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OVERVIEW OF MIXED STRATEGIES IN STACKELBERG EVOLUTIONARY GAME THEORY APPROACH OF POPULATION CONTROL - CASE OF POPULATION GROWTH CONTROL

In this paper we will overview current state of population management simulation using Stackelberg game theory as current development of evolutionary games theory. We will look into both population growth and decline strategies, concentrating on fishery management and cancer treatment accordingly. We will analyze differences in Nash and Stackelberg equilibrium and discuss possibility of usage of mixed strategies. We will outline differences in rational manager approach to population minimization and maximization cases for Stackelberg game.

Evolutionary game theory provides a mathematical framework for the conceptualization and analysis of biological interactions in which an individual's fitness is contingent upon not only its own traits but also those of others. In this context, the participants are generally not explicitly rational actors; rather, they tend to inherit traits as opposed to actively selecting them.

The Stackelberg Evolutionary Game (SEG) theory amalgamates classical and evolutionary game theory to model interactions involving a rational leader and evolving followers within an academic framework. Within this context, the leader's intentions vary; they may seek to sustain the dynamic system, as seen in scenarios such as fisheries management, or alternatively, endeavor to eliminate the system, as observed in cases like pest control. Frequently, a constant aggressive approach assumed by the leader, such as excessive fishing in the context of fisheries management or administering the maximum tolerable dose in cancer treatment, represents a suboptimal strategy. Incorporating ecological dynamics into the analysis typically yields more favorable outcomes for the leader, aligning with Nash equilibria in the realm of game theory [3].

Nonetheless, the leader's most advantageous course of action involves proactive consideration of and influence over the eco-evolutionary dynamics, culminating in the attainment of the Stackelberg equilibrium within the game.

Key words: *game theory, evolutionary games, Stackelberg games, mathematical simulation, cancer treatment, population management.*

Formulation of the problem of the problem and its connection with important scientific or practical tasks.

1.1. Stackelberg games

The outcomes of evolutionary games are primarily driven by the forces of natural selection, encompassing alterations in population size (ecological dynamics) and the prevalence of heritable traits (evolutionary dynamics). However, this dynamic is not universally applicable to games involving human participants. Firstly, humans exhibit rational decision-making capabilities and possess a diverse array of objectives that extend beyond mere matters of survival [15, 16]. Secondly, the rewards associated with these games can encompass a broad spectrum of tangible and intangible factors, including monetary gains, utility, sensory pleasure, and aesthetic considerations [4].

Notwithstanding the disparities between human-driven games and those within the natural realm, they converge under the umbrella of bio-economic or bio-sociologic games. In these scenarios, human

actions exert influence over the eco-evolutionary dynamics of pest species, pathogens, commercially or recreationally exploited species, and species of conservation significance. Historical instances of such interactions can be traced back, as exemplified by an episode involving King James I of Scotland. He was apprised of the diminishing size of cod populations, signifying an early record of the discernible evolutionary changes induced by size-selective fishing practices. These changes encompass alterations in the size at initial reproduction, fecundity, and other life-history traits.

In a parallel vein, a scientist from the United States Department of Agriculture, during the early 1900s, noted the emergence of resistance among various agricultural pests against diverse biocidal agents. The trend persisted, and starting in the 1950s, it was established that different methods of weed control were responsible for shaping crop ecotypes of weeds. These adapted by modifying their seedling phenology in response to manual weeding, adjusting seed size

based on sorting techniques, and synchronizing maturation timing with harvesting schedules.

This phenomenon extends to encompass antibiotic-resistant strains of bacteria [5] and the development of therapy resistance among cancer patients [6]. These instances underscore the fact that the management of evolving species, whether they are considered pests, resources, disease agents, or species under conservation, presents a set of distinctive challenges.

Stackelberg Evolutionary Game (SEG) theory offers a structured approach for the representation and administration of such dynamic and evolving systems [2]. The underlying concept is inherently clear. Individuals, whether occupying roles as managers, stakeholders, or merely engaged citizens, enact actions that exert both direct and indirect influence over the sizes of populations (ecological dynamics) and the evolutionary attributes (evolutionary dynamics) of focal species. These species of interest adhere to the principles of natural selection and evolutionary game theory. As a response to the actions undertaken by the involved parties, alterations transpire within the species' population abundance, along with shifts observed in their evolutionary traits (see Figure 1).

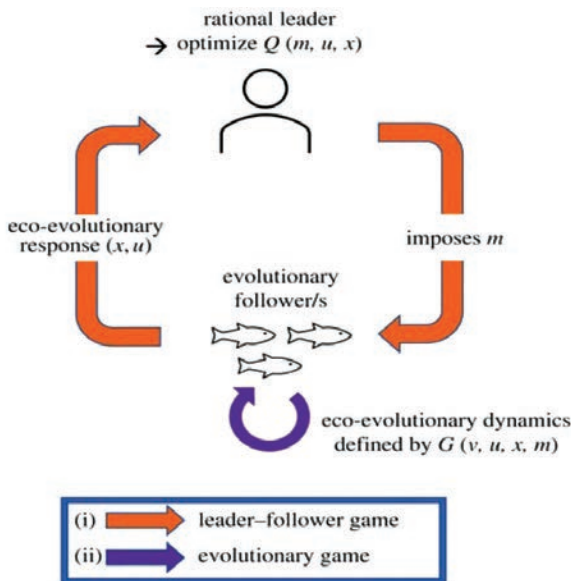


Fig. 1. Illustration of the Stackelberg evolutionary game. It combines two types of games: (i) the leader–follower (Stackelberg) game between the rational leader and evolutionary followers, and (ii) the evolutionary game between the followers. The evolutionary game is defined by the fitness-generating function $G(v, u, x, m)$, which determines the eco-evolutionary dynamics of the followers (§2). In the leader–follower game, the rational leader chooses their strategy m , with the goal to optimize their objective function $Q(m, u, x)$ (§3). The Stackelberg strategy of the leader anticipates the eco-evolutionary response (x, u) , whereas the Nash strategy anticipates the ecological response x only [1]

Leader’s possible strategies. Managers and stakeholders possess a range of strategic options at their disposal. Initially, they might adopt a reactive stance by basing their actions solely on the prevailing state of the species in terms of its population size and trait attributes. Within this context, actions are undertaken in a manner devoid of forward-thinking considerations regarding potential downstream repercussions. Alternatively, a more ecologically-oriented approach can be taken. This involves striving to ensure the sustainability of a fish stock, for example, albeit with a relative disregard for the evolutionary implications.

In a third scenario, the manager exhibits a proactive approach, envisioning and orchestrating both the ecological and evolutionary ramifications arising from diverse strategies for species management. The first instance characterizes a manager who lacks both ecological and evolutionary insights, while the second exemplifies a manager who is ecologically attuned but overlooks evolutionary aspects. The third scenario epitomizes a manager who is well-versed in both ecological and evolutionary dimensions. This latter situation aligns with the Stackelberg strategy of the leader within the SEG framework.

The three possible strategies of the leader can be formalized as follows:

1. Naive strategy

The leader plays a constant and aggressive maximization or minimization strategy ignoring followers’ ecological and evolutionary dynamics

$$m = m_{max}$$

2. Ecologically enlightened strategy corresponding to the Nash strategy A Nash equilibrium (m^N, u^N) is defined as a pair of strategies that correspond to best responses of the leader and followers to each other, which is given by an intersection of the curves $m = m^*(u)$ and $u = u^*(m)$. At Nash equilibrium, no player can improve their outcome by unilaterally changing their strategy [1].

$$m^*(u) = \operatorname{argmax}_m Q(m, u, x^*(m, u))$$

Evolutionarily enlightened leader’s strategy corresponding to the Stackelberg strategy With this strategy, the leader anticipates $u^*(m)$ and $x^*(m, u^*(m))$ and includes them both into objective Q before maximizing it with respect to the action m . It is the following:

$$m^S = \operatorname{argmax}_m Q(m, u^*(m), x^*(m, u^*(m)))$$

Mixed strategies. In some cases (see below) leader may change its approach amid the game. It could be forced by the goal change or be related to the starting position. For example, transferring cancer patient that is already being under treatment.

Power grid case. The RTP between multiple power retailers and multiple consumers can be formulated as a Stackelberg game. At the same time, an evolutionary game is generated for the residential users while a non-cooperative game is proposed for the producers [7].

The existence of Nash equilibrium (NE) is proved for the non-cooperative game among the power retailers. Therefore, after the evolutionary equilibrium is achieved, we also design a distributed algorithm for the power retailers to obtain Nash Equilibrium, and then the Stackelberg Equilibrium is also reached [7], [8].

1.2. Formulation of the goals of the article

1. Analyze current findings in EGT usage for population control
 2. Oversee SEG model for population control
 3. Formulate SEG strategies
 4. Apply strategies to population decline
- Outline of the main research material.

1.3. Population decline

Leader in Stackelberg game may as well aim to reduce the population.

Pests control. One of the most researched subjects in controlled population decline is pest control. For well over a century, the phenomenon of insect pests developing resistance to pesticides has been widely acknowledged. More recently, practitioners have advocated for the implementation of resistance management plans. These plans encompass judicious employment of pesticides, rotational crop practices, strategically timed application of various pesticides, and designated pesticide-free zones [9]. The framework of Social Evolutionary Game (SEG) theory offers a conceptual structure for precisely targeting the resistance strategies employed by pests in response to the pest manager's control strategies. This, in turn, facilitates the selection of optimal control strategies. The adoption of SEG theory holds the potential to supplant the current ecologically informed utilization of pesticides with strategies informed by evolutionary insights. This shift is anticipated to enhance the efficacy of pest containment efforts [10]. Future research endeavors could be directed towards integrating vector-valued strategies employed by pest managers. These encompass diverse pesticide treatments and alternative strategies.

Naive strategy The leader plays a constant and aggressive minimization strategy ignoring followers' ecological and evolutionary dynamics

$$m = m_{min}$$

Nash strategy. Nash strategy remains almost the same – we just look for the minimization:

$$m^*(u) = \operatorname{argmin}_m Q(m, u, x^*(m, u))$$

Stackelberg strategy. With this strategy, the leader anticipates $u^*(m)$ and $x^*(m, u^*(m))$ and includes them both into objective Q before minimization it with respect to the action m . Similar to maximization:

$$m^S = \operatorname{argmin}_m Q(m, u^*(m), x^*(m, u^*(m)))$$

Cancer treatment. Cancer constitutes a malady characterized by uncontrolled cellular proliferation, stemming from aberrant functionality in genes accountable for the regulation of cellular division. The origins of cancer are profoundly intertwined with the evolutionary history of human beings, and its advancement is propelled by the mechanisms of natural selection. This progression is typified by cancerous cells demonstrating the subsequent three conditions:

1. The presence of heritable variation: Diverse hereditary attributes are discernible amidst distinct cancer cells, primarily attributable to genetic mutations, epigenetic alterations, chromosomal reconfigurations, and other mechanisms affiliated with genetic precariousness.

2. A struggle for existence: The expansion of cancer cell populations encounters impediments due to the competition for finite spatial and material resources.

3. The impact of inheritable diversity on the struggle for survival: Broadly, the likelihood of a cell's survival is contingent upon its individual attributes, as well as those of its counterparts. Cells endowed with attributes that bestow heightened probabilities of survival and proliferation ultimately proliferate more prolifically over time (a phenomenon known as frequency-dependent selection).

This view of cancer, rooted in the Darwinian paradigm, corresponds with the foundational principles of evolutionary game theory (EGT). EGT posits that evolution assesses inheritable traits within an ongoing competition for survival [1].

Within the most general game-theoretic framework applicable to cancer, the capacity of a specific cancer cell phenotype to withstand a particular treatment represents a continuously evolving heritable trait. Subsequently, distinctive cancer cells are differentiated based on the magnitude of this trait, subject to the influences of natural selection.

In this context, we will embrace the Darwinian dynamics approach to expound upon such a scenario, augmenting the initial model proposed by Vincent and Brown to encompass additional dimensions.

To describe how the Stackelberg evolutionary game theory can be useful in improving cancer

treatment, let us consider an Stackelberg evolutionary game of cancer treatment between a physician and a polymorphic populace of cancer cells, consisting of both resistant and sensitive variants. The foundational framework for this game is based on the conceptualization put forth by Pressley et al. [11]. SEG contribution involves an extension of this framework that incorporates intercellular competition within the cancer cell population [12]. This augmentation is expected to confer a heightened degree of realism to the model [13] while concurrently enhancing the stability of eco-evolutionary dynamics [14].

The sensitive and resistant cell populations are denoted as x_S and x_R , respectively, and possess distinct resistance traits u_S and u_R . The parameter "m" signifies the dosage of a singular drug. Specifically, $m = 0$ corresponds to an absence of dosage, while $m = 1$ corresponds to the maximum tolerable dose (MTD).

As established in reference [11], the sensitive cancer cells consistently retain their susceptibility to the drug (u_S is consistently 0). In contrast, the resistant subpopulation exhibits a resistance trait that evolves in response to the dose "m" of the drug administered by the physician.

The eco-evolutionary dynamics governing the behavior of cancer cells within each subpopulation, denoted as "i R, S," take the form of a simplified instance of equations (2.3) and (2.4). Notably, in this context, a vector "u" is employed instead of the matrix "U." Within this model, the parameter σ_i represents the evolutionary rate of the subpopulations "i ∈ R, S",

with $\sigma_S = 0$ signifying the speed of evolution for the sensitive population.

The eco-evolutionary dynamics are characterized using the G-function framework, similar to previous treatments.

Naive strategy. Straight minimization of cell population

$$m = m_{min}$$

Nash strategy. The eco-evolutionary dynamics are formally described utilizing the G-function:

$$G(v, u, x, m) = r(v)(1 - \sum_{j \in \{R, S\}} \alpha_{ij} x_j) - d - m,$$

Here, the growth rate, denoted by $r(v)$, is expressed as $r_{max} e^{-gv}$, incorporating a cost of resistance governed by the parameter g . The competitive impact of type j on type i is defined by α_{ij} , while K signifies the carrying capacity, and d represents the natural death rate. The parameter k characterizes intrinsic resistance that may exist prior to exposure to a drug, and b captures the advantage conferred by the evolved resistance trait, resulting in a reduction in therapy efficacy [11].

The assumes that contingent upon the equilibrium population size

$$(x^* = x_S(m, u_S) + x_R(m, u_R))$$

three distinct outcomes are possible:

1. eradication ($x^* \leq 0$), indicative of a successful cure for the cancer;
2. progression (x^* surpassing a certain proportion of the carrying capacity, δK), denoting disease advancement;

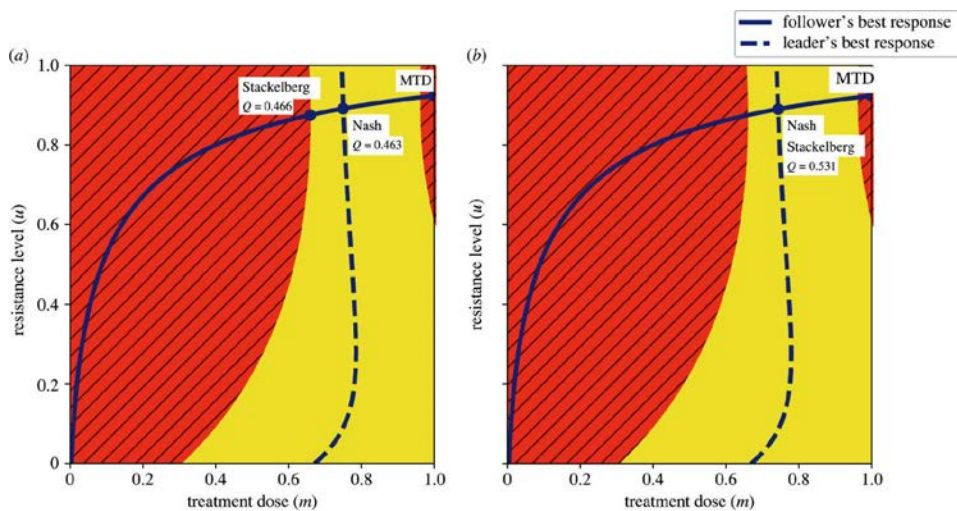


Fig. 2. The outcomes of the maximum tolerable dose (MTD), ecologically enlightened (Nash) strategy and evolutionarily enlightened (Stackelberg) strategy of the physician, when playing an SEG against cancer: the yellow and red/cross-hatched areas represent tumour stabilization ($0 < x^* < \delta K$) and progression ($x^* > \delta K$) regions, respectively[?]. (a) The Nash and Stackelberg outcomes differ when Q defined by (5.3) is an explicit function of u . (b) The Nash and Stackelberg outcomes coincide when $c_2 = 0$. Parameterization: $\delta = 0.7$, $r_{max} = 0.45$, $g = 0.8$, $K = 10\ 000$, $d = 0.01$, $k = 2$, $b = 10$, $\alpha_{SS} = \alpha_{RR} = 1$, $\alpha_{SR} = 0.1$, $\alpha_{RS} = 0.9$, $\sigma_S = 0$, $\sigma_R = 1$, $Q_{max} = 1$; (a) $c_1 = 0.54$, $c_2 = 0.21$, $c_3 = 0.25$, (b) $c_1 = 0.68$, $c_2 = 0$, $c_3 = 0.32$. [1]

3. stabilization ($0 < x^* < \delta K$), representing the potential for cancer to be managed as a chronic condition, accompanied by minimal or no side effects stemming from tumor burden [1].

The evolutionary reaction is expressed as $u = 0$ for the sensitive cancer population, while for the resistant cancer population. This concept is illustrated in Figure 2.

Stackelberg strategy

$$Q(m, u_R, x^*) = Q^{max} - c_1(x^* - K)^2 - c_2u^2 - c_3m^2$$

Here Q^{max} represents the upper limit of quality of life, while the coefficients c_1 , c_2 , and c_3 quantify the degree to which the quality of life diminishes due to factors encompassing tumor burden, the emergence of drug resistance, and the toxicity of the administered drug, respectively. The dynamics of cancer progression under the conventional treatment approach of Maximum Tolerated Dose (MTD), established as the standard of care, are depicted in Figure 2. When the potential for disease stabilization exists, a comparative analysis is conducted between the treatment strategies employed by a physician that are ecologically informed and those that are both ecologically and evolutionarily informed. Figure 2 visually illustrates that, within the selected parameterization, both Nash and Stackelberg equilibrium solutions yield tumor burden stabilization, outperforming the MTD approach, which leads to disease advancement [1].

As illustrated in figure 2a, the evolutionarily enlightened (Stackelberg) strategy corresponds to both a lower treatment dose/toxicity and a lower treatment-induced resistance than the ecologically enlightened (Nash) one. Furthermore, the Stackelberg strategy leads to the best result in terms of patient quality of life, followed by the Nash strategy, while MTD leads to progression.

1.4. Population growth

Fish populations that experience intensive exploitation are anticipated to undergo a gradual reduction in their average body dimensions as time progresses. In this context, we introduce the framework of Stackelberg evolutionary game theory to demonstrate the necessary adaptations in fisheries management practices, aimed at alleviating the potential adverse consequences stemming from these evolutionary shifts. Our analysis revolves around a strategic interplay involving a fisheries manager and a fish population. The former is responsible for regulating the harvesting rate and the mesh size of the nets with the objective of optimizing profits, while the latter undertakes an evolutionary response by adjusting the size at which maturation occurs to maximize overall fitness [2].

Two distinct management strategies employed by a fisheries manager: an ecologically informed approach (Nash) and an approach grounded in evolutionary insights (Stackelberg). The investigation elucidates their respective impacts on fish size and the manager's profit. The Nash equilibrium is achieved at the juncture where the best response curve (ESS) of the fish population intersects with that of the manager (as depicted in Figure 3). At this equilibrium, the fish population attains evolutionary stability, as no individual can enhance its fitness by unilaterally altering its size, while simultaneously maintaining ecological stability, as the expected per capita growth rate for the fish population is null at the point denoted by x^* [2].

For the manager, this strategy engenders no subsequent regret: given the fish size, there exists no incentive for the manager to modify the harvesting rate (mN). In contrast, the Stackelberg equilibrium does not align with a point on the manager's best response curve; rather, it corresponds to a point situated on the fish population's ESS curve where profit is maximized (as illustrated in Figure 3a) [2].

Naive strategy. See Stackelberg games. Naive maximization

Nash strategy and Stackelberg strategies In practical terms, the distinction between the two management strategies is rooted in the foundational assumptions they incorporate. The ecologically informed manager acknowledges the influence of harvesting on fish population size, yet regards the mature size of the fish as a constant, thus omitting evolutionary considerations. For the determination of the optimal harvesting rate (mN), this manager takes into account the impacts of m and x^* , while optimizing the profit function Q while holding u constant (as depicted in Figure 3b).

Conversely, the evolutionarily informed manager anticipates that fish will evolve in response to harvesting. Consequently, this manager integrates both ecological and evolutionary repercussions ($x^*(m, u^*(m))$ and $u^*(m)$) of harvesting into the profit function Q . This manager selects the harvesting rate (m_s) that maximizes profit with these dual considerations in mind (as depicted in Figure 3b). The profit curve associated with this management approach intersects with the profit curve of the ecologically informed strategy at its zenith (reflecting the Nash equilibrium). This signifies that the Nash equilibrium can be attained by the Stackelberg manager, but not necessarily the reverse [2].

In the broader context of the Nash approach, the manager is inclined to adopt an elevated harvesting

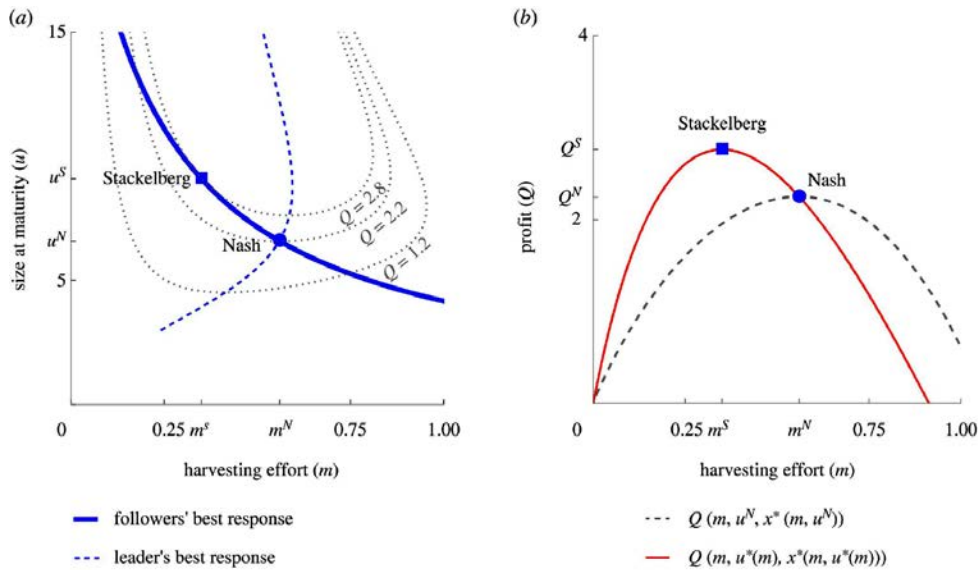


Fig. 3. Figure 3a portrays the best response curve (ESS) for the fish population (depicted by the bold solid line) and the corresponding best response curve for the fisheries manager (illustrated by the bold dashed line). The Nash equilibrium materializes at the point where the ESS curve of the fish intersects with the manager’s best response curve. In contrast, the Stackelberg equilibrium lies exclusively on the fish’s ESS curve and does not coincide with the manager’s best response curve. This disparity emerges due to the manager’s best response being determined by optimizing profit over the best response of the followers. Under the Stackelberg framework, the manager adopts a reduced harvesting effort, thereby engendering an increase in fish size. In Figure 3b, the impact of harvesting effort on profit is elucidated for both the ecologically informed strategy (Nash) and the evolutionarily informed strategy (Stackelberg). Within the ecologically informed approach, the manager assumes a fixed size of fish at maturation ($u = u^N$) and, consequently, selects a harvesting rate that maximizes profit while considering this fixed size (as depicted by the grey dotted curve). In contrast, the evolutionarily informed manager operates under the assumption that the size of fish at maturation corresponds to the ESS ($u^*(m)$), and accordingly, selects a harvesting rate that optimizes profit (as indicated by the red curve). Notably, the evolutionarily informed approach yields higher profits at a lower harvesting rate compared to the ecologically informed counterpart [1]

rate, resulting in diminished fish size over time (as demonstrated in Figure 3a). In contrast, under the Stackelberg framework, the manager opts for a reduced harvesting rate, yielding larger fish sizes and greater profit [1].

Conclusions and future research.

The existing models suggest that, thus far, the Stackelberg solution tends to yield a more tempered management approach compared to the Nash strategy in relation to parameters such as harvesting effort, pesticide application, or drug therapy. This holds true whether the context is cancer, infectious diseases, or other systems. Progressing from a basic understanding to ecologically informed and subsequently to evolutionarily informed management necessitates an expansion of our knowledge concerning the system at hand.

Effectively anticipating and guiding the eco-evolutionary response of a biological system requires an enhancement of our capabilities in predicting

population size and composition before initiating interventions. To achieve this, advancements are imperative in both the estimation and optimization of model parameters. Achieving accurate estimates mandates an ongoing and continuous surveillance regimen. However, a challenge remains in the domain of identifying, quantifying, and monitoring the evolving strategy distribution within heterogeneous populations. This limitation poses an obstacle to fully realizing a Stackelberg solution.

Nonetheless, strides are being made in this direction, particularly within the realms of pest management and cancer therapies. The advent of methodologies such as liquid biopsies, radiomics, organoids, and xenografts is gradually addressing this technological gap. These emerging techniques hold promise in enabling more comprehensive surveillance and characterization of evolving strategies, potentially pushing the boundaries of achieving a Stackelberg equilibrium [15].

The population minimization game (cancer treatment, for example) is more suitable for applying mixed strategies. In fishery management switch between Nash and Stackelberg equilibrium does not yield significantly better result to overall payoff function.

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Баришич Л.М. ОГЛЯД ЗМІШАНИХ СТРАТЕГІЙ У ПІДХОДІ ЕВОЛЮЦІЙНОЇ ТЕОРІЇ ІГОР СТАКЕЛЬБЕРГА ДО КОНТРОЛЮ ЗА ЧИСЕЛЬНІСТЮ ПОПУЛЯЦІЙ – ВИПАДОК КОНТРОЛЮ ЗА ЗРОСТАННЯМ ПОПУЛЯЦІЇ

У цій статті ми розглянемо сучасний стан моделювання управління популяціями з використанням теорії ігор Стакельберга як сучасного розвитку еволюційної теорії ігор.

Ми розглянемо стратегії як зростання, так і скорочення чисельності населення, зосередившись на управлінні рибальством та лікуванні раку відповідно. Ми проаналізуємо відмінності між рівновагою Неша і Стакельберга та обговоримо можливість використання змішаних стратегій. Ми окреслимо відмінності у підходах раціонального менеджера до мінімізації та максимізації популяції у випадку гри Стакельберга.

Еволюційна теорія ігор забезпечує математичну основу для концептуалізації та аналізу біологічних взаємодій, в яких пристосованість індивіда залежить не лише від його власних рис, але й від рис інших. У цьому контексті учасники, як правило, не є явно раціональними акторами; скоріше, вони мають тенденцію успадковувати ознаки, а не активно їх відбирати.

Теорія еволюційних ігор Стакельберга (SEG) об'єднує класичну та еволюційну теорію ігор для моделювання взаємодії за участю раціонального лідера та послідовників, що еволюціонують, в академічних рамках. У цьому контексті наміри лідера можуть бути різними: він може прагнути підтримувати динамічну систему, як у сценаріях, наприклад, управління рибальством, або, навпаки, намагатися ліквідувати систему, як у випадку боротьби зі шкідниками. Часто постійний агресивний підхід лідера, наприклад, надмірний вилов риби в контексті управління рибальством або введення максимально допустимої дози при лікуванні раку, є субоптимальною стратегією. Включення екологічної динаміки в аналіз, як правило, дає більш сприятливі результати для лідера, що узгоджується з рівновагою Неша в теорії ігор [3].

Тим не менш, найбільш вигідний курс дій лідера передбачає проактивний розгляд і вплив на еко-еволюційну динаміку, що призводить до досягнення рівноваги Стакельберга в рамках гри.

Ключові слова: теорія ігор, еволюційні ігри, ігри Стакельберга, математичне моделювання, лікування раку, управління населенням.