Biofortification: lessons from the Golden Rice project

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Biofortification is an umbrella term for a diverse range of projects and possibilities. It is best understood on three levels: as a range of technologies *for developing micronutrient-dense crops; a development* intervention *to improve public health; and an* idea *that links agriculture, nutrition, and health in a particular way. This paper focuses on the Golden Rice project as a well-known example of biofortification. It show how two sets of questions – concerning* effectiveness *of Golden Rice as a delivery mechanism for vitamin A to malnourished populations and its* acceptance *by those populations as a rice variety and staple food item – have been narrowed down to parameters set by an increasingly polarized GM crop debate. It is not too late for these trends to be reversed, however. The Golden Rice project is a case study in the non-linearity of complex innovation processes, which exposes limitations of binaries such as 'upstream' and 'downstream'. Recent developments point to the possibility of a more open debate about outstanding uncertainties and how they might be resolved.*

Keywords: biofortification, Golden Rice, micronutrients, nutrition, agricultural research, GM crops

> Imagine a new breed of crops capable of alleviating malnutrition in even hard-to-reach rural populations – crops such as rice loaded with iron, wheat strengthened with zinc, and sweet potato packed with pro-vitamin A. These staples could be grown on family plots throughout the developing world. (HarvestPlus, 2004: 1)

THE PASSAGE QUOTED ABOVE invites readers to 'imagine' a new generation of crops designed to alleviate malnutrition 'in even hard to reach populations' in remote rural regions of developing countries. This is the vision behind 'biofortification', an umbrella term for a range of projects whose aim is to develop and disseminate micronutrient-dense crops to 'populations at risk' from contracting malnutrition-related diseases. The key premise is that households that make up these at-risk populations subsist on a single, staple crop, which they cultivate primarily for domestic consumption. Whether it is maize in East Africa or rice in South-east Asia, the underlying assumption is that poor families with small landholdings are limited to growing and consuming the harvest from a single crop. It follows, therefore, that their diet (and its deficiencies) is determined by the nutritional content (and deficiencies) of whichever staple it is that is grown on the family plot.

Is this assumption correct? The short answer is 'it depends'. The extent to which households fit this description depends on a wide range of factors arising from

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the geographic, agro-ecological, socio-cultural and political-economic context in which the household and farming system is located. A more pressing question, and one on which this paper focuses, is whether and how such foods, and the health benefits they may offer, can be supplied in a sustainable way to those 'hard to reach' populations that biofortification initiatives explicitly target.

The opening quotation is clearly a view from 'upstream'; in this case a view articulated by architects of HarvestPlus, launched ten years ago by the CGIAR and funded by a range of sources including the Bill & Melinda Gates Foundation (BMGF) under the banner of a 'new paradigm' linking agriculture and health. The term, if not the idea, is relatively new, coined shortly before funding was secured for HarvestPlus as a CGIAR 'Challenge Program' in 2003. What it described, however, was a diverse family of projects, many of which had been ongoing for several years. The earliest of these was maize research initiated in the 1960s at the Mexico-based International Maize and Wheat Improvement Centre (CIMMYT), which led to the Quality Protein Maize (QPM) breeding programme that has continued from the 1970s until today (Mertz, 1997; De Groote et al., 2010). More recently, and since the attention of the international nutrition community became focused on micronutrients, concerted donor-funded efforts have been under way in East and Southern Africa to promote the substitution of beta-carotene-rich, orange-fleshed sweet potato (OFSP) as a more nutritious alternative to the habitually consumed white-fleshed sweet potato (Hagenimama et al., 2001; Low et al., 2007; HarvestPlus, 2012).

These early examples of biofortification research and development highlight some of the dimensions of difference represented by the range of projects that fall under the umbrella of biofortification. Firstly, these projects differ in the extent to which they emphasize upstream 'research' or downstream 'development'. QPM was, at the time it was initiated, an example of cutting-edge crop science. OFSP projects, on the other hand, have been carried out by nutritionists and development practitioners (often from NGOs) using well-developed 'products' as an entry point for community level interventions to encourage behaviour change for better nutrition. Secondly, whether the 'trait of interest' is visible is an important distinction with implications for marketing and promotion as well as monitoring and evaluation. In the case of OFSP, one of the main considerations is how to induce consumer preference for a food item of a different colour (and texture). Promoters of QPM, however, face no such challenge. In the case of QPM adoption, it has proved difficult to establish whether this is in any way connected to nutritional factors (De Groote et al., 2010), and in fact may have more to do with new opportunities to market QPM as livestock feed (Hellin and Erenstein, 2009).

The term 'biofortification' therefore encompasses diverse goals and projects, and this was reflected in the initial design of the HarvestPlus Challenge Program which included six crops: rice, wheat, maize, phaseolus bean, cassava, and sweet potato; and three nutrients: iron, zinc, and vitamin A (CIAT and IFPRI, 2002). (Iodine, also an international nutrition priority, was not included, since near-universal coverage had been achieved though policies for the mandatory iodization of salt.) In this context, a significant accomplishment of HarvestPlus has been the articulation of a singular vision for biofortification which combines three key elements, framing biofortification as: 1) a range of *technologies* designed to alter the nutrient levels in selected crops; 2) a development *intervention* combining goals of improved public health and poverty alleviation; and 3) an *idea* linking agriculture, nutrition, and health in new ways (Brooks and Johnson-Beebout, 2012: 86). While biofortification may not have been 'new' as such, the launch of HarvestPlus was the first time that biofortification (and the 'promise' it represented) had been presented as so complete and coherent a 'package'. Furthermore, as an *intervention,* biofortification was promoted as uniquely cost-effective and sustainable, benefiting from a 'multiplier effect' once biofortified varieties are integrated into seed systems, as compared with other large-scale micronutrient interventions such as industrial fortification of processed foods and pharmaceutical supplements (Nestel et al., 2006; Meenakshi et al., 2010).

It is important to recognize that the gathering together of previously disparate projects under a single heading in this way was above all a political accomplishment. In the process, the 'win–win' vision formulation that proved so compelling to a newly appointed CGIAR Science Council and a – then still young – philanthropic foundation had glossed over a reality of divergent visions of how the promise of biofortification might be realized. For example, the framing of biofortification as a *range* of technologies – and HarvestPlus as a 'neutral' arbiter between them – served to insulate the programme from an increasingly polarized GM crop debate, while at the same time keeping all options open (Brooks, 2010). According to the programme literature, HarvestPlus would focus, in its first phase, on the use of 'conventional plant breeding' (CPB) methods, while exploring the potential for the use of transgenic techniques in later phases (CIAT and IFPRI, 2002). This framing of technological options, at this time, in terms of a 'CPB vs. GM' dichotomy, tended to downplay the multiplicity of research directions *within* CPB (between open pollinated varieties and hybrids, for example) or indeed within the plant and nutrition sciences more broadly.

An additional dimension of difference between crops targeted by biofortification programmes has been the extent to which they are in fact the primary staple for the population concerned. Sweet potato, while valued as a snack food, is supplementary rather than central to diets in East Africa, for example. Similarly, cassava, while important as a 'famine crop' when maize harvests fail, is not an everyday staple food in the target countries (though there are convincing arguments for policies to encourage a greater role for cassava in national and regional food security planning; see Haggblade et al., 2009). Furthermore, both are root crops, so do not fit the logic of biofortification as an inherently scalable (or even scale neutral) intervention via dissemination of *seeds*. Ultimately, the two most significant crops for biofortification as a 'global' effort are maize and rice, since these are the primary staple *grains* cultivated and consumed in target countries in sub-Saharan Africa and South and South-east Asia, respectively. Of these, rice is more important in aggregate terms (being the most widely cultivated, traded, and consumed crop plant worldwide) (FAO, 2003). Rice biofortification initiatives, however, have proved technically complex, both in upstream research and in downstream implementation, due, at least in part, to its consumption (in contrast to wheat and, often, maize) as whole grain.

This article draws on the author's research on rice biofortification, which has examined in some detail two very different trajectories: firstly, efforts within the CGIAR system (prior to and during its incorporation into HarvestPlus) to biofortify rice with the trace minerals, iron and zinc, primarily though conventional plant breeding and also (more recently) though fertilizer application (Cakmak 2008; Brooks, 2011c; Brooks and Johnson-Beebout, 2012); and secondly, the higher profile 'Golden Rice' project which, steered by a public–private partnership, has used a combination of genetic engineering and plant breeding to introduce beta-carotene (the precursor of vitamin A) into *indica* rice varieties habitually consumed in South and South-east Asia (Brooks, 2011b). While not formally incorporated into HarvestPlus, the Golden Rice project has, in a variety of ways, influenced the perception and progress of biofortification as idea and technology and its potential as an intervention. So much so that in 2003, the year HarvestPlus was launched, the BMGF also agreed to fund the 'ProVitaMinRice' research consortium, which builds on the Golden Rice project by 'engineering rice for high beta-carotene, vitamin E and enhanced iron and zinc bioavailability' under its 'Grand Challenges in Global Health' initiative (BMGF, 2003).

This paper focuses on the second of these trajectories, the Golden Rice project, which is now entering the final stages of agronomic and nutritional testing and regulatory approval prior to its planned commercial release, first in the Philippines and subsequently in Bangladesh. Beginning with the initial 'transformation' in a Swiss public research institution, this paper provides a brief overview of this controversial project, from its handover to Syngenta and subsequent 'donation' to a public–private partnership, to its transfer to the International Rice Research Institute (IRRI) in the Philippines for the less glamorous task of 'back-crossing' the donated material into local *indica* varieties, and finally to recent developments including the publication of preliminary nutritional tests and field trials currently ongoing in the Philippines. At the same time, Golden Rice has been afforded a parallel 'virtual' identity, constructed as a potent symbol of what transgenic technologies could – but for burdensome regulations and 'irrational' opposition – contribute to the alleviation of poverty and disease in the developing world (Potrykus, 2010b).

This paper considers the consequences of the superimposition of this virtual identity onto what has been a complex research endeavour, for open discussion about the progress of the research, and in particular the resolution of outstanding uncertainties and challenges as the project progresses through 'downstream' towards the farmer and consumer. While analysis of upstream power-knowledge dynamics and institutional histories shaping the Golden Rice trajectory can be found elsewhere (Brooks, 2010, 2011b), this paper highlights the challenges further downstream, exploring issues around the effectiveness of Golden Rice as a crop variety and nutritional intervention in real-world settings (rather than in the controlled conditions in which findings to date have been generated) and, ultimately, 'acceptance' by farmers and consumers. In light of this analysis, the paper returns to the vision captured by the quotation at the beginning of this paper, arguing that it is not too late for a more open discussion about the challenges involved in making it a reality.

The Golden Rice project

In the early 1990s a group of scientists based in universities in Switzerland and Germany secured funding through the International Program on Rice Biotechnology (IPRB), a programme established by the Rockefeller Foundation to support the development of biotechnology capacity and applications oriented to developing country needs and priorities. While the majority of the projects supported were concerned with improvements in rice yield, seed funding was also allocated to a project which sought to 'genetically engineer the pro-vitamin A pathway into the rice endosperm' (Potrykus, 2001).The rationale for funding the project was that, while the likelihood of success was considered relatively low, the potential benefits would be so significant it was worth the investment. When the scientists achieved the transformation in 1999, on the eve of the closure of the IPRB, the project was hailed as the IPRB's 'greatest achievement' (Normile, 1999).

In 2001 a lead article (and cover) of *Time* magazine announced the arrival of Golden Rice with the claim 'this rice could save a million kids a year' (Nash, 2001). By this time, the project had already become a 'poster child' in a rapidly escalating GM crop debate, and claims that were being made for a technology that was still 'in the lab' attracted contestation and controversy (Nestle, 2001; BIOTHAI et al., 2001). Also controversial was the transfer of the Golden Rice project and materials from a public research institution to the Syngenta company, in return for assistance in negotiating unanticipated intellectual property restrictions, intensifying suspicion that Golden Rice would serve as a 'Trojan Horse' to gain public acceptance of GM crops in general (Pollan, 2001). Meanwhile, the inventors and their new sponsors drew attention to a series of institutional innovations which would allow the free transfer and dissemination of the technology to farmers in developing countries via a 'new type of public–private partnership' (Potrykus, 2001).

Two factors in these formative years of the Golden Rice project have had a lasting effect. Firstly, the project has carried high expectations from the outset. In particular, those closely connected with the project shared a core assumption that once the genetic transformation was achieved, the resulting technology would proceed, in a linear manner and propelled by a sense of urgency, though the stages of technology transfer, farmer adoption, and, finally, consumption by malnourished women and children to beneficial effect. Secondly, the unexpected transformation of the project from an important 'breakthrough' to an object of controversy (particularly in light of its acquisition by Syngenta) led the inventors and other project champions to adopt an increasingly defensive position; a position that, over time, would become firmly embedded in the institutional structures and practices that were evolving around the project at that time, resulting in a lack of openness regarding technical challenges and policy uncertainties that have inevitably proliferated in this pioneering research (Brooks, 2010).

In reality, the transformation was just the start. Potrykus and his colleagues had succeeded in transferring a gene containing a small amount of beta-carotene, a precursor of vitamin A, into a *japonica* rice variety. Whether and to what extent this beta-carotene would prove 'bioavailable' – in other words, in such a form that the human body (in particular, the body of a malnourished adult or child) could convert it into usable vitamin A – was still unknown. Furthermore, while *japonica* rice varieties are adapted to temperate zones, populations targeted by the Golden Rice project (and indeed by the IPRB) live in tropical environments where *indica* varieties predominate. So a way needed to be found to transfer the beta-carotene 'trait' into *indica* varieties grown by 'hard to reach rural populations' in these regions and ensure the trait was both stable and bioavailable in those varieties.

Also unknown, at this stage, were the effects the transformation might have on agronomic performance and eating quality. Rice societies are known for their rich biocultural diversity (Johns and Sthapit, 2004): would farmers and consumers 'choose' Golden Rice from the range of varieties available? The only characteristic about which there was certainty was the colour; Golden Rice, as its name suggests, is yellow. Promoters of Golden Rice have drawn attention to rice dishes (such as *pilau* rice, popular in parts of South Asia) that use spices which lend a yellow colour to cooked rice, as an indication that yellow rice would be acceptable to rice consumers across Asia, ignoring the widespread preference for pure white rice in much of East and South-east Asia. Furthermore, in the case of *uncooked* rice, a yellow colour conveys the presence of mould, indicating that it has been stored for too long and therefore needs to be thrown away. In this context, the challenges and costs involved in educating people to form a 'preference' for yellow rice had yet to be investigated. In addition to agronomic performance, post-harvest stability, and nutritional effectiveness, therefore, questions remained as to the broader acceptability of Golden Rice varieties in different rice cultures (Brooks, 2010).

In 2002, Golden Rice materials were transferred to the International Rice Research Institute (IRRI), a member of an international network of public agricultural research institutes (the CGIAR) based in the Philippines. By this time, a newly formed 'Humanitarian Board', which included the Golden Rice inventors and donors and a Syngenta representative, had issued a 'humanitarian license' enabling IRRI and selected regional partners to begin the process of 'back-crossing' the Golden Rice 'trait' into *indica* varieties (using conventional plant breeding techniques). Concurrent with this adaptive research, overseen by IRRI, a second research pathway was under way in the laboratories of Syngenta. Continuing with *japonica* materials, these scientists were twice successful in raising the beta-carotene level in the rice grain (as well as removing the selectable marker gene). At these moments, the two research pathways would meet, prompting IRRI and its partners to discard the results of earlier adaptive research and start again with the newly transferred *japonica* materials. This process continued until, in 2008, IRRI scientists had stabilized germplasm ready for field testing (Al-Babili and Beyer, 2005; Brooks, 2010).

While Golden Rice continued as a work in progress in research stations in South-east Asia and in Switzerland, it took on a very different identity in policy and public discourse concerning the relative merits of genetically modified crops. In contrast to its messy reality as experimental material in ongoing research efforts, in its 'virtual identity' Golden Rice took shape as a finished product and proven technology. A view increasingly took hold that, but for burdensome regulations and 'irrational' opposition, Golden Rice would already be in farmers' fields and saving lives (Taverne, 2007; Potrykus, 2010a, 2012; McVie, 2013). This view relied on an understanding of the Golden Rice research trajectory as a linear one, in which the output of the inventor's initial discovery has faced a sequence of obstacles – technology transfer, regulatory approval, and consumer acceptance – on the road to its eventual release and adoption (Brooks, 2010). In reality, however, the progress of Golden Rice research has confounded conventional models of linear technology transfer and the conceptual and temporal separation of 'upstream' and 'downstream' in crop research. Rather, the distinction between basic and adaptive research has been 'increasingly blurred, with adaptive research expected to shed light on some of the "surprising" results of basic research' (Brooks, 2010: 87).

In 2011 the BMGF announced nearly $20 m in new grants for biofortification projects, including funds to 'help in the development, testing and marketing of Golden Rice' (Nayer, 2011). Since then, the Philippines Rice Research Institute (PhilRice), in cooperation with IRRI, has carried out two seasons of field trials, which concluded in early 2013 (PhilRice, 2013). Community nutrition studies are planned – to be overseen by a new project partner, Helen Keller International – which, it is hoped, will demonstrate the effectiveness of Golden Rice in improving vitamin A status of malnourished populations (Brooks, 2011a). Nonetheless, the conclusion of field trials and publication of preliminary nutrition studies (carried out in controlled conditions with a group of healthy children) (Tang et al., 2012) have been taken by some commentators as indication that Golden Rice is finally ready for release as a proven antidote to vitamin A deficiency in poor populations, reviving, once again, the virtual identity of Golden Rice as GM crop *'cause célèbre'* (McVie, 2013). On this occasion, however, these claims prompted a swift response from IRRI, clarifying the status of the project as work still in progress:

> It's true that human nutrition research indicates that the beta carotene in Golden Rice is readily converted to vitamin A in the body, providing encouraging evidence that eating Golden Rice could help reduce vitamin A deficiency. However, it has not yet been determined whether daily consumption of Golden Rice does improve the vitamin A status of people who are vitamin A deficient and could therefore reduce related conditions such as night blindness (IRRI, 2013).

The question of whether Golden Rice will prove more effective in addressing vitamin A deficiency than the types of intervention currently in use is therefore still open. The distinction between effectiveness (in 'real world' contexts) and efficacy (in controlled conditions) is an important one, since 'many children exhibiting symptoms of vitamin A deficiency…suffer from generalized protein-energy malnutrition and intestinal infections that interfere with the absorption of beta-carotene or its conversion to vitamin A' (Nestle, 2001: 290). In this case, findings from studies conducted with healthy children shed little light on the likely impact of Golden Rice on the vitamin A status of malnourished populations, since the conversion of beta-carotene to vitamin A depends on the presence of other nutrients, notably fats and proteins, nutrients often lacking in the diets of vitamin A deficient populations. Ultimately, a range of 'biological, cultural and dietary factors act as barriers to the use of beta-carotene, which explains why injections or supplements of pre-formed vitamin A are preferred as interventions' (Nestle, 2001: 290).

Furthermore, vitamin A capsule distribution is conducted through vertical programmes which lend themselves to monitoring – if not impact (Latham, 2010), at least coverage – in a way that embedding nutrient-dense rice varieties in national seed systems would not. This is particularly pertinent to the case of Golden Rice given the outstanding questions about the post-harvest stability of the beta-carotene (GM Watch, 2012). Furthermore, rice systems are highly diverse and decentralized compared with other grains. In the Philippines, for example, rice milling is very much a local activity. While there are a few 'big players' there are an estimated 10,000 rice mills across the country, and monitoring their output is no easy task: a lesson that was learned more than half a century ago by public health officials attempting to introduce mandatory fortification of rice with vitamin B in the 1950s (Florentino and Pedro, 2006). The extent to which Golden Rice can effectively substitute for pharmaceutical supplementation (or indeed other tried and tested interventions at different scales) would depend on how such challenges are tackled, particularly given that biofortification is promoted as an intervention suited to 'out of reach populations' that do not have access to fortified processed foods (HarvestPlus, 2004).

In addition to the confusion over questions of effectiveness, another outcome of the 'poster child' identity of Golden Rice in the GM debate has been the narrow way in which the question of *acceptance* has been understood and addressed. Published literature on *ex ante* impact of biofortification has tended to construct the choice to be made by rice farmers and consumers as between biofortified and non-biofortified varieties (Meenakshi et al., 2010), envisaging a 'switch' from one to the other that bears minimal resemblance to everyday exercise of 'choice' in the context of varietal diversity in local markets and farming systems and the multiple ways in which rice and culture are interwoven in diverse rice societies (Asia Rice Foundation, 2004; Castillo, 2006; Brooks et al., 2013). In the case of Golden Rice, however, this question has been further narrowed by the conflation of farmer and consumer acceptance of Golden Rice with the 'acceptance' of GM crops (PhilRice, 2003), a framing that sidesteps questions about how consumers might react to *yellow* rice (which as discussed earlier is not regarded as a positive characteristic) as well as any effects the beta-carotene content may have on taste and eating quality (Brooks, 2010).

Conclusion

Biofortification is an umbrella term for a diverse range of projects and possibilities. It is best understood on three levels: as a range of technologies for developing micronutrient-dense crops; as a development intervention to improve public health; and as an idea that links agriculture, nutrition, and health in a particular way. Following a brief overview of the biofortification 'landscape', this paper has highlighted the contingency of biofortification in practice by focusing on one initiative that is relatively well known – the Golden Rice project – as it approaches the final stages of product testing and regulatory approval.

A major problem has been the elevation, or rather, reduction of Golden Rice to a 'poster child' in the GM crop debate. This paper has revealed how two important sets of questions about Golden Rice – those concerning its potential *effectiveness* as a delivery mechanism for vitamin A to malnourished populations in 'hard to reach' rural areas; and its *acceptance* by those populations as both a rice variety to cultivate and as a staple food item to consume – have been narrowed down to parameters set largely by an increasingly polarized and impoverished GM crop debate. In the process, considerations likely to have an impact on the viability of Golden Rice, both as a commercial rice variety and as a basis for nutritional interventions, in diverse agro-ecological and socio-economic and bio-cultural contexts, have been framed out of policy and public discourses that conflate efficacy with effectiveness and simplify the challenges involved in securing farmer and consumer acceptance by equating it with the erosion of public antipathy towards GM crops.

It is not too late for these trends to be reversed. As this paper has shown, the Golden Rice project is an exemplary case study in the non-linearity of complex and contested innovation processes, which exposes the limitations of conventional binaries such as 'upstream' and 'downstream'. Attempts to present the project in such linear terms, while shielding it from the reaches of GM crop 'opposition', have led to the 'black boxing' of a range of technical problems and policy uncertainties, which have, as a result, been pushed further and further downstream, to be dealt with 'later'. In this context, the recent clarification by IRRI that resolution of outstanding research questions and completion of approval processes 'may take another two years or more' (IRRI, 2013) is significant and timely. These developments have created a window of opportunity for more open debate about the questions and uncertainties that remain and how they might be resolved.

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