Supplementary Information

Amphipathic environments for determining the structure of membrane proteins by single-particle electron cryo-microscopy

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Keywords: amphipols, detergents, integral membrane protein complexes, lipids, nanodiscs, structural biology

Running title: Trends in the use of amphipathic environments for determining the structure of membrane proteins by cryo-EM.

Surfactants used for vitrification	Surfactants used for solubilization		
	Maltosides	*MNGs*	*Digitonin*
Maltosides	(Grieben et al., 2017; Gopalasingam et al., 2019; Maity et al., 2019; Caspy et al., 2020; Jamali et al., 2020; Kieuvongngam et al., 2020; Perez-Boerema et al., 2020; Wang et al., 2020g)	(Lü et al., 2017; Winkler et al., 2017; Tucker et al., 2019)	
MNGs	(Oshima et al., 2016; Koehl et al., 2018; Bai et al., 2019a; Bai et al., 2019b; Parey et al., 2019; Tang et al., 2019; Timcenko et al., 2019; Tsai et al., 2019; Burendei et al., 2020; Mou et al., 2020; Su et al., 2020; Zhang et al., 2020i; Zhang et al., 2020g)	(Huynh et al., 2016; Liang et al., 2017; Hughes et al., 2018; Jin et al., 2020)	
Digitonin	(Qian et al., 2017; Duan et al., 2018a; Duan et al., 2018c; Gong et al., 2018a; Gong et al., 2018c; Kang et al., 2018; Oosterheert et al., 2018; Qi et al., 2018a; Qi et al., 2018b; Su et al., 2018; Sui et al., 2018; Lee et al., 2019b; Liu et al., 2019c; Qi et al., 2019a; Qi et al., 2019b; Yin et al., 2019a; Cannac et al., 2020; Clark et al., 2020; Huang et al., 2020a; Liu et al., 2020a; Peng et al., 2020; Shaye et al., 2020; Zhang et al., 2020b; Zhu et al., 2020)	(Zhang et al., 2016; Johnson et al., 2017; Lee et al., 2017a; Liu et al., 2017; Zhang et al., 2017; Baradaran et al., 2018; Butterwick et al., 2018; Fay et al., 2018; Johnson et al., 2018; Kefauver et al., 2018; Paknejad et al., 2018; Zhang et al., 2018a; Zhang et al., 2018b; Zhang et al., 2018d; Zhang et al., 2018e; Chew et al., 2019; Lee et al., 2019a; Liu et al., 2019a; Tao et al., 2019; Sun, 2020; Wang et al., 2020c; Wang et al., 2020d; Wu et al., 2020)	
GDN	(She et al., 2018; Hiraizumi et al., 2019; Koehl et al., 2019; Liu et al., 2019b; Nakagawa, 2019; Poweleit et al., 2019; She et al., 2019; Shen et al., 2019a; Zhao et al., 2019c; Chi et al., 2020; Demura et al., 2020; Gao et al., 2020; Jiang et al., 2020; Li et al., 2020c; Li et al., 2020e; Papasergi-Scott et al., 2020; Qi et al., 2020b; Ren et al., 2020; Tsutsumi et al., 2020; Yan et al., 2020; Zhang et al., 2020d)	(Itskanov et al., 2019; Tucker et al., 2019; Yan et al., 2019; Deng et al., 2020a; Deng et al., 2020b; Diederichs et al., 2020; Drożdżyk et al., 2020; Kim et al., 2020c; Li et al., 2020d; Purushotham et al., 2020; Qi et al., 2020a; Wang et al., 2020e; Xie et al., 2020a; Xie et al., 2020b)	(Singh et al., 2018a; Araiso et al., 2019; McGoldrick et al., 2019; Singh et al., 2019; Walter et al., 2019; Zhao et al., 2019b)
CYMAL-7	(Vinothkumar et al., 2014; Zhu et al., 2016; Blaza et al., 2018)		
Amphipathic polymers	(Cao et al., 2013; Liao et al., 2013; Mazhab-Jafari et al., 2016; Shen et al., 2016; Zubcevic et al., 2016; Hirschi et al., 2017; Schoebel et al., 2017; Duan et al., 2018b; Hulse et al., 2018; Huynh et al., 2018; McGoldrick et al., 2018; Myers et al., 2018; Singh et al., 2018b; Vinayagam et al., 2018; Yoo et al., 2018; Zhang et al., 2018c; Zubcevic et al., 2018; Suga et al., 2019; Wang et al., 2019a; Zubcevic et al., 2019a; Zubcevic et al., 2019b; Hou et al., 2020; Johnson et al., 2020; Kuhlen et al., 2020; Long et al., 2020; Owji et al., 2020; Sauer et al., 2020; Vinayagam et al., 2020; Weaver et al., 2020)	(Paulsen et al., 2015; Chen et al., 2016; Fitzpatrick et al., 2017; Li et al., 2017; Wilkes et al., 2017; Zhou et al., 2017; Diver et al., 2019; Letts et al., 2019; Theßeling et al., 2019; Maeda et al., 2020; McDowell et al., 2020)	(Lu et al., 2014; Bai et al., 2015; Lee et al., 2017b; Yin et al., 2019c; Maldonado et al., 2020)
MSP-based nanodiscs	(Gao et al., 2016; Matthies et al., 2016; Shen et al., 2016; Chen et al., 2017; Dang et al., 2017; Jin et al., 2017; Mi et al., 2017; Taylor et al., 2017; Autzen et al., 2018; Jackson et al., 2018; Jojoa-Cruz et al., 2018; Manolaridis et al., 2018; Matthies et al., 2018; McGoldrick et al., 2018; Rheinberger et al., 2018; Roh et al., 2018; Srivastava et al., 2018; Wild et al., 2018; Yoo et al., 2018; Celia et al., 2019; Dang et al., 2019; Feng et al., 2019; Hofmann et al., 2019; Kalienkova et al., 2019; Kern et al., 2019; Khelashvili et al., 2019; Kim et al., 2019; Koehl et al., 2019; Li et al., 2019; Liu et al., 2019b; Rasmussen et al., 2019; Safarian et al., 2019; Saotome et al., 2019; Wang et al., 2019b; Zhou et al., 2019a; Zubcevic et al., 2019b; Arkhipova et al., 2020; Billesbølle et al., 2020;	(Hughes et al., 2019; Laverty et al., 2019; Pumroy et al., 2019; Diederichs et al., 2020; Maeda et al., 2020; Nakane et al., 2020; Wang et al., 2020k; Yin et al., 2020; Zheng et al., 2020)	(Alvadia et al., 2019; Falzone et al., 2019; Guan et al., 2020; Suo et al., 2020)

	Burendei et al., 2020; Fan et al., 2020a; Flores et al., 2020; Glavier et al., 2020; Huang et al., 2020c; Kishikawa et al., 2020; Kumar et al., 2020b; Kumar et al., 2020a; Lee et al., 2020b; Li et al., 2020a; Liu et al., 2020b; Luo et al., 2020; Orlando et al., 2020; Pleiner et al., 2020; Qian et al., 2020; Reid et al., 2020; Roh et al., 2020; Sauer et al., 2020; Shimada et al., 2020; Staus et al., 2020; Tan et al., 2020; Wang et al., 2020i; Wang et al., 2020j)		
Saposin-based nanodiscs	(Kintzer et al., 2018; Nguyen et al., 2018; Gharpure et al., 2019; Nagamura et al., 2019; Du et al., 2020; Kim et al., 2020a)		
Peptidiscs	(Angiulli et al., 2020; Zeytuni et al., 2020)		
Mixed detergents	(Kato et al., 2019a; Krishna Kumar et al., 2019; Qi et al., 2019c; Kim et al., 2020b; Yuan et al., 2020)	(Zhao et al., 2019a; Chen et al., 2020a; Duan et al., 2020; Hilger et al., 2020; Hua et al., 2020; Huang et al., 2020b; Liu et al., 2020c; Sun et al., 2020b; Yang et al., 2020a)	
Others[a]	(Yao et al., 2020)	(Fiedorczuk et al., 2016)	
Same as for purification	(Du et al., 2015; Hite et al., 2015; Bokori-Brown et al., 2016; Iadanza et al., 2016; Meyerson et al., 2016; Oldham et al., 2016; Wei et al., 2016; Whicher et al., 2016; Guo et al., 2017a; Hite et al., 2017a; Hite et al., 2017b; Klusch et al., 2017; Park et al., 2017; Su et al., 2017; Sun et al., 2017; Tao et al., 2017; Wang et al., 2017; Agip et al., 2018; Deng et al., 2018; Du et al., 2018; Garaeva et al., 2018; García-Nafría et al., 2018b; Kim et al., 2018; Lee et al., 2018; Nguyen et al., 2018; Noreng et al., 2018; Parey et al., 2018; Park et al., 2018; Phulera et al., 2018; Pi et al., 2018; Sousa et al., 2018; Sui et al., 2018; Walsh et al., 2018; Wiseman et al., 2018; Xin et al., 2018; Yoder et al., 2018; Yu et al., 2018; Zhu et al., 2018; Zubcevic et al., 2018; Bushell et al., 2019; Chen et al., 2019; Chernyatina et al., 2019; Garaeva et al., 2019; Gharpure et al., 2019; Gopalasingam et al., 2019; Kalienkova et al., 2019; Kato et al., 2019b; Laughlin et al., 2019; Klusch et al., 2017; Lunelli et al., 2020; McCarthy et al., 2019; Miller et al., 2019; Murphy et al., 2019; Parey et al., 2019; Pi et al., 2019; Reddy et al., 2019; Savva et al., 2019; Schuller et al., 2019; Shang et al., 2019; Shen et al., 2019b; Su et al., 2019; Toporik et al., 2019; Zhang et al., 2019; Abbas et al., 2020; Akita et al., 2020; Cao et al., 2020; Coleman et al., 2020; Johnson et al., 2020; Kato et al., 2020; Li et al., 2020b; Lunelli et al., 2020; Mukherjee et al., 2020; Niu et al., 2020; Pan et al., 2020; Rempel et al., 2020; Sauer et al., 2020; Soufari et al., 2020; Sun et al., 2020a; Toporik et al., 2020; Van der Verren et al., 2020; Xu et al., 2020; Zhang et al., 2020a; Zhang et al., 2020c)	(Dang et al., 2017; James et al., 2017; Zhou et al., 2017; Alam et al., 2018; Draper-Joyce et al., 2018; García-Nafría et al., 2018a; Jojoa-Cruz et al., 2018; Kuhlen et al., 2018; Lauber et al., 2018; Liang et al., 2018a; Liang et al., 2018b; Wang et al., 2018; Dosey et al., 2019; Gao et al., 2019; Kampjut et al., 2019; Nguyen et al., 2019; Yu et al., 2019; Chang et al., 2020; Chou et al., 2020; Deme et al., 2020; Dong et al., 2020; Fan et al., 2020b; Fukuhara et al., 2020; Guardia et al., 2020; Kampjut et al., 2020; Kobayashi et al., 2020; Kuhlen et al., 2020; Lee et al., 2020a; Liang et al., 2020a; Liang et al., 2020b; Maeda et al., 2020; Mao et al., 2020; Oh et al., 2020; Park et al., 2020; Pinke et al., 2020; Qiao et al., 2020; Santiveri et al., 2020; Schrecker et al., 2020; Vinayagam et al., 2020; Wang et al., 2020a; Wang et al., 2020b; Wang et al., 2020f; Wang et al., 2020k; Wasilko et al., 2020; Yang et al., 2020b; Yang et al., 2020c; Zhang et al., 2020f; Zhang et al., 2020h; Zhao et al., 2020a; Zhao et al., 2020b)	(Sun et al., 2015; Wu et al., 2015; Gong et al., 2016; Voorhees et al., 2016; Wu et al., 2016b; Wu et al., 2016a; Guo et al., 2017b; Martin et al., 2017; Paulino et al., 2017; Shen et al., 2017; Twomey et al., 2017; Yan et al., 2017; Guo et al., 2017b; Bai et al., 2018; Deneka et al., 2018; Fan et al., 2018; Gong et al., 2018b; Kasuya et al., 2018; Pan et al., 2018; Shen et al., 2018; Singh et al., 2018a; Wu et al., 2018; Yin et al., 2018; Alvadia et al., 2019; Choi et al., 2019; Clairfeuille et al., 2019; Ding et al., 2019; Feng et al., 2019; Gu et al., 2019; Martin et al., 2019; Ramírez et al., 2019; Rathore et al., 2019; Tao et al., 2019; Wu et al., 2019; Yan et al., 2019; Yin et al., 2019b; Yin et al., 2019c; Zhao et al., 2019b; Zhou et al., 2019b; Bai et al., 2020; Chen et al., 2020b; Flygaard et al., 2020; Gérard et al., 2020; Hartley et al., 2020; Kater et al., 2020; McGilvray et al., 2020; Nakamura et al., 2020; Noreng et al., 2020; Qu et al., 2020; Sobti et al., 2020; Wang et al., 2020h; Zhang et al., 2020e; Zhou et al., 2020)

Table S1. References to studies in which the target membrane protein was initially solubilized and purified in either maltosides, neopentyl glycols or digitonin, sorted out according to the surfactant used for vitrification. Note that, in most cases, the latest steps of purification were used to substitute one surfactant with the other.

[a] "Others" refers to liposomes (Yao et al., 2020) and Brij-35 (Fiedorczuk et al., 2016).

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