the still young field of Genetics. He spent most of his career trying to solve "real life" problems related to agriculture and the amelioration of cereals, many of them still growing in some regions in northern Portugal (Fig. 1). These interests made him study the problem of polyploidy in plants and how chromosome movement could be prevented by the action of colchicine (Villax and Mota 1953). He was also a pioneer in the use of the electron microscope to study chromosome structure, with special focus on the centromere (Mota, 1962). Curiously, it was in a theoretical work that he outlined a new hypothesis for anaphase chromosome motion (Mota 1957) for which, only recently, he has received the appropriate credit (Maiato and Lince-Faria 2010). Briefly, in 1957 Miguel Mota proposed, based on very little experimental evidence, that chromosomes might be "propelled" towards opposite poles during anaphase by their own motors localized on centromeres,[1] leaving behind a trace substance, similar to a jet engine (which he knew well due to his other passion for airplanes[2]; Fig. 1).

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[1] The term centromere was indistinguishably used at that time to refer also to the kinetochore region.

[2] Miguel Mota used to live next to the Gulbenkian Institute of Science near Lisbon where the first electron microscope became available in Portugal. However, access to this equipment was often difficult, which made him fly regularly to Porto, in his own little piper cub (Fig. 1), to use the other electron microscope available in the country, and thus satisfy two of his greatest passions.

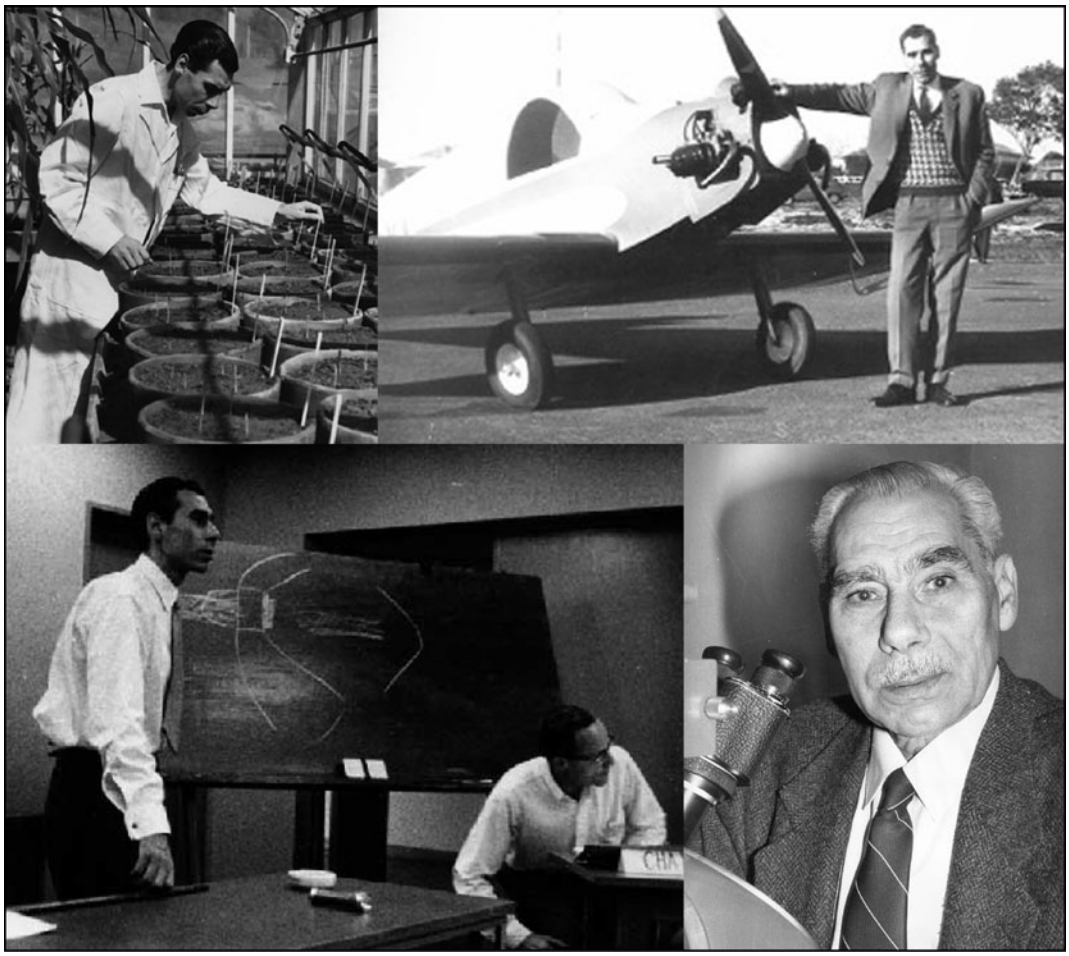

Fig. 1 Miguel Mota working as an Agronomy Engineer to develop better cereals (*top left*). Miguel Mota next to his piper cub that he used to fly from Lisbon to Porto to use the electron microscope (*top right*). Miguel Mota at the meeting of the International Genetics Society in Japan in 1956 (Chaired by Hans Ris on the right) presenting his anaphase model, in which kinetochores were conceived to "propel" chromosomes like a jet engine (*bottom left*). Miguel Mota was a pioneer in the use of the electron microscope to study centromere structure (*bottom right*). Photos kindly provided by Manuel Mota

One might legitimately ask whether Miguel Mota was a visionary or whether his hypothesis was completely naive. The problem of chromosome movement is as old as the discovery of mitosis by Walther Flemming, who clearly posited that the solution might be either on the chromosomes themselves, outside of them, or both (Flemming 1879). The prevalent view in the mid-20th century was that kinetochore fibers "pulled" on the kinetochore with a force that was proportional to their length (Östergren, 1945). My feeling was that the mitosis community never really paid too much attention to the eccentric hypothesis of Miguel Mota, but the truth is that he was ahead of his time. To mention few facts, Mota's hypothesis was proposed several years before any solid evidence for the existence of molecular motors (The first motor, Dynein, was discovered in cilia only 8 years later (Gibbons and Rowe 1965)) and three decades before the identification of molecular motors at the kinetochore (Pfarr et al. 1990; Steuer et al. 1990). Moreover, the substance trace left behind the kinetochores might well be perceived today as a depolymerizing microtubule (note that microtubules were only first identified in 1963 (Ledbetter and Porter 1963)), which pulls chromosomes from the kinetochore-attached end releasing soluble tubulin—the so called "pac-man" mechanism elegantly demonstrated by Gary Gorbsky in Gary Borisy's laboratory in 1987 (Gorbsky et al. 1987). Finally, while microtubule depolymerization is required and sufficient to move chromosomes in many biological systems (Inoue and

Sato 1967; Inoue and Salmon 1995; Grishchuk et al. 2005; Grishchuk and McIntosh 2006; McIntosh et al. 2010), there is also compelling evidence that, in animal cells, several molecular motors, including Dynein and microtubule-depolymerizing kinesins localized at the kinetochores (and poles!), are important players in this process (Savoian et al. 2000; Sharp et al. 2000; Rogers et al. 2004; Yang et al. 2007).

Nowadays, all this knowledge is taken as a pillar in our comprehension of mitosis and the mechanism of anaphase motion, but it was Miguel Mota who dared to think (and publish!) about a possible explanation that hardly anyone took seriously at that time, and he stood by it for the rest of his life. Outside of a long list of publications, the real legacy left by Miguel Mota was his contagious dissatisfaction about how little we understand the things around us and his unshakable determination to think differently, while paddling against the current. And he paddled, until his very last breath at the age of 93, contributing well after his retirement to raise public awareness about the conservation of genetic resources and the definition of intelligent public policies on research and agriculture. He took with him a small piece close to the heart of all those that had the privilege to meet the Man, but he left everybody around him a much, much richer life.

References

Flemming W (1879) Beitrage zur kenntnisse der zelle und ihrer lebenserscheinungen. Archiv Mikrosk Anatomie 18:151–259

Gibbons IR, Rowe AJ (1965) Dynein: a protein with adenosine triphosphatase activity from cilia. Science 149:424–426

Gorbsky GJ, Sammak PJ, Borisy GG (1987) Chromosomes move poleward in anaphase along stationary microtubules that coordinately disassemble from their kinetochore ends. J Cell Biol 104:9–18

Grishchuk EL, McIntosh JR (2006) Microtubule depolymerization can drive poleward chromosome motion in fission yeast. EMBO J 25:4888–4896

Grishchuk EL, Molodtsov MI, Ataullakhanov FI, McIntosh JR (2005) Force production by disassembling microtubules. Nature 438:384–388

Inoue S, Salmon ED (1995) Force generation by microtubule assembly/disassembly in mitosis and related movements. Mol Biol Cell 6:1619–1640

Inoue S, Sato H (1967) Cell motility by labile association of molecules. The nature of mitotic spindle fibers and their role in chromosome movement. J Gen Physiol 50(Suppl): 259–292

Ledbetter MC, Porter KR (1963) A "microtubule" in plant cell fine structure. J Cell Biol 19:239–250

Maiato H, Lince-Faria M (2010) The perpetual movements of anaphase. Cell Mol Life Sci 67:2251–2269

Mazia D (1961) Mitosis and the physiology of cell division. In: Brachet J, Mirsky AE (eds) The cell—biochemistry, physiology, morphology, Vol IIIth edn. Academic Press, New York, pp 77–412

McIntosh JR, Volkov V, Ataullakhanov FI, Grishchuk EL (2010) Tubulin depolymerization may be an ancient biological motor. J Cell Sci 123:3425–3434

Mota M (1957) A new hypothesis of the anaphase movement. In: Proceedings of the International Genetics Symposia (1956), pp 113–116: Cytologia, Supplement

Mota M (1962) The ultrastructure of the centromere. In: Fifth International Congress for Electron Microscopy, Philadelphia, Pennsylvania, 29 Aug – 5 Sept vol 2, NN-11, Academic Press, New York

Östergren G (1945) Equilibrium of trivalents and the mechanism of chromosome movements. Hereditas 31:498

Pfarr CM, Coue M, Grissom PM, Hays TS, Porter ME, McIntosh JR (1990) Cytoplasmic dynein is localized to kinetochores during mitosis. Nature 345:263–265

Rogers GC, Rogers SL, Schwimmer TA, Ems-McClung SC, Walczak CE, Vale RD, Scholey JM, Sharp DJ (2004) Two mitotic kinesins cooperate to drive sister chromatid separation during anaphase. Nature 427:364–370

Savoian MS, Goldberg ML, Rieder CL (2000) The rate of poleward chromosome motion is attenuated in Drosophila zw10 and rod mutants. Nat Cell Biol 2:948–952

Sharp DJ, Rogers GC, Scholey JM (2000) Cytoplasmic dynein is required for poleward chromosome movement during mitosis in Drosophila embryos. Nat Cell Biol 2:922–930

Steuer ER, Wordeman L, Schroer TA, Sheetz MP (1990) Localization of cytoplasmic dynein to mitotic spindles and kinetochores. Nature 345:266–268

Villax E, Mota M (1953) Behaviour of a Triticum x Secale hybrid under the action of colchicine. Nature 172:412–413

Yang Z, Tulu US, Wadsworth P, Rieder CL (2007) Kinetochore dynein is required for chromosome motion and congression independent of the spindle checkpoint. Curr Biol 17:973–980