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The mysterious nature of bacterial surface (gliding) motility: A focal adhesion-based mechanism in *Myxococcus xanthus*

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ABSTRACT

Motility of bacterial cells promotes a range of important physiological phenomena such as nutrient detection, harm avoidance, biofilm formation, and pathogenesis. While much research has been devoted to the mechanism of bacterial swimming in liquid via rotation of flagellar filaments, the mechanisms of bacterial translocation across solid surfaces are poorly understood, particularly when cells lack external appendages such as rotary flagella and/or retractile type IV pili. Under such limitations, diverse bacteria at the single-cell level are still able to "glide" across solid surfaces, exhibiting smooth translocation of the cell along its long axis. Though multiple gliding mechanisms have evolved in different bacterial classes, most remain poorly characterized. One exception is the gliding motility mechanism used by the Gram-negative social predatory bacterium *Myxococcus xanthus*. The available body of research suggests that *M. xanthus* gliding motility is mediated by trafficked multi-protein (Glt) cell envelope complexes, powered by proton-driven flagellar stator homologues (Agl). Through coupling to the substratum via polysaccharide slime, Agl–Glt assemblies can become fixed relative to the substratum, forming a focal adhesion site. Continued directional transport of slime-associated substratum-fixed Agl–Glt complexes would result in smooth forward movement of the cell. In this review, we have provided a comprehensive synthesis of the latest mechanistic and structural data for focal adhesion-mediated gliding motility in *M. xanthus*, with emphasis on the role of each Agl and Glt protein. Finally, we have also highlighted the possible connection between the motility complex and a new type of spore coat assembly system, suggesting that gliding and cell envelope synthetic complexes are evolutionarily linked.

Contents

Abbreviations: IM, inner membrane; OM, outer membrane; OMV, outer-membrane vesicle; T4P, type IV pili; EPS, exopolysaccharide; S motility, social motility; A motility, adventurous motility; FA, focal adhesion; PMF, proton-motive force; Glt, gliding transducer; MASC, major spore coat polymer; TPR, tetratricopeptide repeat; ECM, extracellular matrix; Nfs, necessary for sporulation.

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1. Introduction

The ability of numerous bacterial species to move and change location is a fundamental physiological characteristic that strongly promotes the survival of a given strain in biotic and abiotic environments. Bacterial motility can lead to the detection of food sources in liquid and solid settings, active avoidance of harmful stimuli, spore formation for strain preservation, and for pathogens, infection of host systems. Multiple methods of bacterial motility have arisen over evolutionary time, with each conferring different abilities to suit a particular environment and/or lifestyle. As such, motility systems and associated regulation systems are present in nearly all bacterial clades. Historically, bacterial motility has largely been investigated in the context of swimming in viscous environments through the rotation of flagellar appendages, while cell migration on surfaces has been much less studied. As such, this review will discuss bacterial motility on surfaces.

1.1. Bacterial motility on surfaces

Arguably, the most extensively-studied prokaryotic motility apparatus has been the bacterial flagellum, a rotary machine found in both Gram-negative and Gram-positive bacterial species. The rotation of flagella (which can be reversed) is powered by an inner (cellular) membrane (IM) motor energized via an ion gradient across the IM. Additional components reside in the peptidoglycan for both Gram-positive and Gram-negative cells, and also in the outer membrane (OM) for the latter. Flagella allow individual bacteria to swim and swarm collectively on moist surfaces [1–4], but as they have been extensively discussed in numerous review articles, they will not be discussed herein.

Often referred to as “twitching”, motility mediated by Type IV pili (T4P) has also been broadly studied. This type of surface motility involves the extension, adhesion, and retraction of an extruded polar filament in both Gram-negative and Gram-positive cells. As with the flagellum, multiple proteins in each subcellular compartment constitute the T4P machinery [5,6]. T4P have been adapted for roles in motility, virulence, acquisition of DNA, electrical conductance, secretion of protein substrates, biofilm formation, and attachment to a wide range of surfaces; however, as with flagella, T4P have also been extensively reviewed in the literature [6,7] and will not be discussed in detail herein.

Intriguingly, numerous bacteria have also been shown to move across surfaces in the absence of detectable appendages such as flagella and/or T4P [8,9]; this phenomenon has been broadly termed “gliding” motility and has been observed in a range of phylogenetically-distinct bacterial phyla and/or classes including the *Deltaproteobacteria*, *Cyanobacteria*, *Mollicutes*, and *Bacteroidetes* [10]. Incidentally, studies reveal that distinct gliding mechanisms appear to operate among these different types of bacteria [8,9]. Moreover, certain eukaryotic cell types such as the Apicomplexa move by yet an entirely different mechanism of gliding motility unrelated to any of the known bacterial mechanisms [11], further illustrating the diversity of gliding systems. In this review, we will focus on synthesizing current knowledge and recent advances towards understanding the mechanism of bacterial gliding motility in the Gram-negative bacterium *Myxococcus xanthus*.

1.2. Myxococcus xanthus

Much progress has recently been made regarding the elucidation of motility in the Gram-negative rod-shaped model gliding bacterium *M. xanthus* (order: *Myxococcales*; class: *Deltaproteobacteria*). *M. xanthus* as well as most other identified myxobacteria have been isolated from soils and are not known to be pathogenic. However, a novel tick-borne myxobacterium has recently been identified as the etiologic agent of epizootic bovine abortion (foothill abortion) in pregnant cattle [12,13], illustrating a largely unexplored potential for myxobacteria and disease.

M. xanthus is often referred to as a social bacterium as it displays coordinated behaviours of individual cells in a swarm group (Fig. 1A). When nutrients are scarce, the bacteria can engage in predatory behaviour, resulting in the killing of a range of Gram-positive and Gram-negative prey bacteria and saprophytic usage of the degradation products. In addition, under conditions of nutrient limitation, an alternative developmental cycle is initiated wherein cells aggregate to form fruiting body structures (Fig. 1B), which eventually mature to contain myxospores. Once nutrient conditions ameliorate, these myxospores have the capacity to germinate and form new vegetative cells [14].

1.2.1. M. xanthus *social (S) motility*

The collective motility of swarms, as well as the motility of single cells, are central to the aforementioned phenotypes, and are mediated by distinct motility systems. On soft surfaces (e.g. 0.5%

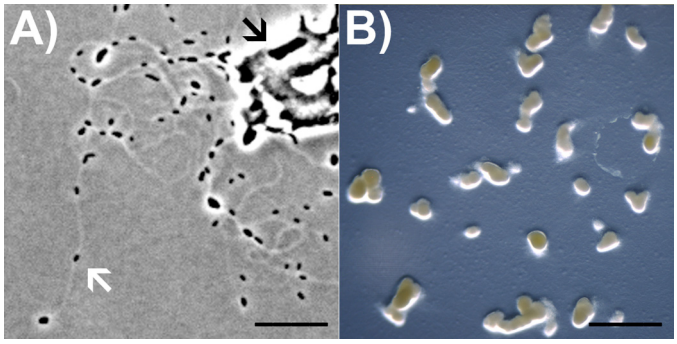

Fig. 1. (A) Micrograph of wild-type *M. xanthus* DZ2 population displaying both T4P-mediated S-motility of cell aggregates (black arrow) and Agl–Glt motor complex-mediated gliding A-motility of single cells on agar (1.5%), with some following a previously-deposited slime trail (white arrow). Scale bar: 50 μm. (B) Fruiting body formation after 72 h on starvation medium. Scale bar: 4 mm.