Biological Information Flow Manipulation: The New Science of Directed Prevention and Control of Crop Diseases and Pests - Postprint

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Abstract

Crop diseases and pests are major natural disasters threatening global agricultural production. Currently, the core philosophy of pest and disease control remains simple eradication, primarily relying on chemical pesticides that target the basic metabolism, physiological and biochemical systems, and neural receptors of pest and pathogenic microorganisms, a process that readily leads to a series of serious problems including human and livestock poisoning, agricultural product contamination, and damage to ecological environments. The major conceptual breakthrough in next-generation pest and disease control will be the manipulation of inter-organism information flow and behavior among crops, insects, and pathogenic microorganisms. In terms of basic research, "Recognition, Decoding, and Manipulation of Inter-organism Information" is also a frontier and hotspot discipline in modern life sciences—once the molecular mechanisms of inter-organism interactions are elucidated, they often drive breakthroughs in the development of universal biotechnology. For instance, scientific discoveries and technological advances such as the RNA interference (RNAi) phenomenon, plant transformation technology, and TALEN genome editing technology have already made significant contributions to the entire field of life sciences. The Chinese Academy of Sciences' Strategic Priority Research Program (Category B) on "Directed Prevention and Control of Crop Diseases and Pests—Inter-organism Information Flow and Behavior Manipulation" has assembled advantageous forces from various disciplines to systematically analyze the processes of interspecies information recognition, decoding, transmission, and control during major crop disease and pest outbreaks, thereby identifying key manipulable nodes and developing new strategies and technologies for next-generation field behavior manipulation of pests and diseases. This program has already achieved a series of major research results, making fundamental and forward-looking contributions to competing for international scientific frontier status and safeguarding China' s grain production security.

Full Text

Preamble

Crop diseases and pest infestations not only threaten food safety and social stability but also cause environmental pollution and health hazards through pesticide misuse. To achieve scientific, green, and efficient pest management without compromising grain yields, we must systematically analyze the interactions among pathogenic microorganisms, insect pests, and crops. By targeting the critical processes underlying pathogenicity and infestation, we can develop revolutionary agricultural biotechnologies—including innovative disease-resistance breeding, novel pesticides, microbiome technologies, ecological suicide mechanisms, and insect sex control—that make significant contributions to national food and food security. This special issue on "Targeted Management of Agricultural Pests" analyzes fundamental research on pest-crop interactions and the advanced biotechnologies they inspire, offering forward-looking recommendations for frontier and applied technology development in this field. This special issue was guided by Academician Kang Le (Institute of Zoology, Chinese Academy of Sciences), Academician Chen Xiaoya (Shanghai Institute of Plant Physiology and Ecology, Chinese Academy of Sciences), and Academician Fang Rongxiang (Institute of Microbiology, Chinese Academy of Sciences).

Bio-information Flow Manipulation: A New Science for Targeted Pest Management in Crops

Crop pests and diseases represent major natural disasters threatening agricultural production worldwide. Currently, the core philosophy of pest management remains simple eradication, relying primarily on chemical pesticides that target the basic metabolism, physiological and biochemical systems, and neural receptors of pests and pathogenic microorganisms. This approach readily leads to a series of severe problems, including poisoning of humans and livestock, agricultural product contamination, and ecological environmental damage. The next major breakthrough in pest management philosophy will be the manipulation of bio-information flow and behavior among crops, insects, and pathogenic microorganisms.

At the fundamental research level, "the recognition, decoding, and manipulation of interspecies information" represents a frontier and hot topic in modern life sciences. Once the molecular mechanisms of bio-interactions are elucidated, they often drive breakthroughs in general biotechnology. Scientific discoveries and technological advances such as RNA interference (RNAi), plant transformation technology, and TALEN genome editing technology have already made significant contributions to the entire field of life sciences. The Chinese Academy of Sciences' Strategic Priority Research Program (Category B) on "Targeted Management of Crop Pests and Diseases—Manipulation of Bio-information Flow and Behavior Among Organisms" has assembled interdisciplinary strengths to systematically analyze the processes of interspecies information recognition, decoding, transmission, and control during major crop pest and disease outbreaks. By identifying key manipulable nodes, the program develops new strategies and technologies for next-generation field manipulation of pest behavior. The program has already achieved a series of major research results, making fundamental and forward-looking contributions to securing a competitive position at the international scientific frontier and ensuring China' s grain production security.

Current Challenges in China' s Crop Pest Management

China is the world' s most populous country and largest agricultural nation. Since Lester Brown raised the question "Who will feed China?" in 1994 [1], this issue has remained a global concern. Food supply represents the most important guarantee for national strategic development worldwide. To ensure China' s food security, the National Medium- and Long-Term Program for Scientific and Technological Development (2006–2020) established "advancing agricultural science and technology to the world forefront, promoting improvement of comprehensive agricultural production capacity, and effectively ensuring national food security" as one of China' s overall S&T development goals. Although the international community recognizes China as a primary region for future global grain production increases (Figure 1A, red areas) [2], comparing this with the distribution map of major pests and diseases on China's staple crops (Figure 1B) reveals that these regions almost completely overlap with the predicted production increase areas. This indicates that China' s grain production and stability face significant risks, severely constrained by the scale and frequency of crop pest and disease outbreaks. Historically, crop pests and diseases have always been major natural disasters threatening agricultural production in China and worldwide, as well as primary causes of social turmoil and dramatic population declines.

China' s current crop pest management situation is extremely severe, characterized by three main features:

(1) **Exceptionally large yield losses**. Even with full prevention and control efforts, annual yield losses due to pests and diseases still reach 40–60 million tons, accounting for 8–10% of total production—enough to feed 150–200 million people for one year. As climate change continues, lightweight cultivation techniques are adopted, and single genetic background varieties are promoted, previously sporadic crop pests and diseases (such as rice sheath blight, dwarf disease, cotton verticillium wilt, wheat scab, and armyworms) have erupted into consecutive annual disasters, with the prevention situation worsening year by year.

(2) **Increasingly severe environmental pollution**. China accounts for approximately one-third of global pesticide use, ranking first worldwide.

Pesticide abuse and residues have caused extremely serious impacts on public health, natural environment, domestic and foreign trade, and socioeconomics, making food safety a major public concern.

(3) **Lack of core technological innovation capacity**. Currently, the vast majority of pest management strategies and technologies were proposed and developed by advanced foreign countries, while China remains largely in a low-level imitation stage. For example, the United States' modern pesticide industry has reached an annual output value of $9.6 billion. Although China is a major pesticide user, its annual output value is only $1.8 billion, with most products lacking core intellectual property rights, indicating a significant gap in technological development capacity.

Under tremendous grain production pressure, the current core philosophy of pest management remains simple eradication, technically relying mainly on chemical pesticides targeting pest metabolism and neural receptors while ignoring interspecies relationships and information transmission—this is the root cause of these serious problems. Although China has launched a zero-growth action plan for chemical fertilizers and pesticides by 2020 and established corresponding national key R&D programs to study scientific and rational pesticide use, achieving these goals will require arduous efforts given current pesticide options and usage patterns. Where will future crop pest management philosophy, basic theory, and technological development head? How can we organically combine the ecological balance advantages of integrated control with the simplicity, feasibility, and effectiveness of chemical control? Meanwhile, developing revolutionary crop pest and disease technologies that abandon the inherent technical defects of low efficiency, complexity, serious environmental impact, and threats to human health represents a major scientific challenge facing contemporary life sciences and applied basic research.

Bio-information Flow and Pest Behavior Manipulation as the Next Breakthrough

In the biosphere, no organism can survive in isolation within an abiotic physicochemical environment—it must interact and establish close connections with surrounding organisms. These connections and interspecies interactions constitute ecological and co-evolutionary relationships such as parasitism, mutualism, symbiosis, competition, and antagonism, while the information flow transmitted between organisms determines the nature of these relationships. The laws governing this transmission constitute fundamental principles for the existence and evolution of all life.

From the perspective of interspecies relationships, re-examining the crop-insect-pathogen relationship reveals that intra- and interspecies relationships and bio-information flow transmission are the most important factors determining their interactions [3]. Bio-information flow refers to the pathways, processes, and controls by which biological signals are generated, transmitted, exchanged, modified, translated, and suppressed between species in physical and chemical forms. Taking the relationship among crops, vector insects, and plant viruses as an example: physical and chemical information released by crops can be recognized by vector insects, attracting their movement, migration, and colonization on plants while transmitting pathogenic microorganisms during feeding [4]. During this process, after plants suffer physical damage, they activate anti-insect defense responses through hormone signal transduction pathways such as jasmonic acid, increasing the content of terpenoids, tannins, flavonoids, or polyphenols. Interestingly, research has shown that viruses carried by insects, when ingested into plants, can interfere with multiple plant signal transduction pathways through virus-encoded proteins, suppressing the expression of plant anti-insect-related genes and compound synthesis, thereby facilitating insect feeding and causing population expansion and disaster [5,6]. This example demonstrates that, on one hand, viruses require insect feeding to infect plant hosts; on the other hand, viral endosymbiosis also helps insects overcome plant anti-insect defense systems, forming complex symbiotic and parasitic relationships among plants, vector insects, and viruses. In these complex biological relationships, how do viruses recognize insects and specifically parasitize them? How do insects recognize specific host plants for feeding while helping viruses infect host plants? How do plants recognize insects and viruses to activate corresponding disease and insect resistance defense systems? These scientific questions concerning interspecies information recognition, decoding, signal transduction, and response determine the degree and scope of crop damage by insects and viruses. Notably, human understanding of these interspecies interactions remains very weak, which limits our ability to precisely manipulate these relationships with advanced scientific methods, forcing us to adopt non-selective "kill-all" approaches to crop pest management—this is a historical limitation in crop pathology and protection disciplines.

Understanding bio-information flow and its regulation can scientifically guide prevention strategies. For example, long-term, single, and repeated use of chemical pesticides has led to resistance and tolerance in multiple pests and diseases. This occurs primarily because most current chemical pesticides employ non-specific toxic killing methods. Under natural selection pressure, spontaneously arising genetic variations related to resistance in pest populations can rapidly gain selective advantage and become fixed, accelerating resistance evolution. Meanwhile, in pathogen populations, horizontal gene transfer allows resistance-related genes to be exchanged among extremely distantly related microorganisms, further accelerating resistance development [7]. Consequently, traditional "kill-all" strategies achieve only extremely limited short-term effects. To address this challenge, scientists have proposed new strategies: when screening novel chemical agents, understanding the direction and regulation of bio-information flow enables purposeful selection of compounds that specifically block interspecies recognition and response processes without affecting other physiological and metabolic processes in pests and pathogens. Such new chemical pesticides would impose less natural selection pressure on pests and diseases, enabling precise population control while slowing the fixation of resistance genes—effectively avoiding rapid resistance evolution. Therefore, deep understanding of bio-information flow is the key to developing revolutionary pest management technologies (Figure 2). Based on this foundation, manipulating bio-information flow and behavior among crops, insects, and pathogenic microorganisms will represent a major breakthrough in next-generation pest management philosophy.

Future Directions: Behavior Control Based on Interspecies Information

From a macro perspective, crop pests and diseases result from insects and pathogens feeding on and parasitizing host plants to meet their survival, development, reproduction, and population expansion needs. In the past, community or population ecology studies of these relationships focused primarily on population numbers, structural patterns, dynamic changes, interspecies relationships, and environmental factors. Although these studies provided basic knowledge for understanding pest outbreaks and environmental constraints, they generally failed to address the fundamental question of species adaptation mechanisms. In recent years, with rapid advances in molecular biology and omics technologies and increasing integration across life sciences, we can now comprehensively and systematically analyze bio-information flow and its molecular transmission mechanisms among crops, insects, and pathogenic microorganisms—studying biological traits themselves rather than just quantitative indicators. This makes artificial simulation, interference, and manipulation of bio-information flow possible with enormous application potential. This development trend represents the future of integrative biology and a crucial pathway for macro-scale biological sciences to achieve major theoretical breakthroughs.

In terms of molecular mechanisms, like animal infection and immunology, the interactions between crop innate immune systems and insects/pathogens constitute a frontier discipline in modern life sciences, with numerous original research papers frequently published in top-tier journals such as *Cell*, *Nature*, and *Science*. In the past, biological sciences using model organisms (e.g., *Drosophila*, nematodes, *E. coli*, and *Arabidopsis*) focused more on major aspects of single life processes such as growth, development, and reproduction. However, as ecology reveals, interspecies relationships form the primary network carrier system for energy flow, information flow, and material flow in Earth' s biosphere and represent the most important dependencies for sustaining life on Earth, containing abundant major scientific questions yet to be understood by humans. Using crop-insect-pathogen systems as research objects to study interspecies relationships and bio-information flow at the molecular level will undoubtedly lead to new biological discoveries and theoretical developments.

How Bio-information Flow Research Drives Biotechnology Development

Modern biological technologies essentially represent artificial simulation and redesign of life. Molecular-level manipulation naturally exists during species interactions, and many major theoretical and technological advances in modern life sciences have emerged from studying and simulating these relationships. Crop pathology and protection have already made significant contributions to the entire life sciences field:

(1) **Discovery of innate immune activation receptors**. The first innate immune activation receptor discovered in higher organisms was the rice Xa21 protein, isolated in 1995 during rice-*Xanthomonas* interactions [8]. Subsequent research on mammalian lipopolysaccharide receptors and insect TOLL-like receptors led to breakthroughs that won the 2011 Nobel Prize in Physiology or Medicine.

(2) **Discovery of RNA interference (RNAi)**. RNAi was first discovered in plant-virus interactions and plant gene "co-suppression" phenomena [9]. After its molecular mechanisms were elucidated in nematode model systems, it won the 2006 Nobel Prize in Physiology or Medicine, making major contributions to understanding molecular biology's "central dogma" and developing modern gene regulation technologies.

(3) **Plant transformation technology**. Research on plant-bacteria interactions revealed that *Agrobacterium tumefaciens* senses plant chemical signals and integrates Ti plasmids into plant genomes to regulate host gene expression [10]. Plant transformation technology, one of the core technologies supporting modern plant molecular biology, was developed through artificial modification of this process.

(4) **TALEN genome editing technology**. Studies of plant-bacteria interactions discovered that *Xanthomonas* TAL effectors can specifically recognize plant gene promoter sequences through a modular coding mechanism [11]. The TALEN technology based on this research is one of the most mature biotechnologies for editing genomic DNA and was named one of *Science*'s top ten scientific breakthroughs of 2012.

These scientific discoveries and technological advances demonstrate that natural, molecular-level manipulation among plants, pathogens, and insects, once elucidated, can radiate throughout the life sciences field and generate major scientific discoveries whose impact extends far beyond the original research area.

The CAS Strategic Priority Project

The Chinese Academy of Sciences (CAS) has assembled a strong research team with significant advantages and international influence in crop disease resistance, insect biology, and pathogenic microbiology, representing one of the leading research collectives in crop pathology and protection. However, because crop disease resistance, agricultural entomology, and pathogenic microbiology belong to different disciplines (botany, zoology, and microbiology), collaborative research has been limited in the past. Existing national key scientific research programs, including "973" programs and major research plans, have not effectively integrated these research teams under a single project to conduct synergistic research on key scientific questions.

Based on these considerations, to break through bottlenecks in pest management basic and applied research, CAS established the Strategic Priority Research Program on "Targeted Management of Crop Pests and Diseases—Manipulation of Bio-information Flow and Behavior Among Organisms" in 2014. Under the overarching academic concept of "bio-information flow and behavior manipulation among crops, insects, and pathogenic microorganisms," the program's overall research direction is to systematically analyze and identify interspecies information and its transmission processes related to pest and disease occurrence, development, and disaster formation; establish finely regulated signal networks of interspecies information flow; and identify important regulatory nodes and critical links in interspecies information transmission. Based on this foundation, the program develops new technologies and methods for artificially manipulating insect and pathogen behavior and pathogenic processes, and uses modern biological approaches—including ecological suicide, sex control, novel antimicrobial compound development, crop immune regulators, and artificial design of crop resistance-related metabolomes—to achieve efficient, specific, environmentally friendly, and cost-effective targeted management of pests and pathogens, making major theoretical innovations and breakthroughs in key technological obstacles for China's major grain crop pest management, and contributing to national food security.

To achieve these goals, the program established five research projects for integrated innovation: (1) Biological effects and artificial manipulation of intraspecies information flow; (2) Recognition and decoding of interspecies information and its artificial manipulation; (3) Regulation and manipulation of information transmission and response; (4) Targeted intervention based on pathogen molecules; and (5) Multi-trophic-level interspecies information interactions and targeted regulation. Each project concentrates CAS strengths in microbiology, modern entomology, plant molecular biology, systems biology, genomics, and combinatorial chemistry, with rational division of labor and collaborative cooperation for in-depth research to accomplish the overall objectives. Concurrently, relying on program implementation, comprehensive research and development facilities have been established, including platforms for genetics, epigenetics, and omics analysis; substance detection and biochemical analysis; static and dynamic cell biology analysis; and integrative biology and bioinformatics analysis.

Major Research Achievements

Since its launch in 2014, the program has achieved a series of major breakthroughs in both basic theory and applied technology.

(1) Basic theoretical research. Through studies on intra-species information flow and its mechanisms, the research team discovered that locust aggregation information flow has transgenerational epigenetic effects, revealing that non-coding small RNAs serve as key regulatory information substances controlling the synchrony of egg development and hatching in offspring, opening new avenues for developing green management strategies for locust plagues [12,13].

(2) Crop-microbe interactions. The team discovered multiple new pathogenic mechanisms, achieving several internationally leading results in plant innate immunity, jasmonic acid- and small RNA-mediated plant immune responses, providing scientific basis for improving crop disease resistance and selecting new pesticide targets [14-18].

(3) Plant-insect interactions. The team discovered that jasmonate response attenuation and phytoalexin accumulation dynamically regulate plant anti-insect resistance at different developmental stages, while developing RNAi-based anti-insect technology to provide technical support and theoretical basis for breeding new insect-resistant crops [19].

(4) Insect-microbe interactions. The team elucidated the genetic evolution and host adaptation mechanisms of insect fungi, as well as oosporein biosynthesis and its mechanism for suppressing insect immunity, providing theoretical foundation for developing environmentally friendly fungal insecticides [20,21].

(5) Multi-trophic-level interactions. The team discovered key molecules for coordinated development among multiple species, elucidated information flow control mechanisms for pest behavior and development, and proposed new early warning and management strategies for crop-pest-virus-natural enemy dynamics under global climate change [22,23].

(6) Major biotechnology breakthroughs. Using genome editing technology, the team directionally modified the MLO gene in hexaploid wheat, internationally pioneering the cultivation of powdery mildew-resistant wheat for the first time, achieving a major biotechnology breakthrough that provides important technical support for crop breeding in China [24]. The team also internationally pioneered the demonstration of a novel plant disease resistance pathway through cross-kingdom small RNA silencing of pathogen target genes in fungi, applying it to germplasm innovation for cotton verticillium wilt resistance, potentially overcoming this major cotton disease [25,26]. Additionally, the team overcame key technological bottlenecks centered on pheromones to successfully control the red turpentine beetle in China [27].

Since program implementation, achievements in publication and application have been outstanding. The program has published over 150 research papers, including 39 in internationally renowned journals such as *Nature Biotechnology*, *Cell Host & Microbe*, *Nature Plant*, *Nature Communication*, *PNAS*, *PLoS Pathogens*, *PLoS Genetics*, and *Plant Cell.* Third-party evaluation results indicate that the program's scientific team has substantially surpassed international averages in entomology and plant pathology, approaching the scientific output and influence of top international research institutions. Furthermore, the program has strengthened data exchange and platform technology sharing, reserving 35 relevant datasets across 8 categories (including genomes, transcriptomes, proteomes, and metabolomes of various pests and pathogens) and 41 relevant technologies across 17 categories (including genome editing and bio-interaction infection methods) for shared use within the program. In terms of management, the program upholds the philosophy of "lean team, stable support, strict evaluation, first-class results," implements a differentiated funding system, encourages major scientific achievements, and conducts innovative management practices, providing institutional guarantees and professional platforms to break down research barriers between disciplines and institutes and facilitate collaborative innovation [28].

After decades of development, China' s modern agriculture has made major contributions to ensuring national and social progress. Looking forward, Chinese agriculture should make entirely new contributions in basic theoretical construction, modern agricultural technology development, and agricultural innovation systems, leading new directions in global agricultural science and technology development. The CAS Strategic Priority Program on "Targeted Management of Crop Pests and Diseases" is a major national project in crop pathology and protection funded as a special S&T program. By assembling high-level research teams, strengthening research cooperation and disciplinary integration, and making important innovations in project management mechanisms and systems, this program will undoubtedly cultivate a world-class innovative team capable of leading disciplinary development, making fundamental and forward-looking contributions to leading frontier life sciences and ensuring major national strategic needs for food and food security.

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