

Making a difference:

the economic and societal impact of Rothamsted Research

– 2008 supplement



1. Introduction

1.1 The Rothamsted Research (RRes) mission is all about achieving impact beyond the scientific community and delivering science that our stakeholders can use and benefit from:

“To be recognised internationally as a primary source of first-class scientific research and new knowledge that addresses stakeholder requirements for innovative policies, products and practices to enhance the economic, environmental and societal value of agricultural land” (adopted 2004).

1.2 In 2006 Rothamsted Research published “Making a difference: the past and future economic and societal impact of Rothamsted Research”.

(<http://www.rothamsted.bbsrc.ac.uk/intopractice/Impact.html>). This provided a retrospective and prospective summary of where RRes has made or expects to make impact.

1.3 This document presents a supplement to the original, containing some newly worked examples of impact across the key areas of Rothamsted Research activity.

2. Who are the expected end-user beneficiaries of RRes activities?

2.1 The following groups of end-use beneficiaries of RRes science have been identified:

- UK arable farmers and their advisers
- The food processing and retailing industries
- Policy makers and regulators
- The agricultural supply sector (seeds, agrochemicals, fertilisers, diagnostics etc.)
- The health-care supply and pharmaceuticals sector
- Farmers in developing countries

2.2 In addition, there are two other areas where there has been significant practical impact from the work of RRes and its progenitors:

- the contribution to the supply of highly trained individuals for employment in many walks of life in the UK and abroad.
- the provision of “generic technologies” that have had significant impact outside the primary RRes user community

3. Arable farmers and their advisers

3.1 Fertiliser recommendations

Rothamsted is the lead partner in the consortium responsible for the revision of the 'Fertiliser Recommendations for Agricultural and Horticultural Crops (RB 209)' published by DEFRA. The new version, likely to be called the 'Fertiliser Manual', is expected to be launched during 2008. It is difficult to put a precise financial value on the contribution of Rothamsted to 'fertiliser recommendations' separate from that of other organisations. However, the scale of the savings resulting from research can be surmised from the following facts. The national fertiliser bill for arable crops is about £350M pa and a national yield loss of 10% in wheat alone is worth about £200M pa (2008 prices). The cost of removing nitrate from drinking water has been estimated at £24M pa. Even a modest contribution from Rothamsted work to reductions in fertiliser use, maintaining yield and quality as well as protecting the environment translates into significant annual savings. More specifically, the savings in lost yield from the research on sulphur nutrition that was led from RRes are valued by HGCA at £50M pa.

3.2 Take-all disease

Take-all is a root disease of wheat that is easily avoided by growing the crop in alternation with non-susceptible break crops. It becomes a problem when (susceptible) cereals are grown consecutively as is now common practise. Losses due to take-all can amount to £50m pa. In long runs of continuous cereal cultivation the disease usually increases to a peak of severity over 2-4 years, after which it typically becomes less severe. This phenomenon, known as take-all decline (TAD), is a form of natural biological control that was first confirmed experimentally by RRes. The phenomenon is now widely exploited by farmers who grow 'continuous' wheat but RRes has now confirmed that although TAD also develops in less susceptible cereals such as barley and triticale, this is not effective in protecting wheat grown subsequently (contrary to a widely-held belief). Grass leys do not currently feature prominently in arable farming systems but their recognised potential to increase populations of fungi that are natural antagonists of the take-all fungus, and thus delay the development of take-all epidemics in subsequent cereals, is largely based on RRes work. Similarly, recommendations to keep soil phosphate at index 2, or above, partly reflect the RRes demonstration that take-all is greatly exacerbated in soils that are deficient in this nutrient.

RRes has played a prominent role in the development of strategies for take-all control using recently introduced fungicide seed treatments. In addition, RRes provided influential evidence for take-all control by foliar sprays of the fungicide azoxystrobin. As part of the wheat genetic improvement network (WGIN), RRes has demonstrated that cultivars can differ in their ability to build up the take-all fungus at the start of an epidemic. This finding could have significant impact on future breeding programmes and disease management.



3.3 Aphid monitoring and forecasting

Suction traps designed in RRes have been used since 1965 to monitor and forecast aphid infestations throughout the UK and are now operated widely in Europe and other countries. Weekly bulletins on aphid distribution and abundance are provided to consultants along with an interpretation of the data for a range of crops. The information is used widely to assist in aphid control decisions in arable crops. A major problem in controlling the main aphid vector of potato and sugar beet viruses, the peach-potato aphid (*Myzus persicae*) arises through its multiple insecticide resistance mechanisms. These mechanisms are identified in trapped aphids using molecular diagnostic techniques and the results help to determine management practices that optimise the balance between immediate control and the safeguarding of product efficacy. The spatially and temporally extensive nature of the suction trap data facilitate predictions of the impact of climate and land-use changes on aphids, which prepare the industry for likely problems in the longer term and inform adaptation strategies. For example, warmer winters and the expansion of the maize growing area are expected to lead to significant problems from the corn leaf aphid (*Rhopalosiphum maidis*), which vectors a specific strain of *Barley yellow dwarf virus* in maize and in small-grain cereals.

3.4 Potato cyst nematodes

In the UK approximately 65% of the potato land is infested with cyst nematodes, which are estimated to cause £50M of damage annually despite the use of control measures. RRes identified potato cyst nematodes as two distinct species, *Globodera rostochiensis* and *G. pallida*, and demonstrated differences in their biology, which affected the effectiveness of their control by crop rotation, chemicals and resistant cultivars. RRes work has resulted in optimised chemical control and application methods which give good distribution of products in soil without destroying structure early in the season. RRes played a key role in the identification of crop tolerance and promoted inclusion of the trait in potato breeding programmes by demonstrating how yield penalties associated with such cultivars could be avoided and thereby increasing grower acceptance. RRes responded to grower pressure for targeted applications of nematicides to reduce costs and environmental impacts but these were shown to be too risky when granular nematicides only were deployed. However, for the growers who must resort to using a combination of fumigant and granular nematicides, spatial application of the fumigant is possible. Temporal and spatial placement of liquid nematicide formulations can provide a more efficient delivery system and have been developed at RRes. Pressure to reduce nematicide use on the UK potato crop has led to RRes work on the use of trap crops to reduce PCN infestations. The use of susceptible potatoes or the resistant wild potato, *Solanum sisymbriifolium*, induces eggs of PCN to hatch but the crop is destroyed before the nematode is able to complete its life cycle. RRes showed that this approach may reduce PCN infestations between 50-80%. However, this practice is too risky using susceptible potatoes but *S. sisymbriifolium* has been the basis of two new products, currently used on c. 250ha in the UK.

3.5 Orange wheat blossom midge

The orange wheat blossom midge, *Sitodiplosis mosellana*, is a sporadic, but increasingly important pest of wheat in the Northern Hemisphere. Larval feeding on the developing seeds causes shrivelling and pre-sprouting damage and facilitates secondary fungal attack by *Fusarium graminearum* and *Septoria nodorum*. This affects both the yield and quality of grain harvested, causing at least 20% loss in years of high infestation. For example, in 2004, when wheat prices were around £60 per tonne, an outbreak in the UK was estimated to have caused crop losses exceeding £60 million. At today's wheat prices and with current wheat prices at around £200 per tonne, we have calculated that an outbreak of orange wheat blossom midge causing 20% yield loss would lead to £600 million in losses. Detection problems mean that it is hard to predict when infestations, which would warrant insecticide treatment, have built up. The egg-laying female remains well hidden in the crop canopy, while the larvae are hidden within the wheat ear. This has led to routine prophylactic spraying with broad spectrum insecticides such as pyrethroids or chlorpyrifos. In a Defra LINK/HGCA funded consortium, RRes has developed a robust pheromone-based monitoring system, which, when used with defined trap catch thresholds, has given farmers confidence to reduce unnecessary use of sprays against lower levels of midge infestation and to time applications more accurately when crops are under threat. In addition, midge-resistant feed wheat varieties have been identified, which can be used in conjunction with the monitoring trap.

4. The food processing industry

4.1 Substantial equivalence of GM and non-GM foods

RRes work based on genetically defined wheat lines is set to provide the Food Standards Agency with detailed comparative data on GM and non-GM wheat at the level of gene expression (transcriptome), protein profile (proteome) and metabolite profile (metabolome). This will allow the agency to advise consumers and the food industry on the equivalence and safety of transgenic crops as well as provide methods for industry to use in routine comparisons of GM and non-GM raw materials and foods.

4.2 Bread-making quality of wheat flour.

There is a correlation between genetic variation in high molecular weight glutenin subunit composition and bread-making quality. RRes has provided an understanding of the molecular basis for these effects which underpins both plant breeding and the industrial process of bread-making. Ongoing work exploits this knowledge to identify molecular markers and biophysical properties that can be used to predict end use quality parameters.

4.3 Establishment of EU regulation on heavy metal (Cd and Pb) presence in grain

RRes data on the occurrence of Cd and Pb in cereal grains and how this related to soil conditions and cultivar provided the basis for formulation of the EU Regulation on Contaminants in Food (Commission Regulation (EC) No 466/2001 Setting Maximum Levels for Certain Contaminants in Foodstuffs). Subsequently, similar advice and information was used for development of the associated Contaminants in Food Regulations 2002 (England).

5. Policy makers and regulators

5.1 Glucosinolates in oilseed rape

UK government decisions and policies on growing oilseed rape were underpinned by RRes work on the physiological basis for glucosinolate accumulation and the influence of agronomic and harvesting practices on the suitability of oilseed rape meal for animal feed. The work resulted in regulations on the varieties to be grown and avoided the need for expensive seed quality testing at the point of sale.

5.2 National and international policy on soil health, quality and conservation

RRes results have been used to advise government on environmental policy and legislation related to sewage sludge utilisation on land. RRes research on ecotoxicology of metals derived from sludge applications lead to new national rules for sewage sludge disposal in the D.o.E. (1996) "Code of Practice for Agricultural Use of Sewage Sludge". RRes research and advice is now being used to develop a new EU Directive on Sewage Sludge (Working document on sludge, ENV.E.3/LM, 3rd draft, Brussels, 27 April 2000). The aim is to ensure utilisation of sewage sludge in such a way as to minimise the risk of negative effects to: human, animal and plant health; the quality of groundwater and/or surface water; the long-term quality of soil; and the bio-diversity of the micro-organisms living in the soil.

RRes work showed that the Draft EU Risk Assessment for zinc, conducted in the Netherlands as a contribution to the EU Existing Substances Directive (Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances) ignored some of important chemical and biological processes affecting the ability to extrapolate toxicity from laboratory to field situations. As a result of RRes research a new risk assessment will be done to take zinc bioavailability into account. RRes advice has been influential on the Environment Agency during the development of their risk assessment for chromate under the ESD.



6. The agricultural supply sector

6.1 Plant breeding

Novel genetic sources of disease resistance and closely associated molecular markers to aid in their selection in breeding programmes have been identified for wheat (soil borne mosaic virus) and beet (powdery mildew). Materials and the means for efficient selection have been transferred to the commercial breeding sector.

Several new RRes-derived willow varieties with greatly increased yield in short-rotation coppice production for bioenergy have been granted Plant Breeders Rights and are being commercially propagated for large-scale planting.



6.2 Environmental fate of pesticides

There are several hundred pesticide active ingredients approved for use in the UK, with new compounds being introduced each year as older pesticides are withdrawn. A framework for understanding many aspects of pesticide behaviour in the environment, including systemicity within plants and leaching in soils to drains or groundwater, has been assembled using the physicochemical properties of pesticides as predictors. This has been developed for the UK Pesticides Safety Directorate into a database/expert system 'Physicochemical Evaluation: the Environment' (PETE), which allows predictions to be made of the environmental behaviour under differing scenarios for over 900 pesticides and other contaminants. This is used by registration authorities and other scientists in many countries to assist in regulation for the safe use of pesticides in agriculture. An example is in predicting the lipophilicity and pKa range that allows systemic movement within plants, both via phloem to new growth and via xylem from roots to shoots; such information has been used by the pesticide industry to focus screening for improved phloem-mobile insecticides and fungicides. Many herbicides, such as 2,4-D, have this transport pattern which is required for them to reach their target site. Equally, the properties conferring such behaviour usually lead to weak sorption by soil and hence the problem of potential leaching to groundwater, but the expert system correctly predicts that this will be mitigated for 2,4-D by virtue of its short persistence in soil.

6.3 New leads for novel active ingredients

Following the discovery of bioresmethrin at RRes in 1967 even more effective new pyrethroid insecticides, notably permethrin, cypermethrin and deltamethrin, were discovered in the Institute during the 1970s. These discoveries were protected by patents assigned to BTG. These insecticides were sufficiently photostable for use in agriculture, had low toxicity to mammals and were benign in their environmental impact. This combination of desirable properties led to their acceptance as a major class of agricultural insecticides and they became one of the three top money-earners for BTG (via patent licence fees) alongside cephalosporins and medical NMR scanning technology. Nearly 30 years after they were introduced, global pyrethroid sales are \$1498 million (£750m), equal to 18% of global insecticides sales of \$8471 million in 2006. In 1986, ten years after they were launched, they comprised 23% of the global insecticides market of \$6016 million. Since 1996 only the neonicotinoids have grown faster and overtaken the sales of pyrethroids.

Of the many new compounds synthesised by RRes subsequently, some, and particularly the “non-ester” pyrethroids, had sufficient activity to justify patenting. This underlined the potential in the pyrethroids and served to stimulate further interest within companies. The result was a range of commercial products with properties suited for new markets including rice. Compounds with enhanced soil activity (the fluorobarenes) illustrated how structural changes could influence physical properties that control delivery to the target.

In the 1990s, another natural product provided the starting point for the discovery of naphthoquinone analogues with high insecticidal and fungicidal activity. These compounds have been protected by world-wide patents assigned to BTG and commercial development is ongoing. Studies on mode of action have led to an understanding of target specificity and the absence of cross-resistance in insects to other classes of insecticide. Studies with the fungicidal naphthoquinone analogues compounds have stimulated commercial interest because they provide the opportunity for rational design of compounds which can minimise problems of resistance.

7.4 Novel crops for production of bioactive molecules

An overarching scientific objective of RRes is to develop new products from crops. Under some circumstances it has now proved possible to produce crop protecting agents directly by cultivation of new industrial crops. This has the added value of exploiting renewable resources and of avoiding disposal problems arising from chemical synthesis. The compounds can potentially be obtained, as required, by exploiting the diversity of natural plant species to find appropriate sources, but also by clean chemical processing once the basic molecular structure has been made available from the industrial crop. Appropriate sources can also be identified where the required isomeric structure is already in place as this aspect often represents a major cost in production by chemical synthesis. This novel approach has already been applied to the production of the aphid sex pheromone.

The sex pheromones enable direct control of aphids by the attraction of wasps that parasitise the aphid pests. They consist of specific isomers of nepetalactone and nepetalactol. One of the nepetalactones is now being produced and formulated on a large scale from the herb *Nepeta cataria*.

Although coincidental, it has long been known that the chemistry described for the aphid sex pheromones also provides potent excitants for animals in the cat family. Further collaborative studies have led to the development of a formulation of nepetalactone for use in devices now being marketed in the US and Europe to provide entertainment for domestic cats and, thereby, their owners.



8. The health-care supply and pharmaceuticals sector

8.1 Control of insect vectors

The development of the pyrethroids insecticides described earlier has had an enormous impact on the control of insects carrying highly impacting pathogens which cause human disease as well as insects that impact on livestock health and welfare. Malaria is a major disease and accounts for approximately 4 million deaths per annum, largely among children, in sub-Saharan Africa. In the African context, the pathogen responsible is mainly *Plasmodium falciparum*, principally vectored by the mosquito *Anopheles gambiae*. An expanding solution to this problem is the use of bed nets impregnated with pyrethroids such as permethrin and the spraying of domestic living quarters with pyrethroids. Although there are problems of resistance, the pyrethroids are still favoured and are potentially the safest insecticides to employ.

With regard to the safety of pyrethroids to humans, recent RRes research in collaboration with the University of Nottingham has shown that the target of insecticide action is structurally different between vertebrates and insects thus justifying their continued use in pathogen vector management.

There is a strong demand for chemicals to control vectors of human pathogens by non-toxic modes of action. RRes was the first to identify a mosquito pheromone, the oviposition pheromone of mosquitoes in the *Culex* genus, such as *Cx quinquefasciatus*. A method to produce this pheromone via ⁵ fatty acid produced in new potential crop plants has been developed and the potential of this approach is under assessment for several *Culex* transmitted diseases.

RRes with collaborators have identified pheromones of the new world sandfly (*Lutzomyia longipalpis*) which can carry the protozoan pathogen of leishmaniasis. Again, an industrially grown plant can be used to produce pheromone in large amounts and its use in control is being evaluated.

9. Farmers in the developing world

9.1 *Phytoplasma diagnostics*

PCR based diagnostic tests developed to enable the detection and discrimination of phytoplasma pathogens that cause devastating diseases of coconut in Ghana, Tanzania, Kenya, Indonesia and Mozambique have become central to rehabilitation of the coconut crop in these regions of the world. RRes work identified the causal agent of Ramu Stunt of sugarcane in Papua New Guinea and prevented closure of a newly established sugar industry funded by the World Bank.

9.2 *Disease resistant oilseeds*

In India, development of disease resistant oilseed brassica germplasm in a project led by RRes has involved 5000 farmers in training programmes at 73 field sites; this has not only increased self-sufficiency in vegetable oil but has also enabled short-duration oilseed production in rotation with rice on previously fallow land.

10. Trained staff and students

RRes provides a training environment which is unique in the UK through its multidisciplinary and yet exclusive focus on questions of relevance to crop-based agriculture. Students and research fellows are able to draw on wide-ranging expertise in biological, physical and mathematical sciences while gaining access to both highly serviced laboratory and field facilities. In addition to the 15-20 PhD students who graduate from RRes each year, Rothamsted International runs three training schemes for scientists from the developing world. The popularity of these schemes is testament to their value.

- Since 1993, over 50 Rothamsted International (RI) Fellows have received high-level training in RRes – all have returned to their countries of origin and many now occupy senior positions.
- The Gatsby Charitable Foundation funds two schemes through RI directed towards capacity building for Africa:
 - o an African research fellows scheme analogous to the RI scheme above;
 - o advanced training in plant nematology conducted from several African centres

11. Generic technologies

11.1 *Aerobiology*

The science of “aerobiology” (the study of airborne biological particles and their effects) was founded in RRes. Studies of a number of occupational respiratory diseases in different environments (farms, mushroom production plants, cork factories, sugar beet factories and waste transfer stations) highlighted the importance of airborne fungal spores in their development. Air sampling protocols developed in RRes have been widely adopted in the evaluation of the effects of biological particles in occupational disease

RRes has also shown that airborne fungal spores may play a previously unrecognised role in allergic disease in non-occupational environments. Over the last two decades there has been an increasing awareness and interest, in many parts of the world, in allergic disease caused by airborne pollen and spores. As a result pollen-monitoring networks have been developed in several countries, particularly Europe, to provide information to both patients and clinicians. The air sampling equipment developed and pioneered at RRes has been adopted as the “standard” for use in many of these networks. Ongoing work is pioneering the use of molecular based technologies for the rapid detection of airborne biological particles which could lead to a new generation of air-sampling equipment for use in the management of allergic disease.

11.2.1 Generalised linear models

Generalised linear models were devised in RRes and extended the classical linear models to situations where the data do not follow a normal distribution, or where a transformation needs to be applied before a linear model can be fitted. They provide a general framework that includes log-linear models for Poisson data as well as logistic regression and probit analysis for binomial data. The original motivation involved the analysis of crop disease data but they have proved useful across a whole range of statistical applications including medicine, insurance and retailing. The GLIM methodology and its associated algorithm have been implemented in Genstat and other leading statistical software packages. These procedures have been influential in raising standards of statistical analysis.

VSN International is the commercial joint-venture company (with NAG Oxford) spun-out from RRes in 2002 which develops and markets innovation in computational statistics - based substantially on BBSRC (formerly AFRC) investment. The company is profitable, truly international (trading in ca. 90 countries and the Chairman, Jim Cooper of Maplesoft is based in Canada), employs 13 people (6 in technical development – 4 ex-RRes), and will have a turn-over in 2008/09 of over £1m. The “Discovery” edition of Genstat (= 9th edition) is provided free of charge to not-for-profit organisations and academics in the developing world, an initiative in knowledge transfer recently publicly endorsed by Professor Sir David King. Genstat is primarily (but not exclusively) used by practitioners in the agricultural, forestry, environmental and ecological sectors. The 11th edition of Genstat will be delivered in 2008 and incorporates the latest scientific developments and innovations demanded by the user base. Roslin/RRes-derived REML methodology is available within Genstat and also as stand-alone software (ASReml). Work is progressing on the refinement of in-demand software for making REML methodology more accessible to an extended user-base.

11.2.2 Spatial statistics

RRes scientists have played a pivotal role in the development of spatial statistics. These were developed for analysis of spatial variation in soil properties but the work provided a springboard for much additional work on spatial analysis in environmental science and human epidemiology including the analysis of pattern in the occurrence of rare diseases such as childhood cancer.

Recent statistical methods developed by RRes scientists, termed SADIE (Spatial Analysis by Distance IndicEs), are the only ones developed specifically for analysing spatial patterns derived from ecological data in the form of counts. The method is also the first that allows mapping of clusters and gaps, and of the strength of spatial associations between organisms, with or without the inclusion of time-lags. An introductory explanation, examples, Windows-based software, documentation, reprints and a dynamic tutorial are available on a series of linked webpages on the RRes server <http://www.RRes.bbsrc.ac.uk/pie/sadie/>. Usage of these methods in ecological studies is steadily increasing.

11.2.3 Biodiversity indices

The measurement of species diversity has been a recurring challenge in quantitative ecology. For species rich faunas and floras the obvious measure, species richness, is so directly related to sample size that little useful information is provided by using number of species in a sample alone without correcting for the number of individuals examined. The first attempt to overcome this problem was provided by the 'index of diversity' suggested by R.A. Fisher and C.B. Williams at Rothamsted in the 1940's. Since then many competing indices have been proposed. Using the spatial and temporal replication in the moth data for the Rothamsted Insect Survey that were available by the 1970s, it was possible to compare the most widely used indices and show the clear superiority of Fisher-Williams index in a number of respects. These included independence of sample size and the power of discrimination. This work has led to widespread use of this measure in many ecological studies including effects of land-use change, comparison of organic and conventional cultivation and, more recently, the environmental effects of GM crops.

