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Muriel Wheldale Onslow and Early Biochemical Genetics

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Abstract. Muriel Wheldale, a distinguished graduate of Newnham College, Cambridge, was a member of William Bateson's school of genetics at Cambridge University from 1903. Her investigation of flower color inheritance in snapdragons (*Antirrhinum*), a topic of particular interest to botanists, contributed to establishing Mendelism as a powerful new tool in studying heredity. Her understanding of the genetics of pigment formation led her to do cutting-edge work in biochemistry, culminating in the publication of her landmark work, *The Anthocyanin Pigments of Plants* (1916). In 1915, she joined Frederick Gowland Hopkin's Department of Biochemistry as assistant and in 1926 became one of the first women to be appointed university lecturer. In 1919 she married the biochemist Huia Onslow, with whom she collaborated until his death in 1922. This paper examines Wheldale's work in genetics and especially focuses on the early linkage of Mendelian methodology with new techniques in biochemistry that eventually led to the founding of biochemical genetics. It highlights significant issues in the early history of women in genetics, including the critical role of mentors, funding opportunities, and career strategies.

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After the rediscovery of Gregor Mendel's paper on hybrid crosses was announced in the spring of 1900, biologists around the world began designing crosses to test the efficacy and extent of Mendel's hypotheses about the purity of the germ cells, segregation and independent assortment of factors, and the dominant-recessive pattern of inheritance of alternative pairs of characters. Color differences were naturally among the first systems to be explored in both plants and animals, with botanists particularly focusing on the heredity of flower color in plants.[1] By 1909, there was extensive evidence that Mendelian heredity was indeed widely applicable, as William Bateson reported in *Mendel's Principles of Heredity* – the leading genetics textbook of the day. Moreover, great advances had been made in understanding the "genetics" of color inheritance. "As the result of extensive research," he wrote, "many Mendelian features of colour have been discovered, and the existence of numerous colour-factors is demonstrated."[2] It was only natural for some to turn their attention to investigating the nature of these "colour-factors."

Bateson was himself very interested in this line of work. Since beginning a study of the nature of variation in plants and animals in the late 1880s, he had considered the possible chemical processes that might be involved.[3] He conveyed this idea to the small band of workers at Cambridge who investigated Mendelian phenomena, and several chose to study color phenomena, including Edith Rebecca (Becky) Saunders (1865–1945), who mainly analyzed flower color in *Matthiola*; Florence Margaret Durham (1869–1948), who worked on coat color in mice; Dorothea C. E. Marryat (1880–1928), who studied inheritance of flower color in *Mirabilis jalapa*; and Muriel Wheldale (1880–1932), who investigated the heredity of flower-colors in snapdragons (*Antirrhinum*). Coloration (or the lack thereof) generally followed Mendelian patterns: albinism, for example, was shown to be a recessive trait. But researchers soon learned that such cases were often complex. As L. C. Dunn noted: "Breeding analysis revealed that many interacting genes were responsible for the wide variety of colors of flowers and leaves."[4] For Bateson and others, however, this line of work appeared promising as a means of exploring the nature of the heredity factors themselves or at least their mode of action.

Wheldale became interested in this problem while still an undergraduate at Cambridge. In 1903 she began to work on the genetics of flower color inheritance. Having quickly provided a factorial analysis that could explain the color patterns, she then turned to the biochemical side of the problem, work that she continued to pursue through the mid-1920s. As Robert Olby noted, Wheldale's work "lent valuable support to the idea that Mendelian differences have a chemical basis, and that genes act as enzymes." Although this problem proved to be much more

[1] See the bibliography of papers pertaining to "Anthocyanins and Genetics" in Wheldale, 1925.

[2] W. Bateson, 1913, p. 37.

[3] Richmond, 2007.

[4] Dunn, 1991, p. 176.

intractable than identifying the patterns of inheritance, nonetheless, in Olby's words, Wheldale's work "formed the starting point for many speculative discussions of the chemical basis of heredity."[5] In the end, the early hope that this line of work would easily link genetic phenomena with biochemistry faded in the face of significant technical as well as theoretical obstacles.

In tracing the roots of biochemical genetics, historians of genetics generally point to work carried out in the 1930s and 1940s. As A. H. Sturtevant observed: "There have been two chief biochemical approaches to the study of genetics – through the biochemical study of the effects of gene substitutions, and through a direct attack on the chemical nature of the genetic material itself. Both approaches have been highly successful in recent years, but both went through a rather long period of slow development that was often rather discouraging."[6] The first approach is characteristic of George Beadle and Boris Ephrussi's study of the development of eye pigment in *Drosophila*, and, of course, Beadle's later Nobel Prize winning work with Edward Tatum on *Neurospora*, which led to the one-gene, one-enzyme hypothesis.[7] So, too, is this applicable to the physiologically grounded genetical study of wing pigmentation pursued by Alfred Kühn and his school in the meal moth *Ephestia*.[8] We know much less about the work of those who attempted a direct attack on the chemical nature of the gene and gene action, especially in the early years of Mendelism, from 1900 through the 1920s.

It is in this regard that Muriel Wheldale's career assumes particular interest. Her genetical study of flower colors in snapdragons was widely cited, and her subsequent focus on the chemical processes involved in the production of color broke new ground in the nascent field of biochemistry, marked by the publication of *The Anthocyanin Pigments of Plants* in 1916. Bateson certainly held Wheldale's work in high regard. As he wrote in 1909, "Not often can we hope to be able to specify the complementary elements which must meet each other in order that a certain compound character may be produced. Nevertheless, by the co-operation of physiological chemistry with genetics there is every hope that in favourable cases of a simple order actual demonstrations of these elements may be carried out. Perhaps the nearest approach to such an achievement is that made by Miss Wheldale in her experiments on

[5] Olby, 1974, p. 135.

[6] Sturtevant, 1965, p. 100.

[7] Sapp, 1987, Olby, 1974, Kay, 1993, and Kohler, 1994. See also Hickman and Cairns, 2003; and Berg and Singer, 2003.

[8] Rheinberger, 2000a, Harwood, 1993, chap. 2.

Antirrhinum (Snapdragon)."[9] Yet she is almost absent in the historical literature. Leading surveys of the history of genetics only mention her work in passing or briefly describe her major results.[10]

Wheldale's research program, even though it did not live up to its early promise, offers historians a particularly valuable vantage point by which to reflect on a number of issues in early genetics. Her scientific papers reveal an interesting and well conceived early attempt to connect genes with their products, specifically linking genes determining flower pigments with the biochemical processes they initiated. Her work thus enriches our understanding of a promising line of early Mendelian research, allowing us to explore in some detail her theoretical assumptions and experimental protocol. It also contributes to elaborating the social history of early Mendelism, providing a particularly insightful glimpse of the interactions of members of Bateson's group and his role as a mentor to students. Because Wheldale eventually migrated to biochemistry, her work also illuminates aspects of Frederick Gowland Hopkin's newly formed Department of Biochemistry at Cambridge. Indeed, it was through her teaching of plant biochemistry that she became one of the first women to secure a position as lecturer at Cambridge. Wheldale's intellectual accomplishments and career trajectory are thus of particular interest to historians of women in genetics as well as biochemistry.

With regard to the history of women in science, the women who worked with Bateson, Wheldale included, provide a good illustration of Margaret Rossiter's observation that women were frequently attracted to newly emerging fields in science. Rossiter offers a very plausible explanation of this in terms of the favorable economic dynamic that benefited both the women and as-yet marginal fields in science.[11] Maria Rentetzi has recently considered yet another variant of this explanation within the field of radioactivity physics, suggesting that new fields were also attractive to women because of their interdisciplinary nature. They provided more opportunities for future work than did established disciplines.[12] Wheldale is a good case in point to explore both hypotheses. For her, however, there appears to be yet another aspect of the inherent interdisciplinarity of newly emerging areas. Indeed, her move into "biochemical genetics" may have reflected an explicit methodological commitment, not simply an expedient career strategy. She actively

[9] W. Bateson, 1913, 279.

[10] Dunn, 1991, pp. 176–78; Sturtevant, 1965, 101; and Olby, 1974, pp. 133–35.

[11] Rossiter, 1982. See also Richmond, 2001.

[12] Rentetzi, 2004.

championed, for example, the advantages of a concertedly interdisciplinary methodological approach in biology, urging different disciplinary communities to broaden the scope of their problem fields as a means of hastening progress. For all these reasons, then, Wheldale's career offers historians a profitable perspective by which to expand our understanding of multiple dimensions of early genetics as well as biochemistry, as well as of women's participation in early 20th-century science.

The Cambridge Mendelians

Muriel Wheldale was among the first generation of British women to receive university training in the sciences and the opportunity to pursue post-graduate research (See Figure 1). The daughter of the Birmingham barrister John Wheldale, she received her secondary education at King Edward VI High School for Girls, a private school founded in 1883 and recognized as the leading British girls' school for scientific training, with

Figure 1. Muriel Wheldale Onslow in her home laboratory at Selwyn Gardens, Cambridge. Reproduced with the kind permission of the Colman Library Archives, Department of Biochemistry, Cambridge.

particular opportunities for advanced work in physiology and chemistry. Many of the school's graduates, Wheldale included, went up to Cambridge for their university training.[13] In the fall of 1900, aged twenty, she entered Newnham College, one of two women's colleges in Cambridge. Since their founding in the late 1860s and early 1870s, Girton (primarily noted for the study of mathematics and classics) and Newnham (with a reputation in the natural sciences) had provided women the opportunity to receive a scientific education on a par with that offered to men, despite the fact that the University denied them admission and hence official degrees.[14] At Cambridge Wheldale read botany, taking a first class in part 1 of the Natural Sciences Tripos in 1902. Two years later she sat part 2, generally taken by those wishing to pursue an academic career in science, again earning first class honors. These results were outstanding, and placed Wheldale among the top tier of scientific women in Cambridge, and hence all England. Upon finishing her undergraduate work, she received a coveted Bathurst Research Studentship, one of the few fellowships available to support promising young women science students who wished to carry out postgraduate research. The project Wheldale chose to pursue was a study of the inheritance of flower color in the snapdragon, *Antirrhinum*.

This choice was strategic. At Newnham, Wheldale had come under the wing of Edith Rebecca (Becky) Saunders (1865–1945), who was demonstrator in botany and director of the Balfour Biological Laboratory for Women. This laboratory was established by Newnham College in 1884 to offer practical instruction in experimental laboratory techniques to women.[15] It was the hub for scientific women. Like her star pupil, Saunders had read botany at Newnham, earning second class honors on part 1 of the Natural Science Tripos in 1887 and first class honors on part 2 in 1888. She too held a Bathurst studentship, having pursued a morphological investigation of the structure and function of plant septal glands (in the red hot poker or torch lily, *Kniphofia*) as her post-graduate project. In 1889, she became demonstrator in botany and

[13] See Stephenson, 1932, p. 915; and Vardy, [Candler] 1928, pp. 25–26. The first head mistress, Edith Creak, was a graduate of Newnham College in classics and mathematics, and her keen interest in science was reflected in the school's curriculum. The Headmistress's Admissions Register 1883–1930 records that Muriel Wheldale sat and passed an entrance exam on 17 June 1890 and was admitted as a fee paying student on 25 July 1890; the Mistress responsible for her was Ada Hadley. The Wheldales lived in Harborne, an affluent suburb of Birmingham. I thank Alison Wheatley, Foundation Archivist, Resources Centre of the school for providing this information.

[14] McWilliams-Tullberg, 1975.

[15] Richmond, 1997.

offered instruction in elementary, physiological, and systematic botany. She also found the time to pursue research, collaborating with Marion Greenwood, director of the Balfour Laboratory and a member of Michael Foster's physiological laboratory, in a study of the role of acid in the digestive processes of protozoa.[16] When Greenwood resigned in 1899 to marry, Saunders assumed the lab's direction. Wheldale arrived the following year.

Saunders was an excellent role model to Wheldale and the other scientific students of Newnham and Girton Colleges. In 1895 she had begun working with Bateson, collaborating in his experimental research program to study variation. To test his views about discontinuous variation and the saltatory nature of the evolutionary process, Saunders designed a series of crosses between different plants that exhibited alternative characters. Her efforts soon paid off; her first publications in this field provided credible evidence that supported Bateson's views about the nature of discontinuous variation.[17] Bateson and Saunders's long-time collaboration was mutually beneficial. For Bateson, he gained a talented scientific partner who shared his views and was able to carry out independently experiments to test their validity. This was particularly important at a time when Bateson was unable to convince any Cambridge men to join him. Not only had his strong criticism of the value of the morphological method for studying evolution alienated members of the Cambridge School of Morphology, but in its stead he pursued hybridization studies, which, despite its association with Darwin, was looked down upon by the morphologists. Saunders's help was thus crucial.

For her part, Saunders's collaboration with Bateson enhanced her scientific credentials at a time when many science dons were hostile to women, in the wake of the acrimonious issue of granting degrees to women. Bateson was a member of a prominent Cambridge family. His father, the Rev. W. H. Bateson, was master of St. John's College, and his mother, Anna Aikin Bateson, was a longtime supporter of the movement for higher education for women, and for many years served as a member of the Newnham College governing board. Moreover, Bateson's sisters Mary and Anna both attended Newnham, Mary gaining distinction in history and Anna in botany. William himself was regarded as a friend of the college owing to his vocal support for the higher education of women and the degrees for women movement. After the defeat of this petition, the general climate of the university was overtly hostile to women, and especially so for those who studied

[16] Greenwood and Saunders, 1894.

[17] Bateson, 1894. See Richmond, 2007.

science. As a result, many found it difficult to find dons who would accept them in their laboratories. Bateson not only offered Saunders and other Newnham and Girton women the chance to carry out advanced research, but also to contribute to a problem they too believed was important.[18] This partnership proved quite fruitful. Bateson undertook crossbreeding in several animal species, while Saunders conducted plant hybridization experiments, with some early success. Saunders's study of variation in *Biscutella*, published in 1897, provided evidence that certain distinct varietal characters – hairy leaves versus smooth leaves – remained "discontinuous" rather than blending in the offspring, which lent support to Bateson's view that evolution could advance by the selection of discontinuous traits rather than the gradual process envisioned by current neo-Darwinian theory.[19] This work, however, was languishing until Bateson learned in the spring of 1900 about Mendel's work. Having been unable to discern any heredity pattern in the characters they monitored prior to encountering Mendel's explanation, Bateson and Saunders were both convinced that Mendel offered the general "law of heredity" that many had long sought.[20] Accordingly, they redesigned their experimental protocol, and by the autumn of 1900 had set themselves the goal Mendel set of determining "whether the law of development discovered for *Pisum* applies also to the hybrids of other plants."[21]

By 1902, Bateson and Saunders were able to publish the results of their hybridization experiments of the past 7 years in the first of what eventually became five *Reports to the Evolution Committee of the Royal Society*.[22] Yet both realized that their ultimate aim – namely, to test the applicability and extent of Mendel's laws of heredity in a wide variety of organisms – required the labor of many other researchers. Bateson was able to convince a few horticulturists and amateur breeders to conduct the extensive hybrid crosses required of Mendelian analysis, but he needed the skills and analytical abilities of academic biologists. With little interest among his fellow morphologists or "regular" Cambridge students, it was in the end a small group of Newnham and Girton students who helped Bateson and Saunders pursue their Mendelian program.

[18] Richmond, 1997.

[19] Saunders, 1897–98. See also Bowler, 1984.

[20] Cock, 1973; Olby, 1987.

[21] Mendel, 1950, p. 28.

[22] Bateson and Saunders, 1902.

A crucial element in attracting students was Bateson's course of lectures on "variation, heredity, and evolution." First offered in 1899 upon his appointment as deputy to the ailing professor of zoology, Alfred Newton, this course became the conduit for attracting followers. In 1901 Bateson incorporated a description of the essential elements of Mendel's work and their bearing on the problem of heredity.[23] He was apparently a convincing advocate of the promise of Mendelism, for before long a "group of eager students soon gathered round him."[24] Nora Darwin, Charles Darwin's granddaughter and a student of botany, was among these, having attended his course around 1905. She well recalled this experience, stating: "My first introduction to the whole subject [of genetics] ... was when William Bateson was giving what we called his Bible Class, in a remote lecture room, in the back of one of the colleges. It was outside the ordinary curriculum. It was a five or six o'clock lecture. And there he introduced a small set of people into the elements of the new Genetics. Mendelism was just coming in. ... He was a brilliant lecturer and, of course, he had an entirely new view of ordinary heredity. ... It was very inspiring indeed."[25]

Wheldale, too, was among the students who took this extramural class. Like Nora Darwin, she was also inspired by Bateson's message. In 1903, while still an undergraduate, she began conducting a series of Mendelian crosses, investigating the inheritance of flower color in snapdragons. Other Newnham and Girton women soon followed suit, eventually joined by a few men, most notably Reginald Crundall Punnett in 1904, who likewise were attracted by the promise of Mendelism.[26] By 1906, Bateson had gathered around him a small band of follower that Robert Heath Lock described as a "school of genetic research founded at Cambridge."[27] In the event, Bateson and Saunders's group of Mendelian researchers provided critical empirical evidence and theoretical concepts that helped establish Mendelism as a legitimate and productive new field of biological inquiry.

[23] Notes from Bateson's lectures, which commenced in 1897, are in the Bateson Collection, John Innes Centre Archive, Norwich (hereafter JICA). The course held in the winter (Michaelmas) term of 1901 was the first to incorporate material on the new Mendelian approach to heredity.

[24] B. Bateson, 1928, p. 62.

[25] Lipset, 1980, p. 26.

[26] Richmond, 2001.

[27] Lock, 1906, p. viii.

Wheldale's Early Research on the Genetics of Flower Pigments

As a student of botany, Wheldale was particularly intrigued by the existence of heritable color variations in flowering plants. With the encouragement of Bateson and Saunders, she set out in June 1903 to investigate "the course of inheritance in regard to flower colour" in *Antirrhinum*, the first year planting snapdragon seeds in Bateson's Grantchester garden and later sharing with Saunders a plot at the Cambridge Botanical Garden.[28] By January 1906 she had completed her initial analysis, and Bateson was very pleased, calling her paper "capital."[29] She determined that of the five flower colors exhibited by snapdragons – white, yellow, ivory, crimson, and magenta – the pattern predicting their appearance could be represented by a Mendelian factorial scheme based on the presumed presence of four different factors responsible for coloration – Y, I, L, and T. As she described this system in her first paper published in 1907: "The factor I modifies yellow, giving ivory. The factor L, superposed upon ivory, gives magenta; with yellow it blends, giving crimson; finally the third factor T is not manifested unless L in addition is present."[30] She speculated that the "original wild Antirrhinum appears to be of the magenta type," since a "reversion" to magenta frequently occurred "when crimson, ivory, or yellow types are crossed with white." Further, she analyzed the production of different shades of color – for example, light versus dark shades of magenta – noting that this depended on which flower colors were crossed. In general, she found that "lighter forms are dominant to darker," which agreed with Bateson and Punnett's findings in sweet peas and Saunders's in stocks.[31] Wheldale also followed the inheritance of striped and non-striped flowers, learning that this phenomenon depended on the presence or absence of magenta sap-color in the tube and lips of the flower.

In providing a Mendelian analysis of the inheritance of coloration, Wheldale initially adopted a "two-factor" hypothesis similar to the one Saunders formulated to describe inheritance of flower color in stocks. By 1906 it was known that "the appearance of colour is due to the

[28] Wheldale, 1907. Bateson, in a testimonial written in 1908, stated that the *Antirrhinum* work "was begun, I think, at my suggestion and we have been in frequent communication during its progress." Wheldale correspondence, 14 February 1908, Bateson Collection, JICA. Bateson (1894, pp. 47–48) considered the chemistry of yellow and red pigments and suggested (pp. 72–73) that chemical processes may be responsible for discontinuity.

[29] Bateson to Wheldale, 26 January 1906, Bateson Collection, JICA.

[30] Wheldale, 1907, p. 292.

[31] Wheldale, 1907, p. 290.

association, in one zygote, of two factors belonging to independent allelomorphic pairs. The presence of either factor alone is insufficient to cause colour in the zygote."[32] Accordingly, the production of color depends on "the meeting of two complementary factors," one of which determines the actual color of pigment and the other whether the color factor is actually expressed. The assumption that multiple factors were involved in the production of color was not new. Indeed Cuénot in 1903, to explain the inheritance of coat colors in mice, "proposed that the two pigments are made from a common *chromogène* as the result of the action of two distinct enzymes."[33] What was new was the elaboration of a different relationship among Mendelian factors than that of dominant and recessive. To describe how the action of one factor coordinated with that of another that was not allelic was a concept that demanded new terminology. This was Bateson's forte. He helped Wheldale delineate the relationship she had identified by coining the new terms *epistatic* and *hypostatic*. As he wrote in a letter of 2 February 1907:

> I think the simplified diagram will do, and that the extension to four pairs can easily be imagined by a reader of ordinary sense. I have tried a great many terms to express the interrelationship of characters which are not allelomorphic, but there are objections to all.
>
> The best I have to suggest so far are: – epistatic and hypostatic but one should have a term for the non-effective characters which have no complement, and parastatic will not strictly fit that idea. Apostatic is just possible in that sense, but has other secondary meanings. If you are bound to introduce the idea with a term I incline distinctly to epi-/hypostatic by preference.[34]

In the end, Wheldale chose not introduce these terms in her 1907 paper. Hence, the credit for identifying epistatic relationships has gone to Bateson, who introduced the terms in a paper he presented at the

[32] See Bateson et al., 1906a, pp. 3–5.

[33] Hickman and Cairns, 2003, p. 839.

[34] Bateson to Wheldale, 2 February 1907, JICA. The reference is to diagram 1, "Scheme of Distribution of three of the Colour-factors in F_2 from white × yellow crimson-striped," in Wheldale, 1907, p. 294. In the text, she noted that a "similar diagram constructed for four factors shows us that, as regards the composition of the F_3 they give on selfing, there are 16 kinds of magentas in F_2." (295).

International Zoological Congress in Boston in August 1907.[35] However, it is clear that it was her analysis that identified the phenomenon.

While the two-factor scheme could represent the production of flower colors in *Antirrhinum*, she also noted that color could be influenced by the presence of yet a third factor, *B*, "which changes the red colour to purple," but has "no effect unless" two other factors, "C and R are also present."[36] This modification reflected the hypothesis, put forward by Bateson, Saunders, and Punnett in 1906, that color factors were in some way connected to the production of enzymes. In sweet peas, for example, they proposed a factor, *C*, which they envisioned as a "colour-forming stuff which gives rise to colour when acted upon by the other factor (R). We should then have to regard this latter as of the nature of an enzyme, but, in the absence of direct chemical evidence, we consider it advisable to use non-committal terms for the present."[37] In the end, it was Wheldale who attempted to provide precisely the "direct chemical evidence" that this line of work demanded.

Wheldale's decision to study the genetics of flower color in *Antirrhinum* was not random but rather reflected current concerns in genetics. Other leading plant geneticists, especially Hugo de Vries in Amsterdam and Erwin Baur in Berlin, were also attempting to analyze the pattern of flower color inheritance in this species. Indeed, it was presumably this knowledge that prompted Bateson to encourage Wheldale to publish her results as soon as possible. Writing to her in November 1905, Bateson asked: "Do you feel disposed to publish anything about Antirrhinum yet? I am not quite sure what stage you have reached with the Delila evidence. It is a nice case and as soon as you have it clear I think you should publish it."[38] He urged her to work up a paper presenting her preliminary results to be delivered at the 1906 London conference sponsored by the Horticultural Society, subsequently known as the Third International Conference of Genetics. As president of this conference, Bateson intended to use this forum as a means of showcasing the accomplishments of the Mendelian workers. In specific, he aimed to bolster his group's credibility in the wake of the severe criticism of their Mendelian assumptions, approach, and interpretations they had

[35] W. Bateson, 1907, p. 653. L. C. Dunn assigns priority for discovering epistasis to Bateson and Punnett: Dunn, 1991, pp. 70–71.

[36] Wheldale, 1907, p. 291.

[37] Bateson et al. 1906b, p. 31n. Wheldale subsequently noted that the production of magenta flowers was due to at least seven pairs of factors. See Wheldale, 1914b, p. 109.

[38] Bateson to Wheldale, 23 November 1905, JICA. The "Delilah" forms, identified by de Vries, "have the lips coloured and the tube or throat white." (Bateson, 1913, p. 87).

endured since 1902 by W. F. R. Weldon and other biometricians.[39] As the letter to Wheldale indicates, Bateson attempted to orchestrate the conference proceedings, wanting to have members of the Cambridge group appear prominently on the program as speakers, exhibitionists, delegates, and awardees.[40] In the event, owing to Weldon's sudden death in April 1906, Bateson ended up placing less emphasis on countering the biometrical threat to Mendelism at the conference and more on establishing the validity of the group's factorial analysis in the face of competing alternative systems recently proposed by foreign geneticists such as de Vries and Erwin Baur.

De Vries, one of the co-discoverers of Mendel, included an analysis of flower color inheritance in *Antirrhinum* in the second volume of *Die Mutationstheorie* (1903), and his factorial scheme was slightly at variance with that proposed by Wheldale. To some extent, the group's relations with de Vries were complicated by a growing animosity between him and Bateson. Although Bateson had been an early supporter of de Vries's mutation theory, which accorded well with his own belief in discontinuous evolution, he increasingly found himself at odds with de Vries's later interpretations.[41] Bateson clearly came to rely on Wheldale to interpret de Vries's findings. As he wrote in a postcard of 11 August 1906, "Have you found in Antirrhinum that tall × dwarf mendelize regularly? You will have read Mutationstheorie II pp. 76–7. Do you agree with this?" He was especially keen to establish his group's competing Mendelian analysis. When the Dutch professor visited Cambridge in November 1906, several months after the London horticultural conference, Bateson wrote to Wheldale, alerting her to the need of convincing de Vries of the correctness of her interpretation: "De Vries comes on Wednesday morning. We expect to have a mendelian lunch at Caius at 1 to which I hope you can come. Bring your pictures.

39 Weldon, Karl Pearson, and others were extremely critical of Mendelism, whose focus on the parental generation excluded ancestral heredity, which was essential to the biometrical analysis of heredity. There criticism appeared in the new journal *Biometrika*. See especially Weldon, 1902a, 1902b, 1903. See also Froggatt and Nevin, 1971, Kim, 1994; and Provine, 1971, pp. 48–55.

40 Richmond, 2001, pp. 74–76. Bateson was honored at the banquet with the award of a gold Veitchean medal, while Saunders was awarded a silver-gilt Banksian medal (along with C. C. Hurst and R. H. Biffen, both members of Bateson's group). The *Gardeners' Chronicle,* 4 August 1906, reported: "A whole series of crosses between varieties of Antirrhinum involving much detail was shown by Miss Wheldane [sic] and Miss Marryat, all giving results bearing on the subject of heredity" (p. 96).

41 Stamhuis, 1996, 2005.

I have some here."[42] In her first publication on *Antirrhinum*, which appeared in 1907, Wheldale described de Vries's results and compared their two systems, glossing over the apparent discrepancies in their factorial analysis by noting that her "ivories and rose delilas are classed together as De Vries' whites and tinged whites."[43] Their results were thus essentially compatible.

For his part, Baur became alarmed, after learning of Wheldale's 1907 paper through the description given in Bateson's 1909 book *Mendel's Principles of Heredity*, that his own priority for his ongoing study of snapdragons might be in jeopardy. In a move seemingly calculated to preserve priority, Baur wrote to Wheldale in June 1909, suggesting that "we both publish as *soon* as possible our investigations up to now, *concurrently* but naturally entirely independent from one another."[44] Bateson helped Wheldale draft a reply to Baur laying out her own claims for this work, which read: "My paper on Antirrhinum was finished some months ago and has been sent to Mr. Bateson for communication to the Evolution Ctee. of the Royal Society. I understand that it would have been passed on for publication before now, but for delays that have occurred in connexion with other papers which are to appear in the same Report. It is in every way satisfactory that the ground should be independently covered by other observers, and especially must this be the case in regard to these more complex phenomena of colour.... Confirmation in this line of experiment is so very important and necessary that even if we do overlap the work will in no sense be superfluous."[45] In the event, both Baur's results on *Antirrhinum*

[42] Bateson to Wheldale, 26 November 1906, JICA. The same day, Bateson wrote to C. C. Hurst, who had pointed out a date error for the citation of a paper by de Vries in proofs of the paper to appear in the conference *Proceedings*, stating: "Thanks for correction of that stupid mistake – I did find it out directly after the Conference and corrected the proof. Yes! it was only some 9 months before the famous rediscovery was announced. I noticed that, when the date turned out to be 1899 and I have often wondered whether all this was in his head at that time. You must remember that he was then chockfull of his own ideas, and to this day he has never really seen the full force of Mendelism. He is coming here on Wednesday for one night on his way to get the Darwin medal." Bateson Correspondence, CUL.

[43] Wheldale, 1907, p. 302.

[44] Baur began the letter: "Bateson schreibt, dass Sie "have succeeded in disentangling the various genetic combinations and showing the factorial composition of almost all," ganz das gleiche kann ich auch von mir sagen." Baur to Wheldale, 7 June 1909, [typescript by Beatrice Bateson], Bateson Collection, JICA (translation mine). See Baur, 1908.

[45] Bateson to Wheldale, [June 1909], Bateson Collection, JICA. The note was headed: "suggested letter to Baur. I have had 2 tries at this and send result W. B."

and a German translation of Wheldale's 1909 paper were published together in 1910 in the journal he edited, the *Zeitschrift für Induktive Abstammungs- und Vererbungslehre*.[46]

As this episode indicates, Bateson served as Wheldale's mentor, promoting her research and her publications in various ways within the nexus of national and international scientific channels.[47] It is clear that he regarded her as an extremely talented young scientist. After completing her undergraduate work in 1904, earning a first class on the Natural Sciences Tripos, Wheldale was able to pursue postgraduate research with the support of a Bathurst studentship awarded by Newnham College.[48] While the studentship was renewed for another year, thereafter she had to apply for other sources of funding to continue her research, and such opportunities were difficult to come by for women at the time. In April 1908, Bateson wrote a recommendation to support Wheldale's application for a fellowship at Newnham College. His evaluation of her work is revealing, both in terms of providing information about her current research agenda and a sense of his assessment of its value and her abilities:

> Miss Wheldale tells me that she is a candidate for a Fellowship at Newnham College. I have pleasure in saying that she seems to me in an exceptional degree well fitted for that appointment. For some years she has been engaged in experiments on heredity in plants and during this time I have been in frequent communication with her about her work. Besides zeal and industry, she has shown distinct power of interpreting results for herself – a much less common quality.

[46] Baur, 1910, Wheldale, 1910a. Wheldale described this paper as a "Comparison of results obtained by the author with those of Baur" (Wheldale, 1925, p. 281). Bateson visited Baur in Berlin over the Christmas break of 1909, 1910, examining his snapdragon specimens. He described this visit to C. C. Hurst: "I was lately in Berlin and saw Erwin Baur – a first-rate man. He shewed me his plants [*Antirrhinum*] and I find that I have made a more serious blunder about them." Bateson to Hurst, 17 January 1910, Bateson Correspondence, CUL. Wheldale noted that "the inheritance of flower-colour in *Antirrhinum majus*" had been worked out independently by her and Baur: Wheldale, 1914a, p. 300.

[47] The abundant ways in which Bateson promoted Wheldale's studies and career are well detailed in the Bateson-Wheldale correspondence, 1903–1919, Bateson Collection, JICA.

[48] On 19 April 1908, Bateson sent her a postcard that reads: "Very glad indeed to see you in the First Class. I should like to hear how the Antirrhinums go on – On Wednesday I shall be away but otherwise am here. | WB." (Bateson Collection, JICA).

> The problem of colour-inheritance in Antirrhinum, which she set out to solve, proved to be far more complex than was expected, and the solution she proposed (Proc. Roy. Soc. vol. 79, B, 1907) is entirely her own work. There is every reason to believe that it is correct and I regard the paper as one of considerable value. In such a line of work results of course come slowly at first, but the investigation is now opening out in several directions. It is most desirable that Miss Wheldale should be enabled to follow up these inquiries.
>
> If she gets the necessary leisure she means also to attempt the task of distinguishing and classifying the various pigments to which the colours of flowers are due, about which almost nothing is known. This is work very urgently needed by students of Genetics, and it would be an important and novel contribution to plant-physiology.
>
> Among those who have collaborated with me I have found few so well qualified for independent work as Miss Wheldale, and she is pre-eminently a student who ought to be given opportunities of continuing in research.[49]

Bateson, then, certainly recognized the importance of Wheldale's research for advancing genetics. Recent historians concur with his judgment, calling her first paper of 1907 "a landmark publication [that] was the first of a flurry of research papers on the linkage between the inheritance of genetic factors and the production of the pigments, the anthocyanins."[50] Bateson thus sought to promote the career of this talented young research scientist. In so doing, however, he was also vicariously advanced his own research agenda, both intellectually and materially. He was of course interested in her attempt to link the genetic factors with the production of pigments, especially as it related to his views about the role of enzymes in this system. It was also in his best interest for her to receive outside funding for carrying out this work. From the beginning, the fledgling Mendelian research program he headed at Cambridge relied on meagre, piecemeal funding opportunities, with what little institutional and private support members received topped up by individuals' reliance on available domestic resources.[51]

[49] Testimonial, 23 April 1908, Wheldale Correspondence, Bateson Collection, JICA.

[50] Rayner-Canham and Rayner-Canham, 2002, p. 49.

[51] Richmond, 2006.

Fortunately for both Wheldale and Bateson, she was successful in obtaining college support for her advanced research, receiving Newnham College's "N" fellowship for the 1907–1908 academic year. Wheldale then embarked on an expressly "biochemical" study of the little-known topic of plant pigments, with Bateson's full backing. In September he wrote to her, offering both encouragement as well as additional financial support:

> I think the pigment inquiry very hopeful. By all means go on with it. So far as I know there has hitherto been no attempt to show the connexion between the chemical and genetic phenomena. There are some minor points of expression which we might talk over.... Certainly buy any reagents &c. you need. I have got a grant from the British Association this year, and I think you can quite well have some of it. How much will you want?[52]

In addition to providing her with intellectual guidance and material support for the experimental work, Bateson also served as a conduit between her and leading Cambridge dons who could advance her research. This included the professor of botany, Albert Charles Seward, and the new head (later professor) of biochemistry at Cambridge, Frederick Gowland Hopkins. Bateson sought out their opinions to make sure that her interpretations were on the right track.[53] In addition, Bateson promoted the publication of her findings, suggesting proper outlets, communicating her papers to scientific societies for publication, and guiding her with the revision process.[54] He was, in the end, a model mentor for Wheldale.

For his part, Bateson well appreciated Wheldale's special intellectual abilities. As he expressed in a recommendation to support her 1908 application for a post in botany at the University of Sheffield:

> I have formed a very high opinion of Miss Wheldale's powers as an investigator. The subject proved by no means an easy one, and the series of results which the experiments provided were unexpectedly intricate. She succeeded in unravelling these complexities for herself

[52] Bateson to Wheldale, 24 September 1908, Bateson Collection, JICA.

[53] Bateson sent the manuscript she had drafted summarizing her results to Seward, stating "I should like to see how the subject strikes a professional botanist," and later to Hopkins to review the chemical analysis. See Bateson to Wheldale, 24 September 1908, and 13 October 1908, Bateson Collection, JICA. Bateson had previously sought Hopkins's help. See Bateson, 1894, p. 73.

[54] In 1909, for example, he arranged with Jan Paulus Lotsy for her summary paper to be published in *Progressus* rei *botanicae,* Wheldale 1910b. See Bateson to Wheldale, 29 November 1909 and 8 December 1909, Bateson Collection, JICA.

> and there can be no doubt that the solution she published in Proc. Roy. Soc. is correct. I may say that in my experience of this kind of work she is one of the few who have shown themselves thoroughly capable of independent research.[55]

That his assessment was not simply gratuitous, however, also seems clear. While Wheldale and other Newnham women formed the backbone of Bateson's early Mendelian program at Cambridge, by 1908 he had been able to attract a number of university men to this work – including (in addition to Punnett) William Lawrence Balls, Leonard Doncaster, Reginald Philip Gregory, Robert Heath Lock, and Thomas Barlow Wood.[56] Still, most of the critical early evidence supporting Mendelism had come from the Newnham College women.[57] In any event, it is not surprising that Bateson conscientiously facilitated Wheldale's experimental work and helped to shepherd it into print.

There is some irony, then, that in moving into working out the basis of flower coloration in *Antirrhinum*, Wheldale increasingly began to move away from a purely genetic study of the production of pigment in plants, and thus deviate from Bateson's Mendelian fold. More and more, this line of work on the chemical nature of the factors responsible for the production of color variations moved her out of genetics and into biochemistry. This can be seen in the description of the genetics of flower color provided in a paper of 1909:

> The original type of *Antirrhinum* has magenta (anthocyanin) flowers. Loss of the reddening substance, which may be represented by a Mendelian factor (M), gives a variety bearing ivory-white flowers containing no pigment (except in the palate and hairs), but a glucoside-like body giving the reactions with acids, alkalis, and lead acetate described above. Further loss of a substance, again represented by a factor (I), from the glucoside-like body in the superficial cells of the lips gives a yellow xantheïc pigment, and the variety thus bears yellow flowers. Loss of yellow pigment, represented by yet another factor (Y), gives an albino, containing no pigment and no glucoside-like body.... The albine may carry I or M, or both, since these factors are invisible unless the fundamental

[55] Testimonial, 14 February 1908, Wheldale Correspondence, Bateson Collection, JICA.

[56] Richmond, 2006, pp. 580–581.

[57] The authors of papers in the five reports in the series *Reports to the Evolution Committee of the Royal Society*, included, in addition to Bateson and Punnett, two men – C. C. Hurst and Leonard Doncaster. In addition to Saunders, four other women contributed articles: Wheldale, Florence M. Durham, Dorothea C. E. Marryat, and Igerna B. J. Sollas.

> colour Y is present. Moreover, the reddening factor can exist with Y, the decomposition product, giving a mixed colour, *i.e.*, crimson. Each variety may breed true or may throw itself and one or more varieties below it in the scale of colour, according as it is homo- or heterozygous in the various factors. Magenta can throw all varieties; crimson can throw yellow and white; ivory, yellow and white; and yellow, white only.[58]

Because of this interesting pattern, Wheldale came to believe, in the words of her subsequent student, "that the red and magenta anthocyanin pigments might be derived from the yellow and ivory flavones, and that the white varieties, from which these pigments are absent, might carry the factors which act on the flavones to form anthocyanin."[59] Although titled "The Colours and Pigments of Flowers with Special Reference to Genetics," Wheldale categorized this paper as a contribution to the "Chemistry of Anthocyanins" rather than to genetics per se, viewing it as an attempt "to show that there is some correlation between the chemical reactions of pigments and their behaviour in genetics."[60] Thus, it is clear that her interest in pursuing the underlying chemical relations was gaining an upper hand over purely genetic concerns.

In *Mendel's Principles of Genetics*, Bateson referred to Wheldale's work as complementing his study of the factorial basis of flower color in sweet peas and Saunders's in stocks. It well supported, for example, his and Punnett's "presence and absence" hypothesis, by indicating how the presence or absence of a "ferment," "chromogen," or an "epistatic factor" accounted for the production of flower coloration.[61] These terms pointed to a growing yet still elusive attempt to understand the genetic control of pigment formation, with early contributions coming from Lucien Cuénot and his study of coat color in mice and Carl Correns's reflection on his botanical results.[62] Bateson, too, contributed to Wheldale's early analysis of color factors and their interrelationships. In a letter of 23 January 1909, he provided the following comparison of her results with his in sweet peas:

> After our conversation to-day I tried again to compare Sweet Pea with Antirrhinum. We may take it that in Sweet Pea the factors are

58 Wheldale, 1909a, p. 46.
59 Scott-Moncrieff, 1930, p. 753.
60 Wheldale, 1925, p. 234.
61 Bateson, 1913, p. 98.
62 Buican, 1982, Saha, 1984, p. 159; Rheinberger, 2000b.

C. chromogen

R. ferment

B. blueing factor.

CR gives red. CRB gives purple.

In Antirrhinum, you have, as I understand:

R. ferment (carried by white)

C. the bright yellow chromogen–namely the "tannin-like" body in lowest form.

B. the factor which makes C into the "tannin-like" body of higher form.

For since white × ivory may give yellows in F_2 the distinction between the two chromogens, yellow and ivory, must be detachable, and we must not say simply that there are two kinds of chromogens, a yellow and an ivory.

So I think on the whole my description was correct. May I not therefore draw up the comparison as enclosed?

Yours truly, | W. Bateson

Sweet Pea	Antirrhinum
Ferment. R. } together producing anthocyanin	R.
Chromogen. C. }	C. visibly present as a bright yellow.
Factor which turns Anthocyanin blue, B	I factor which turns C ivory and turns crimson into magenta

After her early success in working out the genetics of flower colors, it was natural for her to wonder about the chemical processes involved in the production of different flower colors, or, as she expressed it, "whether there is any connection between the genetic behaviour of pigments and their chemical reactions and constitution."[63] At a later point, Wheldale elaborated on this notion more fully, stating: "It must also be patent to those who have been working on the subject of

[63] Wheldale, 1909a, p. 44.

Genetics that a proper conception of the inter-relationships and inheritance of the manifold characters of animals and plants will be greatly facilitated by a knowledge of the chemical substances and reactions of which these characters are largely the outward expression.''[64] While geneticists may have contemplated this problem, however, few actually had the necessary skill set to enable them to pursue it. The American geneticist W. J. Spillman articulated precisely this point in 1912:

> While a large part of the work on which Mendel's principles of heredity depend has been done with pigments, very few investigations have been undertaken in order to determine the connection between the phenomena of inheritance of these pigments and the chemical reactions which underlie these phenomena. This is quite natural, since few of those who have conducted the investigations relating to Mendelian inheritance have had the training, and hence the opportunity, to study the chemical side of the question. Likewise, those relatively few individuals who have become well versed in the highly complex and difficult subject of physiological chemistry have seldom had any direct interest in the phenomena of inheritance.[65]

Wheldale, however, with her strong background in chemistry, could do precisely this. Moreover, she also apparently had the desire. As a friend and associate of Wheldale's characterized the nature of the transition she made at this time: ''She soon decided that a mere counting of numbers and construction of genetic formulae built up of imaginary factors was a slightly arid occupation, and that progress would only come by discovering the real nature of the hypothetical materials concerned. She was one of the first geneticists who turned to biochemistry for assistance.''[66]

Whether Wheldale was disenchanted with the methodology of genetics or simply interested in pursuing the problem along different lines is uncertain. However, it is clear that her early work on the genetics of flower colors soon evolved into a dedicated study of the chemistry of plant pigments. She did not, however, simply envision her work as a contribution to the nascent field of biochemistry.[67] It would also advance genetics. As she explained in 1910, ''if the study of heredity is to occupy a central position among the biological sciences, the necessity

[64] Wheldale, 1916, p. v.

[65] Spillman, 1912, p. 117.

[66] D. J. L., 1932.

[67] Kohler, 1982.

for identifying Mendelian factors with the chemical or physiological constituents of the animal or plant cannot be too strongly emphasised."[68] It was her hope that genetics could provide clues that could expedite the analysis of the chemical side of the problem, and that this, in turn, would enrich genetics.

Wheldale soon arrived at a hypothesis about the chemical reactions underlying flower pigments, involving the formation of the "soluble red-purple-blue pigments known as '*anthocyanin*.'"[69] In a series of papers that appeared in rapid succession after 1909, she formulated and developed the view that a "colourless chromogen, of the nature of a tannin" present in plant tissues "eventually may become coloured" when coming into contact with the pigment "anthocyanin" and "that the aromatic chromogen forms a component of anthocyanin."[70] In genetic terms, she attempted to determine the chemistry connected with the hypothesized genetic factors, *C* and *R*. The assumption that the chromogen was a glucoside (sugar) of the nature of a tannin was novel. Indeed, it was so novel that Bateson warned her that Hopkins was somewhat skeptical of this hypothesis:

> Hopkins thinks that the existence of the glucoside can't be proved without isolating it, and then getting the sugar reaction after H_2SO_4. Just now he is very busy seeing men. You ought to have a talk with him as soon as he is more free.
>
> I may not have expressed the point about the glucoside rightly, but I think there is a point, which will have to be considered. If you can look in this afternoon. Hopkins doesn't think the "tannin-like" substance account probable. As I understand, it should be a ferment that acts on the other substances.[71]

Nonetheless Wheldale felt confident enough in her interpretation to persist. She was convinced that there was "a connection between the chemical behaviour of the classes and their inheritance."[72] Specifically, she proposed that "the various red and blue plant pigments (anthocyanin) are oxidized products of substances of the nature of flavones, the agents of oxidation being oxydases."[73]

[68] Wheldale, 1910b, p. 457.
[69] Wheldale, 1909a, p. 44.
[70] Wheldale, 1909c.
[71] Bateson to Wheldale, 13 October 1908, Bateson Collection, JICA.
[72] Wheldale, 1909a, p. 48.
[73] Wheldale, 1909b, p. 27.

Wheldale recognized that proving the hypothesis that "anthocyanin is the product of oxidation of a colourless aromatic chromogen" represented "a difficult chemical problem," requiring an analysis of "the flavone and xanthone classes of natural colouring matters." These were currently being studied by Arthur George Perkin (son of the organic chemist William Henry Perkin, discoverer of aniline dyes) and his colleagues at the University of Leeds for their properties as dyes.[74] Her work thus intersected with cutting edge research in chemistry, a remarkable accomplishment for a young woman at the time. She believed she had an advantage, however, in using her knowledge of genetics to guide her biochemical approach. Still, this could not help her circumvent technical problems she encountered. For example, she tried a number of different methods of isolating the presumed oxydase from the petals of colored flowers and analyzing its elemental composition, none of which were entirely satisfactory. Nonetheless, over the course of the next few years, Wheldale worked hard to provide evidence to support her theory that the production of anthocyanin required the presence of two factors, "an aromatic chromogen of the flavone series and a reddening factor, in all probability an oxidizing ferment," the genetic factors *C* and *R*.[75] In so doing, she attracted the attention of biochemists and botanists alike.[76]

The Interdisciplinary Nature of Wheldale's Research Program

Increasingly, Wheldale's work focused on the "physiological" aspects of the expression of Mendelian factors rather than their simple transmission. Her approach was highly interdisciplinary, combining methodological components and theoretical elements from the disciplines of botany, physiology, chemistry and biochemstry, as well as genetics. An illustration that this was a concerted decision can be seen in Wheldale's publication strategy. She published a series of papers in a variety of disciplinary journals, each directed at different audiences. In each, she couched her message about the significance of this line of work in terms that could be readily appreciated by the different disciplinary cohorts. For example, she informed botanists that "if the study of heredity is to occupy a central position among the biological sciences, the necessity for identifying Mendelian factors with the chemical or physiological

[74] Wheldale, 1909c, pp. 152, 144–145, 151.

[75] Wheldale, 1909c, p. 160.

[76] See the description of her "interesting theory" in Spillman, 1911, p. 507.

constituents of the animal or plant cannot be too strongly emphasised."[77] She encouraged plant morphologists to engage with such problems by expanding their traditional approach to include a knowledge of biochemistry, stating that "increased knowledge in the field of morphology, however exact and comprehensive it may become, must, from the nature of its methods, fail to give an insight into the underlying causes of specific form. To gain this insight the plant should be viewed from the biochemical standpoint."[78] Speaking to biochemists, Wheldale challenged them to deviate from their current concentration on investigating the chemical makeup of plants that were useful for medicinal or commercial purposes. She urged them to infuse their studies with insights that could come from considering evolutionary relationships among plants. For example, she recommended investigating "whether any isolated plant product is peculiar to certain species only, to all species of a genus or to allied genera of a natural order. The differentiation of species upon a purely chemical basis would require a store of information which we are at present very far from possessing."[79] Such inquiries, she believed, would be mutually beneficial to all. In retrospect, we can see that it was just such an interdisciplinary research program that Wheldale pursued over the course of the next few years, with some notable successes.[80]

In 1913, Wheldale published the first of a series of papers on the flower pigments of *Antirrhinum*, the first describing the methods she used in preparing and purifying the crude pigments.[81] Later the same year, in a paper co-authored with Harold Llewellyn Bassett of Trinity Hall, Cambridge, came the identification of apigenin, a flavone, as the basis for the ivory pigment of *Antirrhinum*.[82] The next year, 1914, brought the announcement that another flavone, luteolin, was responsible for the yellow pigment.[83] But then their progress slowed, primarily hampered by technical difficulties – especially their inability to isolate the anthocyanins associated with red and magenta pigments as a crystalline product so that they could determine their chemical formula.

[77] Wheldale, 1910b, p. 457.

[78] Wheldale, 1911a, p. 446.

[79] Wheldale, 1911a, p. 448.

[80] One manifestation of this interdisciplinary perspective is the extensive, annotated bibliography provided in Wheldale (1916). The entries, which numbered 879 in the second edition (1925), are divided into categories, including the pure chemistry of anthocyanin, the physiological significance of anthocyanins, and anthocyanins and genetics.

[81] Wheldale, 1913.

[82] Wheldale and Bassett, 1913.

[83] Wheldale and Bassett, 1914a, 1914b. See also Wheldale, 1914a and 1915a.

But it was not just technical problems that hindered progress. Wheldale's assumption that anthyocyanin is an oxidation product of flavonols came under attack by several chemists. The British chemical research team of F. Keeble, E. F. Armstrong, and W. N. Jones, for example, accepted Wheldale's oxidase hypothesis of anthocyanin formation, but differed with her interpretation in a few key areas. They believed, for example, that there was a reduction process prior to the oxidation of anthocyanins.[84] A more damaging critique came from the German organic chemist and future Nobel laureate, Richard Willstätter, and his associate Arthur Ernest Everest, a lecturer in chemistry at University College, Reading, who had taken his Ph.D. at Basel in 1913.[85] Willstätter and Everest, studying the pigments in cornflowers, put forward a diametrically opposed point of view to Wheldale's. Unlike Wheldale, they had been able to crystallize the anthocyanin they derived from cornflowers. This led to Willstätter's view that the production of anthocyanin proceeded by *reduction* from a flavone precursor, not by *oxidation*, as Wheldale proposed.

This criticism did not, however, daunt Wheldale. She was unable to bring her *Antirrhinum* results into alignment with those of Willstätter and Everest, and for this reason, and because their views did not harmonize well with the data of Mendelian experiments, she continued to uphold her theory.[86] In this respect, her faith in results produced by the

[84] Wheldale, 1916, pp. 11–12.

[85] See especially Wheldale, 1915b. Everest published on this topic with Willstätter, whose collaborative study of anthocyanins continued independently until the outbreak of the First World War (Willstätter and Everest, 1913; Willstätter, 1958, pp. 220, 221). On the biochemical orientation of many German organic chemists, see Kohler, 1982, p. 36.

[86] In 1915, Wheldale provided her reasons for rejecting Willstätter's criticism, noting that her "hypothesis is more within the province of plant physiology than chemistry and was the outcome of observations upon the distribution of pigment in the tissues and the effect of factors such as light, temperature, drought, injury, sugar feeding, etc., on anthocyanin formation" and was based on a study of "*the living cell,*" not a chemical analysis based on the test tube (Wheldale, 1915b, p. 376; her emphasis). The following year, she restated her position: "The author has been so far unable to bring the results provided by the case of *Antirrhunum* into line with Willstätter's views. ... Willstätter's views provide a very different interpretation of Mendelian factors for coloration from that of Keeble & Armstrong and the author. For we must suppose, should Willstätter be correct, that the factors for colour are the chromogen (flavone) and the power to reduce the chromogen with a complete change of structure from the pyrone grouping of the flavone to the quinonoid structure of anthocyanin. ... Thus we have a reversion to the ideas of the earliest writers, and it is less easy to correlate such a view with the results of cross-breeding." Wheldale, 1916, pp. 15, 16. This approach paralleled Hopkins's focus on the biochemistry of the living cell (Baldwin, 1972).

consilience of different disciplines not only influenced her methodology but also her theoretical interpretations. For example, she was impressed by the agreement between the "symbolic representation of compositions" she constructed on the basis of her chemical analysis and the factorial scheme developed by Bateson, Saunders, and Punnett using the methodology of genetics; this appeared to offer a good indication of the ability of both methods to model different aspects connected with the hereditary factors.[87] Because of her belief in the mutual relationship between genetics and chemical phenomena, Wheldale continued to believe that the genetic analysis of plant pigmentation could provide a guide in identifying the biochemical reactions taking place in the living plant.[88]

For his part, Bateson's support for Wheldale's research did not waiver, even after her work became more biochemical in nature and, as he admitted, was "getting rather out of my depth."[89] Leaving Cambridge in 1910 to assume the direction of the new John Innes Horticultural Institute in Merton, Bateson recommended to the governing council that Wheldale be appointed to one of the two proposed studentships. He also arranged to have a small chemical laboratory outfitted at the new institute to support her work.[90] He was thus naturally disappointed when she decided to work for a time in the laboratory of the specialist on tannin chemistry, Maximilian Nierenstein, in Bristol, in an attempt to clarify the connection between the two glucosides, tannins and anthocyanin.[91] Despite her seeming abandonment of genetics for chemistry, Bateson nonetheless continued to accommodate her needs,

[87] See, for example, the chemical scheme she substituted for the factorial representation suggested by Bateson Saunders, and Punnett: Wheldale, 1906b, p. 30.

[88] See Wheldale, 1916, p. 10, where she notes that the study of flower-color inheritance "is not only highly important in its connection with heredity, but it also provides us with well-defined material for the solution of the problem as to what chemical processes are involved in anthocyanin formation. Conversely, these processes once discovered, we should also be provided with a chemical interpretation of the Mendelian factors for flower-colour." In the second edition (Wheldale, 1925, p. vii), Wheldale lamented that this problem had not yet been solved, but stated that "recent work on Genetics, nevertheless, has considerably broadened our general conceptions of Mendelian factors and has prepared the way towards that elucidation which, unquestionably, in the course of time, will be found of the relations between the chemistry and biochemistry of the anthocyanin pigments and the factors for colour-inheritance."

[89] Bateson to Wheldale, 27 December 1908, Bateson Collection, JICA.

[90] Professor Bateson's Report to Council [John Innes], 25 November 1909, Bateson Collection, JICA.

[91] Wheldale, 1909c which aimed at "finding out whether, and if so, in what way anthocyanin is related to tannin."

arranging for her to hold a half-time position at the institute and work at Merton during the summer months.[92] He also actively supported her research agenda in other ways. Late in 1912, responding to Wheldale's news that she was thinking of preparing a book on the anthocyanin pigments, Bateson encouraged her enthusiastically, saying: "When the time comes for your book on anthocyanin to be planned in detail and you decide to offer it to the Press, let me send a letter in support. I think it an excellent idea. Of course it won't pay, but that you must not expect."[93] He read the manuscript carefully, suggesting a number of editorial changes. When *The Anthocyanin Pigments of Plants* appeared in 1916, published by Cambridge University Press, Wheldale offered her "sincerest thanks" to Bateson "for the great interest he has taken in much of my work which is included in this volume, and for his many valuable suggestions and criticisms."[94]

Bateson continued to serve as Wheldale's mentor, helping her navigate the treacherous waters of scientific controversy. In 1914, when Everest began to criticize her oxidation hypothesis, Bateson helped her strategize about how to proceed. In March, he alerted her to a lecture Everest was to give on anthocyanin at the Royal Society. In May, he sent a postcard telling her to "look at Everest's article p. 369 of Gardener's Chronicle this week," commenting that "par. 3 is rather artless."[95] In this passage, Everest, having described Willstätter and his collaborators' work on the chemistry of the red and blue pigments, then

[92] Bateson wrote to Wheldale on 7 September 1910, "I expect you are right to take a period with Nierenstein. It is a pity we missed each other here. To what extent we shall be able to organize chemical work on an extensive scale I hardly know, but I see no reason why we should not." See also letters of 10 January 1911, 10 March 1911, and 23 March 1911 (Bateson Collection, JICA). Apparently Wheldale did not get on well with Nierenstein. Rose Scott-Moncrieff, a student of Wheldale's in the 1920s, reported that Nierenstein "was an old antagonist of Mrs Onslow's, with heated arguments as to whether tannins did or did not come into anthocyanin biosynthesis." See Scott-Moncrieff, 1981–1983, p. 146.

[93] Bateson to Wheldale, 12 December 1912, Bateson Collection, JICA. Bateson was a member of the Syndics of Cambridge University Press.

[94] Wheldale, 1916, p. vi. She also thanked Frederick Frost Blackman (1886–1947), reader in botany at Cambridge who studied plant respiration and photosynthesis, "for criticisms and assistance with the manuscript." Blackman, like Bateson and Hopkins, supported the work of scientific women at Cambridge.

[95] Bateson sent a postcard on 21 March 1914 that read: "I see in Nature that there is an Anthocyanin paper at R.S. next Thursday. The author, I think, is Everest of whom I know nothing. I have asked for abstract to be sent to you. WB." See also Bateson to Wheldale, 29 May 1914 and 6 June 1914, Bateson Collection, JICA. The reference is to Everest, 1914a.

claimed that "in all investigated cases, these colouring matters (the anthocyans) are members of one class of chemical compounds, and, moreover, that they are closely related to the colouring matters of many yellow flowers. This latter result is a confirmation of similar conclusions arrived at independently by various other workers."[96] This was an indirect rebuff of Wheldale's hypothesis that anthocyanin was an oxidation product of flavonols. Bateson suggested that Wheldale respond to Everest's criticism. "Why shouldn't you," he recommended, "put your answer to Everest as an Appendix to Journal of Genetics paper now in proof?"[97] At issue was whether his and Willstätter's chemical analysis was more credible than Wheldale's opposing interpretation based on combining data from chemistry, genetics, and plant physiology and reasoning about conditions present "*in the living cell*" rather than the test tube.[98] Because this topic was of some interest to geneticists, Bateson's co-editor R. C. Punnett accepted a paper by Everest as well as Wheldale's for publication in the *Journal of Genetics*. But in so doing, the journal unwittingly became a vehicle that publicized rather than diminished the controversy.[99]

In 1915, Willstätter received the Nobel Prize for chemistry for his work on chlorophyl along with anthocyanin and other plant pigments. This did not convince Wheldale to abandon her oxidation hypothesis. As she recounted in the second edition of *The Anthocyanin Pigments of Plants*, published in 1925, "The chemical work on anthocyanin has not given the solution as to its mode of formation. The constitution of anthocyanins and flavones is known, but it is not clear whether, *in the plant*, the anthocyanins are derived from the flavones or formed independently." It was clear, however, that she was disappointed by the failure of her interdisciplinary approach to reap definitive results. As she noted, "From the point of view of Genetics it is helpful to know from Willstätter's work the nature and constitution of many anthocyanins, and also that the same pigment may be common to different genera and species. ... Genetics, on the other hand, has given us no knowledge as to the origin of anthocyanin."[100]

[96] Everest, 1914a; Willstätter and Everest, 1913.

[97] Wheldale, 1914b, 1915b. In a concluding note to the latter paper, Wheldale corrected errors (an embarrassing misquotation of Everest's statement and an erroneous chemical formula) in Wheldale and Bassett, 1914c. Bateson worked with her to come up with the best "face-saving" way to acknowledge the mistakes: Bateson to Wheldale, 18 and 19 February 1915, Bateson Collection, JICA.

[98] Everest, 1914b, c; Wheldale, 1914b.

[99] Everest, 1914d, 1915.

[100] Wheldale, 1916, pp. 18, 19.

In pursuing this problem, Wheldale increasingly moved away from the research concerns of Bateson and his group and more towards those of the newly appointed Cambridge professor of biochemistry, F. G. Hopkins. Like Bateson before him, Hopkins soon gathered around him a committed circle of followers, many of whom were women (See Figure 2).[101] Entering Hopkins's laboratory in 1914, having been one of the first women elected to the Biochemical Club (later Society), Wheldale began focusing on identifying the oxidases she believed acted on anthyocyanin.[102] This research fitted in well with the biological orientation of Hopkins's lab, particularly his interest in exploring the chemistry of biological oxidation.[103] Her work subsequently shifted, however, following her marriage in 1919 to Huia Onslow (1890–1922), son of the 4th Earl of Onslow and a talented life scientist who had been paralyzed as a result of a diving accident. Wheldale and Onslow shared mutual interests in problems connected with the genetics and biochemistry of pigment formation. Serving as a conduit between her husband (working in a laboratory in their home) and workers in the Department of Biochemistry, Wheldale shifted her focus to other topics, including "the presence of amino acids in germinating seedlings" and "the distribution of the enzyme, tyrosinase, in plants."[104] She also turned her course lectures into a textbook, *Practical Plant Biochemistry*, tailored to botany students whose "knowledge of plant products is usually obtained, on the one hand, from Organic Chemistry, on the other hand, from Plant Physiology," in the belief that "between these two extremes there is a gap, which, it is hoped, the following pages may help to fill." In 1931, shortly before her death, she published the first part of a planned two-volume work on *Principles of Plant Biochemistry*.[105]

Wheldale eventually began to lose faith in the ability of biochemistry to solve the problem of the nature of plant pigments, and apparently so did Hopkins. When a new student, Robin Hill, entered the department

[101] On Hopkins's biochemical program at Cambridge and his support for women, see Kohler, 1982, pp. 47–55, chap. 4; Creese, 1991 and 1998, and Weatherall and Kamminga, 1992, pp. 46–48.

[102] Rayner-Canham and Rayner-Canham, p. 50.

[103] Cambridge was somewhat unique in associating biochemistry with general physiology (histology, embryology, and chemical physiology) rather than medicine, a result of Michael Foster's influence in shaping the life sciences disciplines at Cambridge after 1870. "Foster brought Hopkins to Cambridge in 1898 in the belief that chemical physiology was the key to further understanding of living matter." (Kohler, 1976, p. 332). See also Needham and Baldwin, eds., 1949 and Geison, 1978.

[104] Wheldale Onslow, 1924, pp. 220, 225; Hopkins, 1923, p. 3.

[105] Wheldale Onslow, 1920, preface; Wheldale Onslow, 1931.

Figure 2. Members of Frederick Gowland Hopkin's Department of Biochemistry, 1917? Standing: George Windfield, Ginsaburo Totani, Sydney W. Cole, F. G. Hopkins. Seated: H. M. Spiers, Elfrida Cornish, Harold Raistrick, Elsie Bulley (later Mottram), Dorothy Jordan-Lloyd, Muriel Wheldale (later Onslow). Reproduced with the kind permission of the Colman Library Archives, Department of Biochemistry, Cambridge.

in 1922 wanting to study plant pigments, having been "inspired by his knowledge of natural dyes and the book on Anthocyanins by Muriel Wheldale," Hopkins discouraged him and instead "'directed' Robin to work on hemoglobin and its derivatives," which resulted in Hill's important discovery of cytochrome *f*.[106] By the time Wheldale Onslow published the substantially updated second edition of *The Anthocyanin Pigments of Plants* in 1925, she had effectively ended all work on the biochemical basis of plant pigments.

Although Wheldale was not able to solve the problem she set for herself in 1909, her conviction that genetics held the key to unraveling biochemical processes and her related interdisciplinary approach did bear fruit. Indeed, a combination of a direct chemical and genetical approach—investigating the connection between genes and their physiological activity by means of carrying out a chemical analysis of both the pigment and the presumed transformative oxidase—succeeded in tracing the biochemistry of the magenta anthocyanin pigment. In 1926, Wheldale became the supervisor of a newly arrived research worker in the Biochemical Department, Rose Scott-Moncrieff, who became interested in working on this problem.[107] Fittingly, Becky Saunders

[106] Bendall, 2004, p. 266.

[107] Stephenson, 1932; Kohler, 1982, p. 83.

assisted her work in growing the flowers.[108] Between 1926 and 1939, Scott-Moncrieff, with the encouragement of J. B. S. Haldane, collaborated with geneticists working at the John Innes Horticultural Institute, as well as the Oxford research team of Oxford chemists under the direction of Sir Robert Robinson and Gertrude Robinson. This collaboration ultimately succeeded in making major headway in illuminating the "chemical genetics" of flower pigmentation. In the event, the chemical relationships Wheldale proposed based on her knowledge of Mendelian genetics proved untenable. As Scott-Moncrief concluded, "The identification of antirrhinin as a cyaniding compound contradicts the theory of a simple relationship between this pigment and the ivory flavone apigenin, which is indicated by a study of the Mendelian factors for flower colour in *Antirrhinum*."[109] However, her belief in the value of an interdisciplinary approach did bear fruit, leading to "the first systematic uncovering, on an extensive scale, of the biochemical nature of gene action, and thus set in motion the contribution which biochemistry was to play in genetical research from then onwards."[110]

Conclusion

Wheldale's work on the genetics of flower colors and the biochemistry of plant pigments provides an interesting illustration of an early attempt to analyze the chemical nature of the factors identified by Mendelian genetics. Preceding by 20 years G. W. Beadle and E. L. Tatum's one gene-one enzyme hypothesis, this work joins other recent attempts to expand our knowledge of efforts to explore the "physiology" of the gene prior to the 1940s.[111] Reflecting the thinking of the Bateson group at Cambridge, Wheldale identified the Mendelian factors with precursors

[108] Scott-Moncrieff, 1930, p. 755.

[109] Scott-Moncrieff, 1930, p. 766.

[110] Scott-Moncrieff, 1981–83, p. 125; and Lawrence, 1950. See also Olby, 1974, pp. 134–137.

[111] See Buican, 1982; Harwood, 1993; Rheinberger, 2000a, and Saha, 1984. Kohler certainly recognized that focusing on the work of the 1940s "is not the whole story," stating: "Many others were designing organisms and practices to unite genetics with embryology and physiology: intersexes of the gypsy moth *Lymantria dispar* (Richard Goldschmidt); eye color in the meal moth *Ephestia kühniella* (Alfred [sic] Kühn, Ernest Plagge); eye color in the freshwater shrimp *Gammarus* [sic] (Julian Huxley); skeletal deformations in lethal mutants of mice (J.B.S. Haldane, Hans Grüneberg); plant pigments (Muriel Wheldale Onslow); cysteinuria in Dalmatian hounds (Erwin Brand); and coat color pigments in guinea pigs (William E. Castle, Sewall Wright), to mention only the main competitors." Kohler, 1991, p. 90.

in pigment formation and used genetics to guide her attempt to analyze the chemistry involved. While encouraged by the Bateson group's speculation about the chemical action of genetic factors, Wheldale was the one who had the skills and inclination to develop a methodology by which to carry out such a study. Her approach was ultimately biological. She believed that an integration of the findings and techniques of genetics, morphology, and physiological botany – all based on studying the living organism – would provide a better guide to the actual biochemical processes involved than would chemistry alone. In the end, she reached an impasse owing to limitations of the chemical techniques available to her. However, the development of new techniques to isolate and purify the components of plant pigments in the 1930s permitted a renewed assault on this problem. Although the hypothesis she developed proved not to be true, the interdisciplinary approach she advocated ultimately bore fruit. As one contemporary who was well familiar with Wheldale's early work noted, "The genetical material was available: the chemical knowledge and technique were not."[112] Rose Scott-Moncrieff, in her delightful reminiscence of the work on this problem from the distance of five decades, concurred: "Though the level of sophistication has changed dramatically since that time, subsequent results have not disproved the rules of genetic control of anthocyanin pigmentation in higher plants and the theories of biosynthesis which were first glimpsed by Wheldale and elaborated in the thirties."[113]

The interdisciplinary aspects of Wheldale's scientific work and career are also of interest. Not only was her methodological approach to scientific problems interdisciplinary, but so too were her standards for the interpretation of data. That she did not abandon her belief that anthocyanins were products of oxidation reactions in plants, even in the wake of the Nobel-prize winning work of Willstätter, was not simply stubbornness. Rather, it indicated her strong convictions that a solution would more likely come from a consilience of multiple lines of evidence, and not simply from analytical chemistry. Interestingly, it was also the interdisciplinary nature of her work that served to advance her scientific career. After Bateson left Cambridge in 1910, many of the women who

[112] Lawrence, 1950, p. 3. Kohler argues that an essential piece of the puzzle necessary for developing a successful experimental approach to this problem was the transformation of an essentially genetic system of production [like *Drosophila* or *Antirrhinum*] into an instrument for biochemical diagnosis. "In hindsight, the most important result of this work was the transformation of Drosophila itself into a new kind of laboratory instrument. Tatum took an instrument of developmental genetics and refashioned it into a reagent for quantitative biochemical analysis." Kohler, 1991, p. 112.

[113] Scott-Moncrieff, 1981–83, p. 150.

had worked with him found it difficult to continue their work in genetics. Several, including Wheldale for a time, followed him to the John Innes Horticultural Institute and continued to work in plant genetics.[114] Yet, her situation illustrates the problems these women faced. While, as an assistant, she had a research position at the Innes, Wheldale could not expect a permanent post that could have sustained her research work indefinitely. In 1915, having received a Prize Fellowship from the British Federation of University Women, she returned to Cambridge and joined Hopkins's research group at the Department of Biochemistry. This move proved to be fortuitous. Not only was she able to continue her research, but in 1926 she gained the distinction of becoming one of the first women to receive a university lectureship (in biochemistry).[115] Certainly, then, Wheldale's scientific career greatly benefited from the mentorship she received, first from Bateson and later from Hopkins. But she also profited from working in two newly emerging specialties – genetics and biochemistry – that lacked the hierarchical and male-dominated structures characteristic of more established fields at the time. Thus, like the case of Marietta Blau highlighted by Maria Rentetzi, Wheldale appears to illustrate, "how research on the border zone" – in her case, the border zone between genetics and biochemistry – offered "the flexibility to shift careers," allowing her to enjoy a long and successful career in science.[116]

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[114] Richmond, 2001.

[115] D. J. L., 1932. Her later work was supported by the Food Investigation Board, the Cambridge Low Temperature Station, and the Department of Scientific and Industrial Research.

[116] Rentetzi, 2004, p. 366. Another member of Bateson's group and his sister-in-law, Florence M. Durham, moved from plant genetics to medical genetics, working for the Medical Research Committee (later Council) after the First World War. See Richmond, 2001.

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