Article:

Radick, G. (2024) Alternative paths for genetics, then and now: Q&A with Gregory Radick about Disputed Inheritance. Trends in Genetics, 40 (1). pp. 1-14. ISSN 0168-9525

https://doi.org/10.1016/j.tig.2023.10.005

TrendsTalk

Alternative Paths for Genetics, Then and Now: Q&A with Gregory Radick about *Disputed Inheritance*

Gregory Radick, School of Philosophy, Religion and History of Science, University of Leeds, Leeds LS2 9JT, UK

Correspondence: G.M.Radick@leeds.ac.uk

Despite the complexity of biological inheritance, most students are introduced to genetics using simplistic concepts that can be traced back to the mid-nineteenth-century work of Gregor Mendel and its subsequent “rediscovery” in 1900. But what if history had played out differently? How would the practice and teaching of genetics look today? What would have been the implications for society more broadly? The possibility of alternative paths for genetics, past and present, is a theme explored in detail in *Disputed Inheritance: The Battle over Mendel and the Future of Biology* [1], by Gregory Radick, professor of history and philosophy of science at the University of Leeds. In this Q&A, he answers questions from the editor of *Trends in Genetics*, Maria Smit.

The cover of your new book shows a collection of peas, but they're not Mendel's peas. Whose peas were they, and what is their significance?

> Those peas belonged to the English zoologist Walter Frank Raphael Weldon FRS (1860–1906), who from 1899 was Linacre Professor of Comparative Anatomy at Oxford University. Nowadays he's probably best remembered for pioneering studies he did in the 1890s showing how, through a combination of precision measurement, statistical analysis, and clever experimentation, it's possible to catch Darwinian natural selection in the act of adapting a population to changing conditions – in Weldon's case, the shore crabs of an increasingly polluted Plymouth Bay. From autumn 1900, he became one of a number of people who took an interest in the excited buzz over Mendel's old paper on his pea-crossing experiments.
>
> In 1901, as part of research for a planned review article on Mendel's paper and the scientific literature burgeoning around it, Weldon acquired samples of pea seeds from hybrid varieties then available commercially, to help him make sense of what he was reading. When his article [2] appeared in February 1902 in *Biometrika* – a journal that he'd recently co-founded with London allies in the new statistical biology, the mathematician Karl Pearson and the polymath Francis Galton – it included two photographic plates of pea seeds selected from those samples. One plate, in black and white, illustrates degrees of wrinkledness. The other plate – on the cover of my book – illustrates a deep-green-to-deep-yellow color range.

For Weldon, the significance lay in the manifest gap between the variable colors of actual pea seeds and the binary, "green"-or-"yellow," unit-character categories that Mendel proposed. The point for Weldon was not that it's impossible ever to observe patterns tolerably close to basic Mendelian patterns. Rather, he saw himself as drawing attention to how much can get missed out, from our descriptions of inherited characters and so from our explanations of them, when complexly heterogeneous experience gets replaced with a simplified, homogenizing idealization. In Weldon's view, the patterns that Mendel reported, instructive as they are in a limited way, didn't so much open a window onto biological inheritance in general as reflect back the particular methodological choices he'd made: the individual varieties he selected, his purifying them to the n^{th} degree, and so on. For Weldon, other choices could yield other patterns that the student of inheritance, curious to know about all of the causes that can impinge on inherited characters, and about the full range of variability that can result, would find at least as instructive.

I've discovered that, appropriately enough, the cover image elicits a spectrum of responses. At one pole are geneticists who seem to want it struck from the record, and certainly not publicized [3]. But there are plenty of geneticists at the opposite pole, including William D. Stansfield, Emeritus Professor of Genetics at California Polytechnic State University, and author of the classic *Schaum's Outline of Theory and Problems in Genetics*. For some while, Prof. Stansfield's been concerned that students trained on textbook representations of Mendel's peas are left ill-prepared for dealing with the fuzzy data that any researcher in genetics confronts. I'm permanently thrilled that he published a letter in *American Biology Teacher* recommending that an article of mine featuring the Weldon green-to-yellow peas plate "should be assigned reading to all students for 'broader critiques of Mendel's legacy.'" [4] Even so, my absolute favorite response so far is from a non-geneticist friend who, when I described the cover image to him, said: "That's what life is like."

Your book reflects an enormous amount of archival research and analysis. How long has this project been incubating? What did it take to research and subsequently write the book?

There's a tradition in Britain as elsewhere of giving an "inaugural" lecture after you've been promoted to a full professorship. I used the occasion of mine, at Leeds in June 2012, to lay out my basic vision for the book [5]. At that point I'd been thinking and researching off-and-on for over ten years about a new history of what's come to be called the "biometrician-Mendelian debate," with the aim of going beyond previous treatments chiefly by giving far more attention – and far more sympathetic attention – to the losing, Weldon-led side of that debate. But transforming that vision into *Disputed Inheritance* took me another ten years – and would have taken even longer if not for two spells of research leave: in 2013-14, funded by the British Academy; and again in 2017-20, funded by the Leverhulme Trust and my department, the School of Philosophy, Religion and History of Science at Leeds.

The challenges were mainly of two kinds. There was the task of getting my eyes on, and then my head around, all of the relevant material, published and unpublished. The good news and the bad news for the historian of Weldon, his arch rival in the Mendelism debate William Bateson, their shared mentor Galton, and all of the other people that I write about, from Darwin onward, is that they were often immensely prolific, with much of their backstage correspondence, manuscripts, and so on surviving. Once that work was well underway, there was the task not merely of figuring out what I wanted to say about it all but of inventing a structure suitable for organizing all of that material into a single argument.

What I eventually settled on is a three-part structure, topped with an Introduction and tailed with a Conclusion and then three loose-end-tying postscripts. Part 1, "Before," comprises four interlinked interpretive essays, taking the reader from the 1860s to the 1900s, and putting in place the background needed to understand the world in which the Weldon-Bateson "battle over Mendel" of my title played out. For example, in the first chapter, entitled "Who Needs a Science of Heredity?," I introduce Mendel's pea-hybrids paper and Darwin's pangenesis hypothesis as historians of science see them, stripped of the several layers of anachronism that now obstruct our view. (Neither Mendel nor Darwin saw himself as trying to establish a science of heredity; Darwin didn't need Mendel in order to make natural selection work; the distinction between "blending inheritance" and "particulate inheritance" is ahistorical nonsense; and so on.) In Part 2, "Battle," I offer a blow-by-blow account of the ever-escalating debate between Weldon and Bateson and the others they drew in from 1900 until Weldon's death in 1906. Although readers will indeed learn much more about how it all looked from Weldon's vantage point, they'll also come to see Bateson's achievement differently – appreciating

> for instance that his coming to be remembered for his one-liner "Treasure your exceptions!" is deeply ironic, because one of his many gifts to nascent Mendelism was a basketful of exculpatory explanation that served to protect it from empirical disproof. Finally, in Part 3, "Beyond," there's another set of four interlinked interpretive essays, standing back from the Mendel battle to assess its significance for everything from politics to pedagogy.

Some of your work involves exploring history-of-science "counterfactuals" – i.e., how history might have played out if circumstances had been different. What is the counterfactual scenario that you explore in your new book?

> Nothing in our culture looks less like it could have been otherwise – and so is harder to unthink – than textbook science. That's where counterfactual scenarios come in. The particular scenario that I take up in *Disputed Inheritance* is whether, had Weldon lived long enough to publish the brilliant "Theory of Inheritance" book manuscript he was working on at his death, our biological science would have relegated Mendelian patterns to the status of the special case, rather than treating them, as our textbooks still do, as the exemplary starting point. So, instead of a biology organized around genes that come either in a dominant or a recessive version, associated with unit characters, we would now have a biology whose central conceptual lesson on heredity is that genes have variable effects depending on contexts, internal and external. Where the emblem of our science of heredity is a Punnett square, the emblem of the science that might have been is a norm-of-reaction curve.

I hope that one of the pleasurable surprises for a lot of readers will be the discovery that what Weldon objected to in emerging Mendelism was not its emphasis on experiments over statistics, or its postulation of invisible entities to explain visible patterns, but its marginalizing of the modifying effects of environments on inherited characters. Over and over again, Weldon stressed how backwards it was, given the circa 1900 state-of-the-art of biological knowledge (which for Weldon, unlike Bateson, included chromosomes as well as natural selection), for biologists to use the phrase "acquired character," as if there are some characters that are wholly germinal in origin and others that are wholly environmental. On the contrary, according to Weldon, every character is the joint outcome of the germinal and the environmental in complex interaction: and *that*, surely, has to be the starting point for any science of heredity worth having.

So when we consider the possibility of biology taking a Weldonian direction circa 1906, we contemplate what's later called "phenotypic plasticity" coming to be not a peripheral, never-fully-integrated concept, but the central, integrated-into-everything concept. And as I try to show in the book, biology's going Weldonian rather than Mendelian in its overall framing and ethos was a close-run thing. In the months before Weldon's death, Bateson was seriously rattled. I want my readers to see that, far from being a foregone conclusion, a historical inevitability, Mendelism's success was something of a historical accident.

I expected that the counterfactual element of the book would be controversial, and in the otherwise enthusiastic reviews that the book's received so far, the reviewers have indeed raised a collective eyebrow at the counterfactualism [6] [7] [8]. But as I emphasize, asking about what might have been just comes with the territory once we concern ourselves not just with what happened in the past – with the "what?" and the "how?" of history – but with the "why?". Why did events unfold as they did, rather than in some other way? In answering those "why" questions, we pick out, on the best evidence that we can find, and the most plausible inferences that we can draw from that evidence, what seem to us the cause or causes that were responsible. And in so doing, we pass – in historical inquiry as much as in scientific inquiry – from description to explanation. But because our explanatory claims carry counterfactual implications. we also, and whether we like it or not, pass into the domain of the counterfactual. If you think that a cause or set of causes X brought about Y, then you seem to be saying, if not for X, then no Y. Scientists routinely follow up investigatively where their counterfactual reasoning leads, and I think historians benefit from doing likewise.

To be sure, historical counterfactuals have a not-entirely-undeserved reputation for inhabiting an evidence-free zone. But, as I try to show, there's often quite rich evidence that we can, and should, avail ourselves of in assessing them. Suppose you're of the view that, however interesting Weldon's perspective, and however well-positioned he was to get a serious hearing for it and also to recruit able and willing Weldonians to build the program, ultimately little would have come of his finishing and publishing his manuscript because biology was bound to go genic after 1900. And if I then press you to say *why* you think that, you could maybe point to the famous triple convergence of Hugo de Vries, Carl Correns and Erich Tschermak on Mendel's patterns and explanations in 1900 as a sign that the Mendelian gene's time had come. (In the book I quote someone who says: if it hadn't been three people in 1900, it would have been six in 1901.) Or you could point to the infamous catastrophe of anti-Mendelian Lysenkoism in the mid-twentieth-century Soviet sphere – an episode that ended with the Communists, having wrecked their agriculture, eventually slinking back to Mendelian genetics. Or you could point to any number of biotech wonders where it seems like, just as Bateson foretold, we can pull a gene for some amazing character out of one organism and plug it into another and get that same character; an example I give in the book is of transgenic goats that produce spider silk in their milk. Put all of that together, and that's a fairly substantial empirical basis for the claim that our biology went genic after 1900 because the Mendelian gene concept captures reality, and that, provided a biological community is mature intellectually and not deformed ideologically, it will sooner or later organize its science of inheritance around that concept. Accordingly, I devote quite a number of pages to evaluating the above in order to show that, on inspection, it doesn't actually support gene inevitablism at all well. But whether the reader ends up convinced, what's under discussion is evidence from the actual past and the plausible inferences that this evidence supports.

But there's also, plainly, an imaginative aspect to counterfactual reasoning, and I embrace that too, to the extent of closing the book with an extract from the entry for Weldon in a counterfactual edition of the *Dictionary of Scientific Biography*. In history as in science, imagination is part of creative inquiry, and it's always impressive to me how the asking of what-if or what-might-have-been questions can help jolt thinking out of accustomed grooves, and also how valuable such questions can be independently of the value of any answers.

How do you think a Weldonian "win" might have impacted the practice of genetics or the discoveries made over the past century?

Let me first of all emphasize a couple of important ways in which I think the impact *wouldn't* have been all that large. For one thing, there would have been plenty of cross-breeding á la Mendel, in part because cross-breeding as a research method circa 1900 already had so much momentum behind it (hence De Vries, Correns and Tschermak finding their way to Mendel's pea paper around then), in part because Bateson and his Mendelian allies would have continued to promote its use so vigorously, and in part because Weldon himself was so positive about it. In the "Theory of Inheritance" manuscript, he presented Mendelian cross-breeding as complementary to Galtonian biometry, in that the former concentrated on controlled mating of homogenized lineages whereas the latter concentrated on statistical studies of freely breeding populations. In Weldon's view, cross-breeding was troublesome only when it was treated as establishing that dominance was something that a version of a character either has or doesn't have, independently of context. So long as we guard against overinterpreting in that way, the method's useful – and a Weldonian biology would have esteemed it. In my book, I underscore this point in that counterfactual *DSB* entry by suggesting that, had biology taken a Weldonian turn, the Morgan group's classic fruit-fly investigations into the chromosomal basis of heredity would have taken place much as they actually did, but published in a book entitled *The Mechanism of Weldonian Heredity*.

If we turn next to consider the growth of knowledge about the biochemical and ultimately molecular nature of inheritance, what's so striking about it, as a number of historians and philosophers of science have stressed, is how little it owed to or otherwise extended distinctively Mendelian knowledge. The discovery of the double-helical structure of DNA by Watson and Crick, for example, depended not on Mendelian cross-breeding pushed to the molecular level but on X-ray crystallography, nucleic-acid chemistry, the mathematical theory of helices, and a willingness to play about with physical models. The general point holds for the working out of the details of transcription and translation, for the invention of nucleotide sequencing, and for all of the extraordinary manipulative advances from recombinant DNA to CRISPR. Despite a familiar iconography of pea plant tendrils spiralling up into a double helix, the knowledge we classify as "biochemical genetics" and "molecular genetics" would have come about in much the same way without the Mendelian turn of the early twentieth century. Indeed, when we take into account how much more bullish Weldon was on chromosomes compared with Bateson, I think the problem of understanding chromosomal structure and function would if anything have commanded a greater share of workers and resources sooner than it did.

So what would have been different research-wise? For me, the answer lies with working out what a research science organized not around the Punnett square but the norm-of-reaction curve would have looked like. As I show in the book, in 1902, seven years before Richard Woltereck introduced the norm-of-reaction curve in a paper on experiments on the water flea *Daphnia*, Weldon gave an evening discourse on "Inheritance" at a British Association meeting in which, near the start, he described similar experiments done also using *Daphnia*, and to similar ends. As Weldon put it to his audience: if you want to increase average spine length in *Daphnia*, you either change the solution around a particular *Daphnia* variant or you keep the solution the same and change the *Daphnia* variant. For Weldon, the take-home message was that whenever you're thinking about an inherited character you should also be thinking about the environment, because all characters are joint products of what's within and what's without an organism. Now, if we suppose that, after a Weldonian "win", that message really did hit home, I think we'd be considering a science where everyone takes for granted that if you're not including variability in internal and external environments in the study design, and so making room for phenotypic plasticity empirically and conceptually, then you're not really studying inheritance, but some isolated subset of it. And that really would be very different from genetics as we've known it.

What about society as a whole? How do you think early uptake of Weldonian ideas might have influenced society in positive or negative ways?

It's easy to overplay the social consequences of scientific ideas, but easy to underplay them too. In trying to get the balance right, I take inspiration from the work of the historian Sir Richard Evans on social Darwinism in Nazi Germany. What Evans concludes is that, even without Darwinian concepts and language, the Nazis would have done the awful things they did. But it doesn't follow therefore that Darwinian talk of struggle between the races and so on was just a kind of window dressing, unpleasant but ultimately ineffective. Rather, that talk functioned to reconcile men and women to the awfulness by encouraging them to see it as sanctioned by nature, science, and history [9].

I think something like that holds for what the historian of science Amir Teicher has aptly called "social Mendelism" [10]. Eugenics of some form would have emerged as an international movement in the twentieth century no matter what happened with the science of heredity. But, as detailed in the book, with no Weldonian ideas on a par with Mendelian ones in the public culture, Mendelian simplisms about complex characters went un-countered in America in the 1920s and Nazi Germany in the 1930s, when they were used to legitimate increasingly harsh eugenic interventions. And Mendelism's availability for that role was well prepared in the social polemics of the early Mendelians, who, from Bateson onward, routinely went out of their way to stress that the upshot of their science for society – beyond the economic benefits prophesied for Mendelized agriculture – was a thorough-going hereditarianism. Education and sanitation improvement schemes, they counselled, were a waste of time and money if the hereditary stock was bad. (A Scottish soldier once told Bateson that what he preached was "Scientific Calvinism," and Bateson thought that was right.)

So, at a minimum, had Weldonian ideas been circulating more conspicuously, they could have diminished – maybe even dissipated – the air of authority that came to settle over Mendelian hereditarianism, with consequences potentially for, e.g., who got denied a visa, or involuntarily sterilized, or murdered. And had those ideas continued to circulate, they could have helped habituate us sooner to all sorts of increasingly familiar notions belonging as much to biology and medicine as to social justice: that actual people vary in important ways not well captured by simple uniform categories; that developmental potential on the whole can't be reliably read off from genotype; that the phenotypic differences which variant genes make can be larger or smaller or non-existent depending on environment. Although I struggle to see any downsides to that counterfactual prospect, we shouldn't discount how hard it might have been for the upsides just outlined to be realized. Norm-of-reaction curves and, more ambitiously, GxE diagrams can be taught in socially empowering ways, or they can be taught as just another piece of knowledge that Punnett-square-minded genetics students can master for the exam and then forget.

What are some things you hope the genetics community will learn from your book?

One thing that I hope my geneticist readers take away is a much richer sense of what was up in biology circa 1900. The standard history of genetics, as it's presented in textbooks but also in pop-science bestsellers, tie-in TV documentaries and the like, is a story in which basically all was chaos until Mendel's discovery of the gene was belatedly recognized and – once some tedious nay-saying overcome – built upon, eventually enabling connection-making first with chromosomes and then with Darwinism. In itself the story is very satisfying, so much so that, if it's all you know, you'll have zero motivation for questioning it. But once you're given more information, of the sort that my book supplies in abundance, you can see how problematic that story is, and relatedly, how far from a foregone conclusion was a twentieth-century science of inheritance whose foundational concept – the Mendelian gene – effectively shunted knowledge of the modifying role of environments, internal and external, to the margins.

A related hope is that the book can help reset the community's relationship with Mendel himself, as part of a more general shift towards engaging with the past in a critical spirit. Consider, for example, the well-known question about whether Mendel's data are improbably close to his theoretical predictions, given the number of trials he did, i.e., "too good to be true." If your Mendel is the Mendel of the textbooks, and your knowledge about the controversy over his data is limited to the for-and-against scientific literature, you're bound to feel that you've got to take sides on that issue, and then either to come out as a vindicator of the unfairly maligned Mendel or as reluctantly concluding that alas your former hero wasn't so heroic after all. But if, by contrast, your Mendel is the actual Mendel of history, and furthermore you know the cultural history of the data controversy as reconstructed in the book and more extensively in a recent paper of mine [11], then you're able to see that the "good Mendel or bad Mendel" choice is a bad choice. Actual Mendel was actually great, but his pea-hybrids paper wasn't an attempt to found a new science of inheritance. It was a virtuoso sorting out of the fate of hybrid character in a scientifically fascinating and commercially important class of plant hybrids. Appreciate that, and you appreciate at a stroke why his use of binary categories and his exclusive concentration on germinal causation – so problematic for any science of inheritance – were brilliantly apt *given his aims*.

Mendelism has a lot to answer for, scientifically and socially. But Mendelism wasn't Mendel's creation, it was the creation of Bateson and his allies, who extracted the bases for their science from Mendel's otherwise-directed paper. Likewise, the statistical dodginess of Mendel's data should be seen not as due to a character flaw but, as Weldon stressed, as flowing from that decision to deal in binary categories. Weldon's perspective got lost in part, I suggest, because Ronald Fisher in his famous 1936 paper on the data problem treated it as largely to Mendel's intellectual credit, since Mendel must have worked out theoretically what the ratios should be, and in part thanks to the peculiar cultural dynamics of the Cold War period, in science and in the wider culture, which ended up entrenching and then promoting the fraud-or-not framing. I very much hope that geneticists who become acquainted with this historical perspective can liberate themselves from the received version, in their thinking and research but, perhaps most powerfully for the immediate future, in their teaching. I'd love for students to learn more about the actual, historical Mendel, in a way that might enhance their sense that even the best science – including their own – is always rooted in time and place in ways that we should be curious about. Equally, I'd love for their teachers to feel that it was in keeping with the best of what Mendel stood for to draw students' attention to the actual phenotypes of real-world organisms – peas included – as variable in expression because complexly multifactorial in causation.

There's a connection between an underdeveloped sense of what the options were for biology around 1900 and an underdeveloped sense of what the options are for biology now. You can see the linked constraints at work, for example, in a tribute to Mendel published last year, commemorating his two-hundredth birthday [12]. In an impeccable passage, the geneticist author, Aoife McLysaght, inventoried all of the ways in which genetics in general was not at all like the textbook-Mendelism version of it:

"Genetics is incredibly (beautifully, fascinatingly, bewilderingly) complex. We now know that most traits – physical, biochemical, behavioral – are influenced by many different genetic variants, individually of small effect, acting in combination with the environment and stochastic processes during development. Even identical twins, who share all their genes, are not actually identical."

The rest of the article delivers a devastating critique of genetic determinism ("very easy to learn and very difficult to abandon"). Yet the passage quoted above begins: "I could not imagine trying to teach genetics without starting with Mendel." To imagine trying to teach genetics without starting with Mendel, it helps a lot to spend time getting to know Weldon's work, because Weldon, unlike us, didn't have to unthink the Mendelian organization of knowledge of inheritance.

A few years ago, you ran an experiment [13] to see what would happen if introductory genetics was taught as if its curriculum emerged from a more Weldonian biological past. Can you tell us about this experiment and what we learned from it?

Here we come to the best illustration I know of how curiosity about the might-have-been world can increase knowledge of the actual world. In that vision-outlining inaugural lecture of mine, I suggested that a good place to test the proposition that a science of inheritance organized around Weldonian emphases could have worked, and would have been interestingly different in its effects on cognition from our Mendelian science, was the classroom. I invited my audience to imagine designing an introductory curriculum in genetics as if it came not out of the actual Mendelian past but out of the Weldonian past that might have been.

So, we don't start students off with Mendel's unit-character peas and then proceed to complicate it, but instead start them off with the idea that, for most characters in developing, environmentally situated creatures like humans, there's lots of variability owing to multiple causes interacting in complex ways. In giving the students a DNA-influenced character to think with, we give them not seed color in the pea but the health or otherwise of the human heart, dwelling in detail on the range of causes that potentially bear, in and out of the body. Then throughout the course, the constantly reinforced message is that variability is the norm because multifactorial causation is the norm. When these students eventually do meet elementary Mendelian patterns, they meet them accordingly as a special case – as what happens when, due to human-contrived or (more rarely) natural circumstances, all the internal and external variability that might otherwise obtain is dialed down to the point where there's just, in the simplest case, one difference at one locus on one chromosome.

> Suppose you could develop that course, and students signed up for it, and they didn't just run screaming from the room at the first meeting but actually found that message about variability and complexity intriguing and so stayed through to the end. What would they be like? In particular, might they be less deterministic in their attitudes to genes than students doing the traditional start-with-Mendel's-peas course?
>
> To my amazement, the next month, my collaborator Jenny Lewis, a genetics education expert then based at Leeds, and I actually got a grant to run the experiment – or, as I now know to call it, quasi-experiment, since in educational psychology any intervention short of a randomized controlled trial is a quasi-experiment. Jenny and I recruited the developmental biologist turned historian of science Annie Jamieson, who did the heavy lifting in writing the new curriculum and then basically ran the study, including teaching the new curriculum to undergraduates. Our results indicated that whereas students completing the traditional course were on average as determinist about genes at the end of teaching as they were at the start, students who completed Annie's Weldonian course were on average less determinist. On the face of it, then, the Weldonian organization seemed to do a better job of ensuring that students learn genetics without inadvertently picking up a heredity-is-destiny message which, in the twenty-first century even more than in the twentieth century, we know to be pernicious hokum.

What do you think a genetics course curriculum should look like in 2023? Should it be different for budding scientists versus the general public? How much history should be included?

To my mind, the most exciting story coming out of genetics in 2023—or so far anyway (I'm writing this in the summer)—is about the development of a CRISPR-based therapy for sickle cell disease [14]. Today's students will have to navigate a future in which such innovations come thick and fast. If we ask: what kind of introductory curriculum in genetics will best help these students rise to the challenge not merely of understanding these innovations but of making best use of them, and more generally of all the new knowledge, techniques, and technologies that will emerge from the genomic, post-genomic, epigenomic etc. research forefronts in their lifetimes?, then I don't think a great answer is: the current curriculum, just with more stuff at the end about CRISPR, and maybe a health warning about the dangers of eugenics.

The sickle-cell therapy story is an especially good one to think with because, although this hasn't been emphasized in the press coverage, it's a beautiful vindication of the "context matters" perspective – and I actually wrote about it in this spirit in *Disputed Inheritance*. The therapy hinges on the discovery of people who, according to textbook genetics, should have suffered from sickle cell disease, since they'd inherited a double dose of the disease-causing mutation, but were in fact healthy. It turned out that they owed their healthiness to a mutation in another gene which ordinarily functions to switch off fetal hemoglobin shortly after birth. The CRISPR therapy works not by fixing the alleles that encode faulty adult hemoglobin but by introducing a fault into the alleles blocking the production of fetal hemoglobin. So it's an innovation story that illustrates how important it can be to take on board the Weldonian point that, in general, phenotype can't just be read off from genotype.

Designing an introductory curriculum reliably capable of instilling that point in students is work in progress. At Leeds I've had the rare good fortune for a historian of science not only to be asked to join the teaching staff for our Genetics 101 course but to be introduced to the students as someone who'd changed the course leader's mind about how the subject should be taught! His name is Tom Bennett, he's a plant geneticist, and he'd so completely taken for granted the centrality of Mendelian genetics that when he first heard me give a talk on my research, his reactions – as he told the students – were "surely not!" and also "how *dare* you!" But he continued to mull it over, and by the time he was asked to teach the introductory course, he'd decided – and he said this to the students too – that I was right after all, and that, for all the immense utility of Mendelian genetics for research purposes, it was a disservice to newcomers to present the science of inheritance as if it was nothing but the study of genes.

It's still early days for the revised Leeds course; but between Tom's steer at the start, followed by three lectures from me on, respectively, the history of genetics (along *Disputed Inheritance* lines), phenotypes as multifactorial upshots of genes in developing and environmentally located bodies, and human genetics and the problem of genetic determinism (including coverage of eugenics), I reckon we're on our way to rethinking what a "context matters" university-level introductory genetics course for the mid-2020s can be. And similar rethinkings are in train for school biology, where Kostas Kampourakis [15] and Brian Donovan [16] have been especially active. None of us, to my knowledge, thinks that the basics should be different for budding scientists, since they will go on to do research and to teach in a world that needs bio-scientists who are as creatively "context matters" as can be.

As for history: individual teachers will have varying levels of confidence in integrating history beyond the "it all goes back to Mendel's mind" textbook cliché. But in my experience there will always be some proportion of students in a class who find that some humanizing historical perspective on how and why a science *got that way* – how and why, say, Punnett-square problems perpetuating what have long been known to be myths of human genetics (e.g., that dimples/no-dimples is a simple Mendelian character) became ubiquitous – really empowers them, simultaneously boosting their understanding and super-charging their motivation. Attention to Mendel's paper can be valuable too, just so long as it's presented not as the Beginning of Genetics—with Mendel as the Law Giver, a kind of scientific Moses – but as an outstanding response to a problem about plant hybrids that was lively in Mendel's day but not in ours [17].

In most settings, anyone teaching introductory genetics will have very limited room for maneuver, given all of the hand-me-down materials and expectations. Even so, there'll be opportunities to raise consciousness and pique curiosity about real-world phenotypic variability and causal complexity – and I think these should be seized with both hands. An easily incorporated suggestion that I make in the book concerns a staple of basic genetics teaching: the Punnett square problem. Because Punnett squares represent phenotypes as the result of nothing but allele distribution, with each allelic combination giving rise to unit-character "yellowness" or "sickle cell disease" or whatever, they're

> deeply misleading. But if teachers first of all emphasize that every Punnett square has an invisible sign over it that reads ALL ELSE BEING EQUAL, and illustrate with examples so that students see, literally and figuratively, how many sources of variability have to be excluded for Punnett-square reasoning to hold, then potentially there's less of a chance that students will leave the classroom thinking that inheritance is Punnett squares writ large.

If educators are interested in learning more about your Weldonian approach to teaching the science of inheritance, are there specific resources that they can tap into?

> Towards the end of the final chapter of *Disputed Inheritance*, educators will find a range of proposals for folding the Weldonian approach into existing curricula. Beyond what's set out there, I recommend the resources at three online sites: the website from the 2012-14 Leeds Genetics Pedagogies Project, where the course materials – including the PowerPoints that Annie Jamieson put together for lectures – are available [18]; a recently published CourseSource lesson by Kelly Schmid and colleagues entitled "Honoring the complexity of genetics: Exploring the role of genes and the environment using real world examples," and making use of Weldon's 1902 peas image among the examples [19]; and the lectures-and-lab unit outline published as a supplement to a 2020 article [20] by biology educators at Illinois State who, drawing on the Leeds work, put the Weldonian approach and indeed story at the heart of a culturally inclusive, socio-politically *engagé* revamp of their genetics teaching. They are so forthright on why biology students need

to know about Weldon's approach, and also about why, in the heyday of Mendelian hereditarianism, that approach got sidelined, that I'd like to quote them at length:

"Reflect[ing] upon the history of the development of our genetics knowledge. . . . would require instructors to be aware of and teach about the culturally laden history of Mendel, Weldon, and Bateson as detailed above, which may create discomfort in some instructors. However, we argue that it is entirely appropriate to include this history, as we often teach about the history of scientific knowledge regarding the discovery of the double helix, atomic structure, evolution, and numerous other scientific concepts. Shying away from the impacts of culture on scientific knowledge only serves to reinforce deterministic, essentialist, and racist views of human genetics. It is far more appropriate to embrace the complexity and context-dependent nature of science education and of genetics itself to promote greater learning gains and begin to move toward culturally relevant genetics education."

And it isn't a resource per se, but Robert Johnston's reflections [21] on forty years of teaching what he now sees as "an oversimplification of the truth" make for sobering reading. Especially worth dwelling on, I think, is the following observation: "When I taught Mendelian genetics for all those years, I felt I was teaching mathematical logic rather than Biology." If you can imagine what it would be like to teach genetics so that it felt less like mathematical logic and more like the rest of biology – along the lines of the way other "context matters" biological subjects like evolution or ecology or, well, pretty much everything else gets taught – then you're well on the road to reimagining genetics along Weldonian lines.

How does your new book relate to some of the work you've done in the past (e.g., on Darwin and Darwinism)?

Mainly I see the book as bringing to a sort of climax and synthesis my research on the history and philosophy of genetics and on what, slightly grandly, could be called my reflections on historical evidence, explanation, and counterfactuals. But I also drew in all kinds of ways on insights I've gleaned from my work in other areas. In researching my first book, *The Simian Tongue: The Long Debate about Animal Language* (2007) [22], for example, I learned a lot about how new scientific disciplines become entrenched, not least via the power they acquire over the imaginations and ambitions of the people trained up within them. That helped me to appreciate the brilliance of Bateson's innovations in extracting from Mendel's paper what I identify as the teachable principles, tractable problems, and technological promise which made Mendelism the outsized success it became. Lessons I learned even further back from an amazing paper on laboratory science [23] by the late, great philosopher of the sciences (as he always called them) Ian Hacking – a paper that I read while trying to understand Darwin on evolutionary progress, and what had gone wrong with Stephen Jay Gould's analysis of it [24] – live on in the book in my analyses of the permanent usefulness of Mendelian genetics as well as its remarkable extendability as "applied science." And my long acquaintance with the challenge of getting inside Darwin's thinking on everything from the evolutionary origins of language [25] to the nature of analogical argument [26] was a help in getting inside his much-derided pangenesis hypothesis, which Darwin first wrote up in 1865, the same year that Mendel gave lectures on his pea experiments. By the time I'd finished drafting the first chapter of *Disputed Inheritance*, I was sufficiently at home in pangenetical reasoning that I could anticipate what Darwin was going to say about whatever explanatory problem he turned to next.

Did you discover any surprises while researching or writing the book?

All the time! Lots of them turned out, as I researched further, to have been surprises for me but not for scholarship at large. The reasoning set out in the book's second postscript is a good example. There I follow Weldon's lead in showing how, on assumptions that were biologically plausible in circa 1906, the classic Mendelian pattern can be explained without Mendel's assumptions, and with the non-Mendelian result that most of the green seeds in the F_2 would harbor yellow-making factors. Other scholars had known about that, notably Bernard Norton (from whom I learned it) and, later on, Michael Bulmer. But I reckon that it will be unfamiliar to most of my readers, and it will be as eye-openingly surprising to them as it was to me when I first encountered it. No less revelatory was seeing for myself – though again, others had seen these things before me – how misleadingly Galton had been caricatured as a hereditarian; how firmly the chromosome theory of heredity was in place by 1900 (as I show, it featured in a popular-science lecture that March in London); and how thoughtful Morgan's fly group was about the ties binding their claims about what genes were "for" to their particular experimental set-up.

But then there were the real-deal, genuinely new-to-scholarship surprises. One that's especially close to my heart was my realization, quite late in the writing, that an unpublished manuscript of Weldon's had been misclassified in the archive, and was actually the draft of something that I'd despaired of ever finding: the text of that 1902 popular lecture on inheritance, given as an evening discourse at the British Association meeting in Belfast. That discovery is dear to me in part because I made it while pursuing the counterfactual question of what a successful Weldonian science might have looked like – so it's a concrete instance of how knowledge of the actual past can benefit from inquiry into the might-have-been past. But it's also dear to me because it's in this manuscript that we find the clearest instance of what Weldon thought beginners on inheritance should be organizing their understanding around: not Mendel's pea experiments, in which nothing matters but the combination and re-combination of germ-line factors, but – as I've already mentioned – experiments on the water flea *Daphnia*, showing that spine length depends both on the particular variety of *Daphnia* used and on the quality of the solution that the individuals are raised in. Again, for Weldon, you can change spine length either by changing the solution or by changing the *Daphnia*, so it makes no sense to think of spine length as determined germinally or environmentally. A mature character is the complex product of germinal-environmental interaction.

What are your future plans? Do you intend to expand upon this work?

Currently I have several book-expanding projects on the go. There are some draft papers about aspects of the general method of counterfactual history, and I hope to continue developing my work in that area. There are also three collaborations that I'm very excited about. With fellow history and philosophy of science scholars Charles Pence and Yafeng Shan, I'm working on a scholarly edition of Weldon's "Theory of Inheritance" (which Annie Jamieson did foundational work on some while ago). With biomedical colleagues in the Leeds Centre for Disease Modelling I'm exploring prospects for taking the Weldonian approach into the disease-modelling laboratory. And with science education specialists Brian Donovan and Michelle Smith I'm involved in a large-scale NSF-funded project that's taking the genetics curriculum work we did at Leeds to the next level of rigor.

If I may close with an invitation to readers of *Trends in Genetics*: thanks to supplementary funding from the University of Leeds, Brian and Michelle and I are now in a position to enroll college and university students anywhere in the world in the teaching experiment. In brief, students who participate will be assigned at random to one of several self-guided, hour-long, online tutorials in introductory genetics, with the tutorials differing in how much emphasis they put on trait malleability and multifactorial causation. So if, in academic year 2023-4, you're teaching introductory genetics and might be interested in participating in our research, please get in touch with me at the email address above. As Weldon knew so well, the wider and more diversely representative the sample, the better the science!

References

1. Radick, G. (2023) *Disputed Inheritance: The Battle over Mendel and the Future of Biology*, University of Chicago Press.

2. Weldon, W. F. R. (1902) Mendel's laws of alternative inheritance in peas. *Biometrika* 1, 228-254.

3. Davey Smith, G. (2022) https://twitter.com/mendel_random/status/1550073946220920835. 21 July.

4. Stansfield, W. D. (2016) Letter to the editor. *American Biology Teacher* 78, 185.

5. Radick, G. (2012) Scientific inheritance: How history matters for the sciences. 16 May. https://www.youtube.com/watch?v=D3nyB2lqmRo

6. Comfort, N. (2023) Review in *FASEB Journal* 37:4.

7. Hall, B. K. (2023) How a scholarly spat shaped a century of genetic research. *Nature* 619, 690-691.

8. Ings, S. (2023). Mendel's new place. *New Scientist* 259:3453, 29. Also: A truth told backwards. 28 August. http://www.simonings.net/?p=3749

9. Evans, R. J. (1997) In search of German social Darwinism. In *Rereading German History: From Unification to Reunification, 1800-1996*, Routledge, 119-148.

10. Teicher, A. (2020) *Social Mendelism: Genetics and the Politics of Race in Germany, 1900-1948*, Cambridge University Press.

11. Radick, G. (2022) Mendel the fraud? A social history of truth in genetics. *Studies in History and Philosophy of Science* 93: 39-46.

12. McLysaght, A. (2022) The deceptive simplicity of Mendelian genetics. *PLOS Biology* 20 (7): e3001691.

13. Jamieson, A. and Radick, G. (2017) Genetic determinism in the genetics curriculum. *Science & Education* 26, 1261-1290.

14. Le Page, M. (2023) Cut, paste, cure. *New Scientist* 259:3446*,* 39-42.

15. Kampourakis, K. (2022) Should we give peas a chance? An argument for a Mendel-free biology curriculum. In *Genetics Education: Current Challenges and Possible Solutions*, eds. M. Haskel-Ittah and A. Yarden, Springer, 3-16.

16. Donovan, B. M. et al. (2019) Towards a more human genetics education: Learning about the social and quantitative complexities of human genetic variation research could reduce racial bias in adolescent and adult populations.

17. Radick, G. (2016) Teach students the biology of their time. *Nature* 533: 293.

18. Jamieson, A. Leeds Genetics Pedagogies Project teaching materials. https://geneticspedagogies.leeds.ac.uk/

19. Schmid, K. et al. (2023). Honoring the complexity of genetics: Exploring the role of genes and the environment using real world examples, https://qubeshub.org/community/groups/coursesource/publications?id=3603&tab_active=about&v=1

20. Sparks, R. A., Baldwin, K. E., and Darner, R. (2020) Using culturally relevant pedagogy to reconsider the genetics canon. Journal of Microbiology & Biology Education 21:1-6, plus supplementary materials.

21. Johnson, R. (2023) Is it time to remove Mendel from the school curriculum? *Journal of Biological Education* 57, 707-708.

22. Radick, G. (2007) *The Simian Tongue: The Long Debate about Animal Language*, University of Chicago Press.

23. Hacking, I. (1992) The self-vindication of the laboratory sciences. In *Science as Practice and Culture*, ed. A. Pickering, University of Chicago Press.

24. Radick, G. (2000) Two explanations of evolutionary progress. *Biology and Philosophy* 15: 475-491.

25. Radick G. (2008) Race and language in the Darwinian tradition (and what Darwin's la5guage-species parallels have to do with it)." *Studies in History and Philosophy of Biological and Biomedical Sciences* 39: 359-70.

26. White, R., Hodge, M. J. S., and Radick, G. (2022) *Darwin's Argument by Analogy: From Artificial to Natural Selection*, Cambridge University Press.