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Myxococcus xanthus, a unique predatory myxobacterium: Gliding, hunting and feeding together

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Abstract
Myxococcus xanthus, a unique soil dwelling myxobacteria is omnivore in nature which feeds on other microbes. Having a multicellular social lifestyle, this bacterium is unique in its own way. The multicellular behaviour involves scouting, gliding, branching, fruiting and rippling. Being omnivore in nature it uses its attacking strategy to attack and lyse its prey for nutrient absorption. Its complex life cycle involves a growth phases which mainly depends upon environmental conditions. This bacterium produces myxospores which makes them heat-resistant, UV and desiccation resistant. *M. xanthus* is known to be producing secondary metabolites such as antibiotics and hydrolytic enzymes to kill and lyse prey cells. Low molecular weight antibacterial produced by them autolyse self-cells (autocides) and other microbes (paracides). The important paracides produced by them are myxovirescin A and myxalamid B and important autocides are AMI and AMV. Due to its antimicrobial producing efficiency, it is used as natural bio-control agent against many pathogens.

Keywords: myxobacteria, multicellular behaviour, myxospores, secondary metabolites, bio-control agent

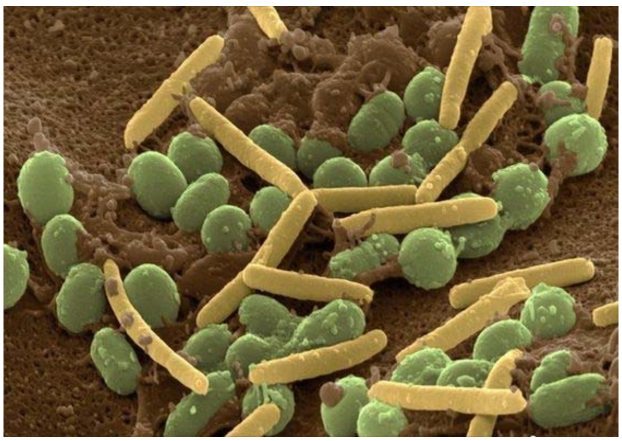
1. Introduction

Myxococcus xanthus is a myxobacterium belongs to phylum Proteobacteria and family Myxococcaceae. It is an aerobic, rod-shaped, Gram negative predatory bacterium that can kill, lyse and grow on other bacteria (Berleman and Kirby, 2007; Hillesland *et al*., 2007) [1, 2]. It behaves as predatory, saprophytic single species biofilm known as swarm under normal conditions but follows multicellular development cycle under nutrient deficient conditions. Members of the colony forms simple patterns to generate complex group behaviours and this process is known as 'stigmergy'. It acts as a model system for defining the social behaviour in bacteria. They form thin biofilms in which cells work together to colonize new place, to kill and lyse prey cells and to invade in prey colonies (Kaiser, 2003) [3]**.** The biofilms formed by them have macroscopic fruiting bodies where vegetative cells further differentiates into spores. The cells of the *M. xanthus* are covered by an extracellular matrix (ECM) formed by exopolysaccharides and proteins which facilitates motility, cell-cell cohesion and fruiting body formation (Lux *et al.*, 2004) [4].

Under nutrient deficient or stressful conditions, they undergo a process in which the single individual cells come together to form aggregate structure called the 'fruiting body'. The fruiting bodies are species specific and multicellular in nature. The rod shaped cells present inside the fruiting body differentiates into spherical thick walled, heat-resistant structures called 'myxospores' (Velicer and Vos, 2009) [5]. The myxospores enables myxobacteria to survive under harsh environments or under starvation conditions. These spores are UV-irradiation, desiccation and heat resistant. Once the conditions become favourable, these myxospores germinate by shedding spore coat into rod shaped vegetative cells (Julien *et al*., 2000) [6]. The vegetative cells are flexible, rod-shaped and motile in nature, while the spores are spherical in shape and are non-motile (Justice *et al*., 2014) [7]. This bacterium have unique ability to glide on solid surfaces by a unique mechanism called gliding (Shi and Zusman, 1993) [8]. This gliding motility helps the bacterium to move on solid surfaces without the help of a flagella (Kaiser, 1979) [9]. *M. xanthus* is a social bacterium, found ubiquitous mainly in soil. These bacteria are commonly found in animal dung or in organic rich neutral to alkaline pH soils, so commonly called as soil dwelling bacterium. They grow by utilising cellulose from the surrounding medium but due to their predatory nature they feed on other bacteria by secreting antibiotics to kill them. They also produce certain hydrolytic enzymes which lyse the prey cells making the nutrients available to them.

This myxobacteria have a unique characteristics of having multicellular structures and their cellulolytic and proteolytic activities (Hyun *et al*, 2008) [10]. Cellulolytic myxobacteria are important for global carbon cycle for having cellulose degrading property as cellulose is present abundantly in plant cell wall, While their proteolytic activity makes them micropredators that impacts the composition of other microbial communities (Lueder *et al.*, 2006) [11].

2. Life cycle of *Myxococcus xanthus*
2.1 Complex life style
M. xanthus is a common soil dwelling bacterium with an intricate multicellular lifestyle (Fig. 1). It has complex life cycle including gliding on solid surfaces, fruiting bodies formation and predation. The prominent example of multicellular behaviour of this species involves scouting, branching and rippling used to access nutrients for growth and predation. When nutrients are available abundantly, the bacteria take a rod-shaped form and under nutrient deficient conditions bacterial cells aggregates into multicellular fruiting bodies containing spores as shown in Fig. 1.



***Source*:** https://www.pinterest.com/pin/481603753881236458/?autologin=true

Fig 1: *Myxococcus xanthus*, rod-shaped form (yellow) and fruiting bodies containing spores (green).

2.2 Gliding motility
M. xanthus have a striking trait of moving on solid surfaces in the direction of its long axis without using the flagella refered to as gliding motility (Jarrell and McBride, 2008) [12]. It helps them to actively search for prey and to regulate the mechanism of cell killing and lysing in a targeted manner which requires lytic factors in low concentrations. This gliding is controlled by two genetically distinct synergistic systems social (S) and adventurous (A) (Sun *et al*., 2000) [13]. S-motility is powered by polar type IV pili and exopolysaccharides, while A-motility relies on focal adhesion complexes. These two synergistic gliding motility systems may contribute to the morphological patterns (Mauriello *et al*., 2010) [14]. During predation, the bacterial cells organize to form rippling wave structures. This rippling behaviour controls cell movement in which a group of $>10^8$ cells working as a unit. Rippling is induced during predation on various microbes or for degradation of macromolecules such as protein, peptidoglycan and chromosomal DNA act as growth substrates (Shimkets and Kaiser, 1982) [15]. Individual cell movement is slow as compare to groups, so unique rippling behaviour act as a balance between maintaining the close contact with the neighbouring cells to achieve maximum gliding velocity and also to maintain contact with prey cells for maximum feeding.

2.3 Fruiting behaviour
M. xanthus, under high cell density conditions forms fruiting body aggregates having $\sim 10^5$-10^6 cells. When nutrients availability is poor, vegetative rods within the fruiting bodies starts differenting into non-motile spores called as myxospores (Fig. 2). A striking manifestation of multicellular behaviour is the formation of dynamic cell groups. The coherent motion of cells allows this soil dwelling bacterium to attack its prey by cooperatively producing antibiotics and digestive enzymes (Kaiser and Warrick, 2011) [16]. Under nutrient deficient conditions, a swarm of cells initiates a complex, multistep process that leads to the formation of aggregates known as fruiting bodies within which cells sporulate. This process of fruiting body formation is a multi-step process and involves distinct stages of group behaviour (Higgs *et al*, 2014) [17]. Unlike other aggregation phenomenons which shows reduce mobility and forms static aggregates, *M. xanthus* cell groups remain mobile throughout the process moving as fruiting bodies over long distances. The thick outer wall of the myxospores consists of spore coat protein S, glycosaminoglycan, N-acetylgalactosamine, glucose and glycine that allows them to survive under harsh stressful environmental conditions being in dormant state (Holkenbrink *et al.*, 2014) [18].

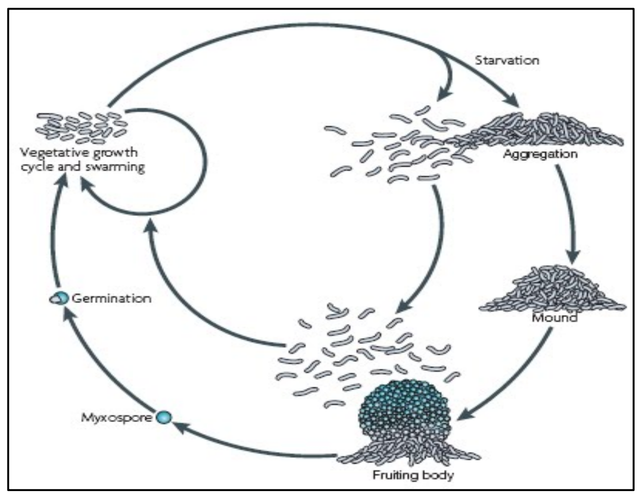


Fig 2: Vegetative cells of *M. xanthus* under un-favourable conditions forms fruiting bodies containing myxospores. These spores germinate when conditions become favourable allows bacterium to survive under harsh conditions (Zusman *et al.*, 2007) [19].

2.4 Hunting and feeding strategy
M. xanthus was first isolated from cow dung which shows its preference for growth on macromolecules (Beebe, 1941) [20]. It secretes lytic enzymes in the culture extracts which shows its predatory potential (Hart and Zahler, 1966) [21]. In vegetative growth phase, it grows on dead organic matter as a saprophyte by decomposing polymers or by lysing bacteria as well as fungi (Morgan *et al.*, 2010; Muller *et al*., 2014) [22, 23]. The feeding style of this bacterium is a multicellular process and also seems to be density dependent (Rosenberg *et al*., 1977) [24]. High cell density facilitates predation process by increasing the concentration of lytic enzymes (Berleman and Kirby, 2009) [25]. The gliding motility of the bacterium plays

an important role in the predation as predator cells require close contact to the prey (McBride and Zusman, 1996) [26]. They actively swarm towards prey using its two motility systems A and S. The proximal contact with the prey cells stimulates various factors that are responsible for cells being trapped in micro-colonies of the prey, until the lysis of the prey cells complete (Keane and Berleman, 2016) [27]. The rippling during predation process serves to increase the predation efficiency and nutrient scavenging. The hunting strategy of this bacterium seems to depend upon the nature of the prey. The attacking strategy of *M. xanthus* resembles frontal attack in which groups of predators penetrates the colonies of the prey and lyse them (Perez *et al*., 2011) [28]. The other strategy used by it is unique to this bacterium known as 'wolf-pack' attack (Hillesland *et al.,* 2007) [2]. In this strategy, the bacterium cells surrounds the prey and ripple before killing and lysing it. A swarm of hydrolytic enzymes are secreted during predation which includes antibiotics and other secondary metabolites to kill and lyse the prey cells, thus releasing the hydrolysed products used by bacterium (Xiao *et al*., 2011; Evans *et al*., 2012) [29, 30].

3. Conclusions

By reviewing literature regarding the *Myxococcus xanthus*, it was found that this unique myxobacterium has many striking features. Its novel mechanism of predation involves many secondary metabolite, hydrolytic enzymes and extracellular vesicles that promotes prey cell lysis. Due to its large genome it serves as a reservoir of biochemical potential. It is used as a natural biological control agent against many pathogenic microbes due to its antibiotic producing potential.

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