SHOULD I PAUSE OR SHOULD I GO

A c-di-GMP mediated motility arrest before cell division in *Myxococcus xanthus*

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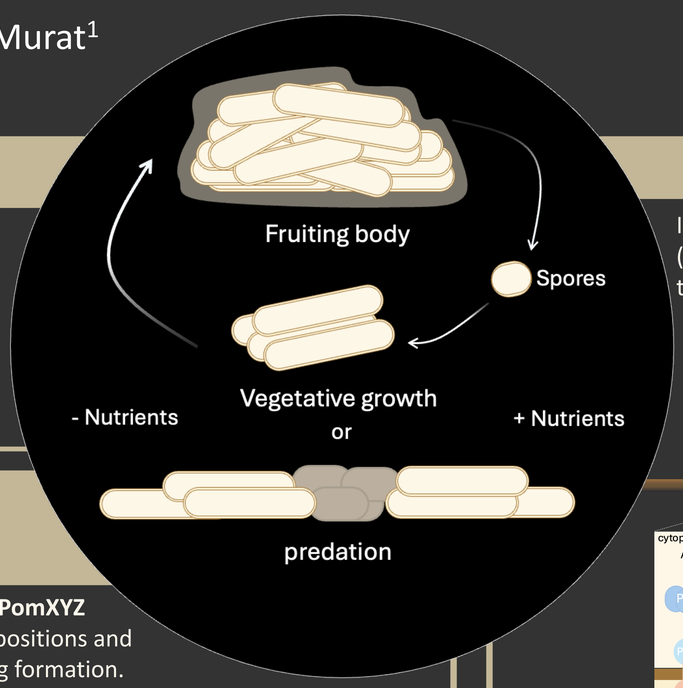
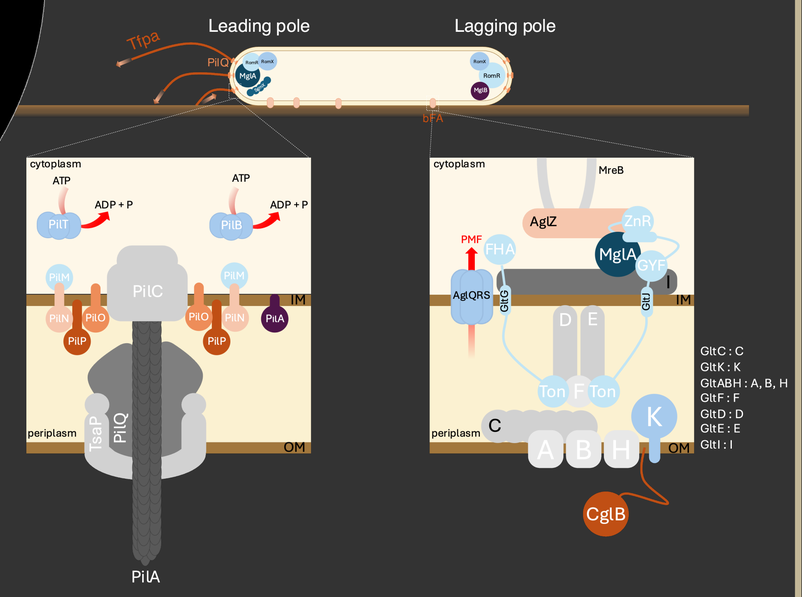
Myxoccocus xanthus has a complex life cycle including multicellular stages

M. xanthus is a ubiquitous soil bacterium and a model organism studied for its social behaviors and complex life cycle. Motility plays a central role in this life cycle, allowing *M. xanthus* to predate on other microorganisms. As a facultative predator, *M. xanthus* can use available nutrients in its milieu as well as kill and feed on nearby preys, thus allowing *M. xanthus* growth and **division**. When ressources become scarce, *M. xanthus* cells converge and aggregate to form multicellular structures called fruiting bodies, which can sporulate again when conditions improve to resume vegetative growth.



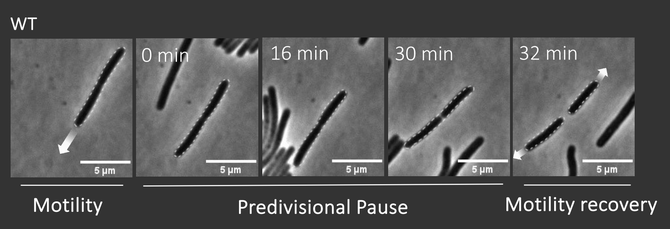
M. xanthus has two motility systems

It possesses two distinct motility systems : Twitching via type IV pili (Social motility) and gliding with an Agl-Glt complex linking an adhesin to the cytoskeleton (Adventurous motility).



Unlike other extensively studied life processes of *M. xanthus*, cell division remains poorly characterized

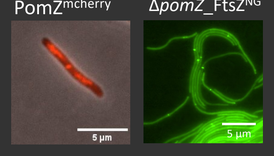
Before dividing, *M. xanthus* undergoes a pause *(Harvey et al. 2014).* Motility and its regulation are well-studied in *M. xanthus*. However, functionnal correlation between motility and cell division is not understood.



There is a correlation between motility systems and cell division

M. xanthus employs a unique **PomXYZ** protein complex that directly positions and stimulates cytokinetic FtsZ-ring formation.

***ΔpomZ* :** presents **division defects** with the formation of **chromosome-free minicells** and **filamentous** cells. Lack of PomZ also caused **reduced formation of Z-rings** and **incorrect positioning** of the few **Z-rings formed**. *(Treuner-Lange, Aguiluz et al. 2013).*



Surprisingly, It is not essential, even though it is the only known factor involved in FtsZ localization and recruitment.

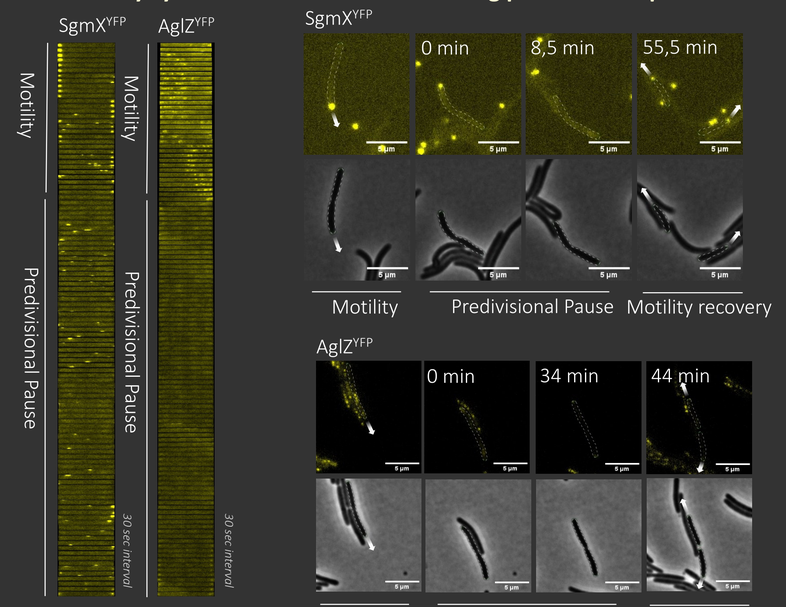
Does this suggest the existence of an additional player?

How are cell division and motility coordinated in *Myxococcus xanthus* ?

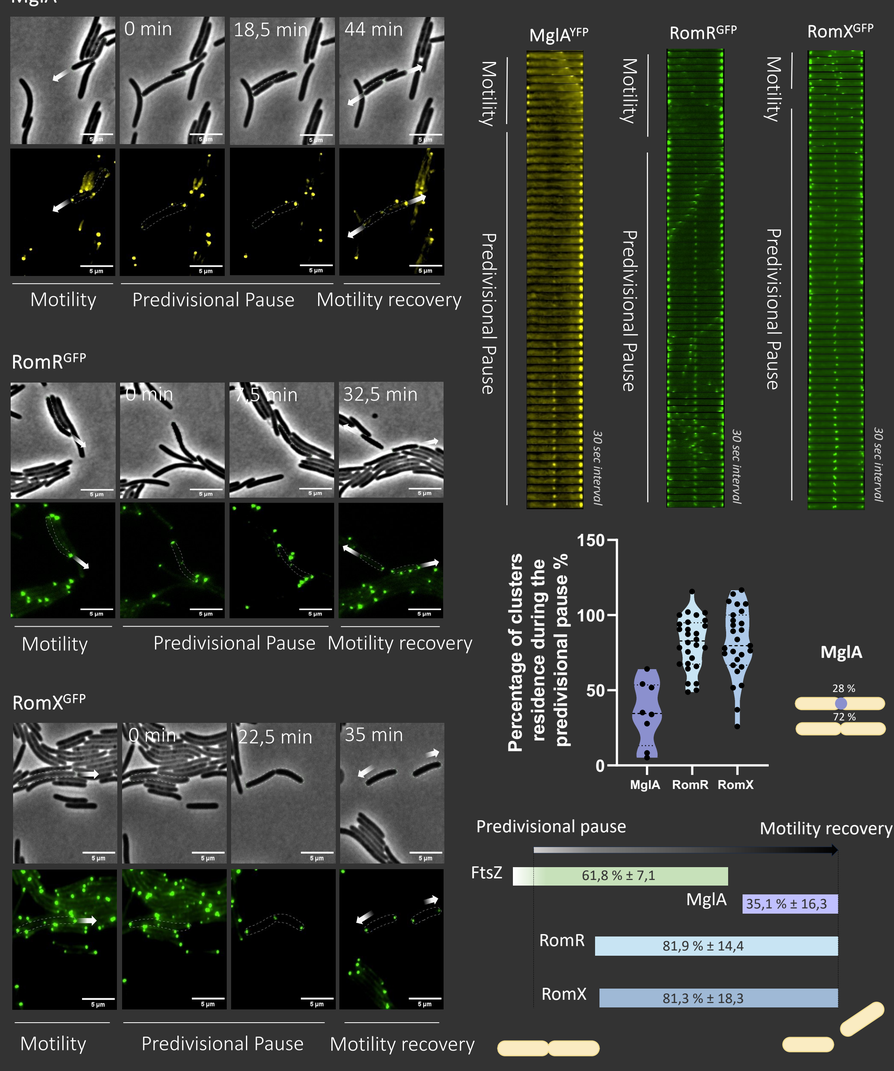
1 MOTILITY PROTEINS DURING CELL DIVISION

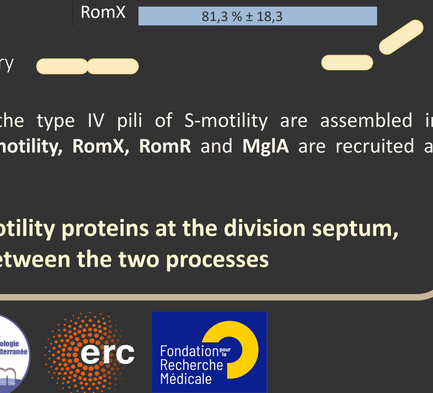
Locating and capturing division events in *M. xanthus* is difficult. Indeed, this bacterium is motile and has a doubling time of 5 hours. However, cell division is favored in a predation context. *(Panigrahi et al. 2021)*

Motility systems are disassembled during predivisional pause



But three motility regulators are recruited at the future division site





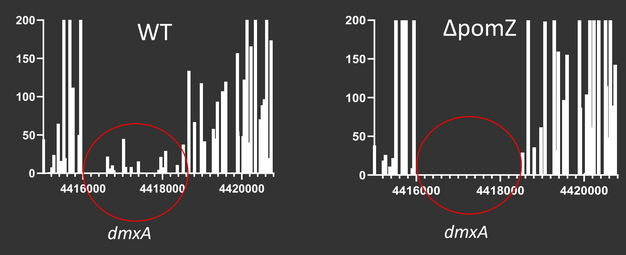
Neither the Aglt-Glt complex of A-motility nor the type IV pili of S-motility are assembled in predivisional cells. However, **three regulators of motility, RomX, RomR** and **MglA** are recruited at midcell.

There is a successive recruitment of motility proteins at the division septum, suggesting a correlation between the two processes

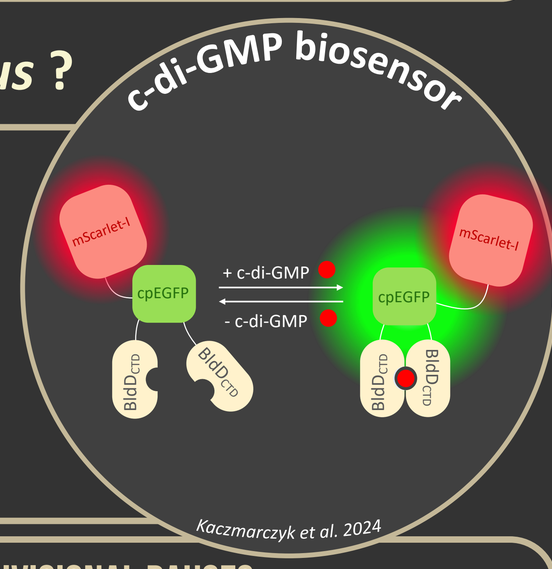
2 DISCOVERING OF NEW PLAYERS IN CELL DIVISION USING TN-SEQ

Fifty mutants are less abundant in the Δ*pomZ* library, suggesting synthetic lethality and potential functional redundancy.

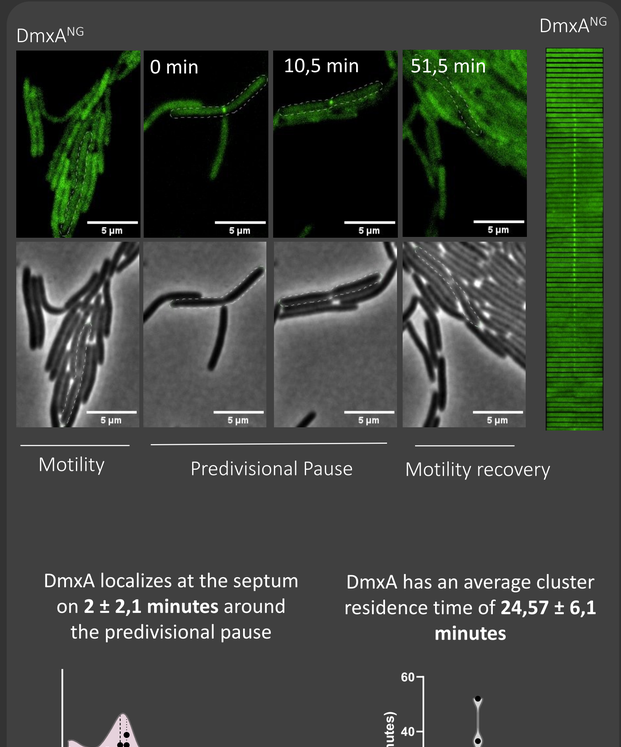
One of these mutants is known to play a role in the distribution of motility proteins after cell division in *Myxococcus xanthus* ***dmxA.*** *(María Pérez-Burgos, 2024)*



The *dmxA* mutant is synthetically lethal in a *ΔpomZ* background

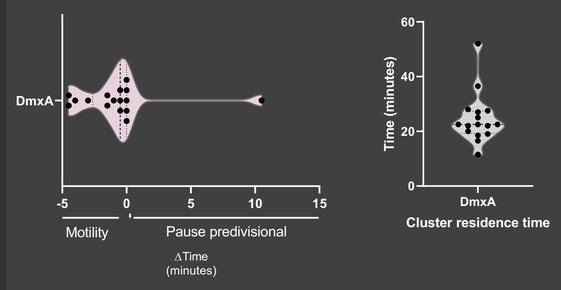


3 A DIGUANYLATE CYCLASE IS RESPONSIBLE FOR PREDIVISIONAL PAUSES



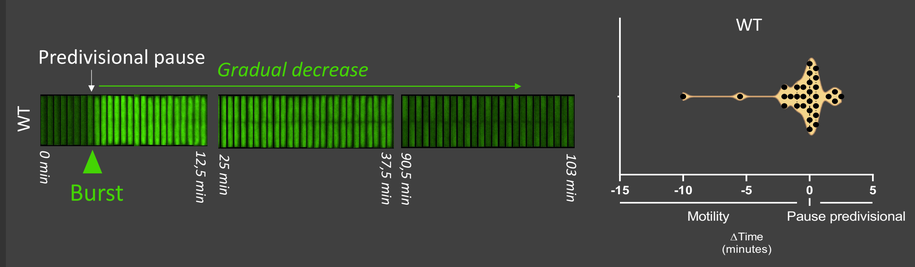
DmxA localizes at the septum on **2 ± 2,1 minutes** around the predivisional pause

DmxA has an average cluster residence time of **24,57 ± 6,1 minutes**

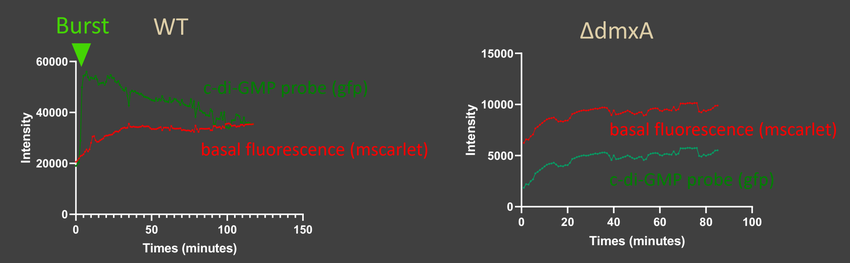


DmxA localizes to the division site prior to cytokinesis, suggesting a role in the early stages of cell division

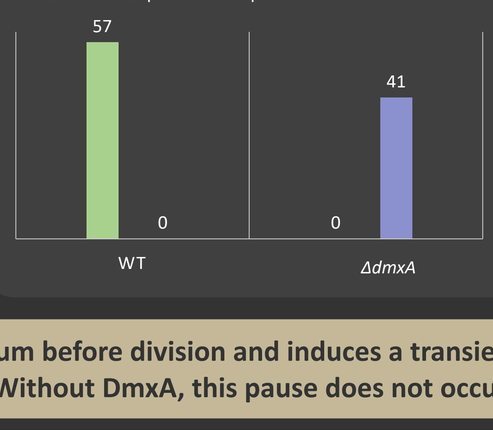
A transient increase in c-di-GMP coincides with the division pause and is lost in *ΔdmxA* cells, indicating a role for DmxA in c-di-GMP signaling during division



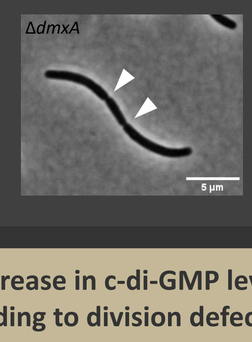
The c-di-GMP peak appears on average **1,26 ± 1,2 minutes** around the predivisional pause



***dmxA* deletion results in the absence of predivisional pause**

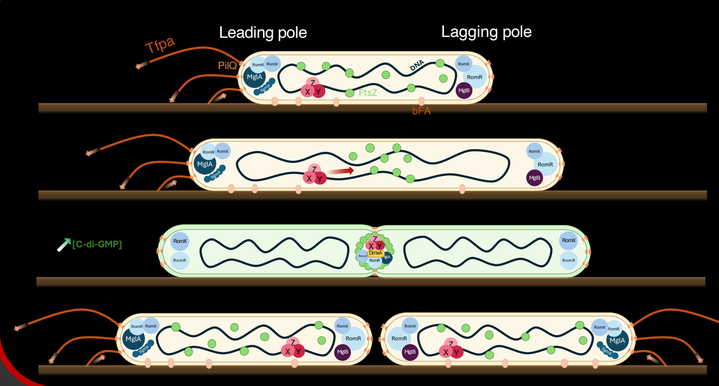


Defects in cell division are also observed including asymmetric divisions and faulty septation



DmxA, a diguanylate cyclase, localizes to the septum before division and induces a transient increase in c-di-GMP levels, promoting a predivisional pause in *M. xanthus*. Without DmxA, this pause does not occur, leading to division defects.

Conclusions & perspectives



For the first time, we link predivisional pause of *Myxococcus xanthus* to a burst of c-di-GMP triggered by the diguanylate cyclase DmxA.

This transient signal precedes the disassembly of both motility systems, suggesting that c-di-GMP acts as a checkpoint linking motility shutdown to cell division. The relocalization of key motility regulators to the septum further suggests a shared regulatory mechanism for both motility systems (A-motility and S-motility), although the downstream effectors remain to be identified.

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