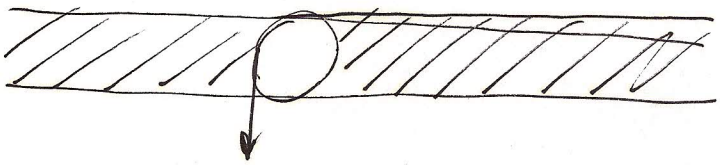
Composizione di alcuni tipi di membrane

(valori percentuali)

	Proteine	**Lipidi**	**Glucidi**
Membrana plasmatica Degli eritrociti	49	43	8
Guaina mielinica	18	79	3
Membrana mitocondriale interna	76	24	0

Da: D'Angelo e Peres (a cura di), Fisiologia, edi-ermes, 2011

GLUCOSIO



GLUCOSIO

ESOCHINASI ↓ ↑ G6-FOSFATASI (SÍ: FEGATO intestino rene

NO: muscolo neuroni)

GLUCOSIO-6P

GLUCOSIO-1P

GLICOLISI

SINTESI DEL GLICOGENO

TRASPORTO FACILITATO DEL GLUCOSIO

Rassegna: G.D. Holman. Structure function and regulation of mammalian glucose transporters of the *SLC2* family. *Pflügers Archiv – Eur J Physiol* 472: 1155-1175, 2020.

SLC2: 14 geni (GLUT1-GLUT14)

Classe I	**Localizzazione e funzione**
GLUT1	assorbe il glucosio, eritrociti, vasi cerebrali K_m ($K_{0.5}$) = 1.5 mM (influsso di D-glucosio) 3.0 M (L-glucosio) 20 mM (D-mannosio)
GLUT2	epatociti, intestino, cellule β del pancreas, rene, etc. K_m = 20 mM (glucosio) 67 mM (fruttosio)
GLUT3	assorbimento nei neuroni K_m = 1-2 mM (glucosio)
GLUT4	assorbimento nel muscolo e negli adipociti K_m = 5 mM (glucosio)
Classe II	apparentemente preferenza per il fruttosio
GLUT5 (esempio)	intestino, rene, altri tessuti. Affinità più alta per il fruttosio

FLUSSO DI GLUCOSIO UNIDIREZIONALE

(supponiamo $[\text{GLUCOSIO}]_{\text{INTRACELL.}} \approx 0$)

$$T_E + GLUC_E \rightleftharpoons T_E GLUC_E \rightleftharpoons T_i GLUC_i \rightarrow T_i + GLUC_i$$

T = TRASPORTATORE

GLUC = GLUCOSIO

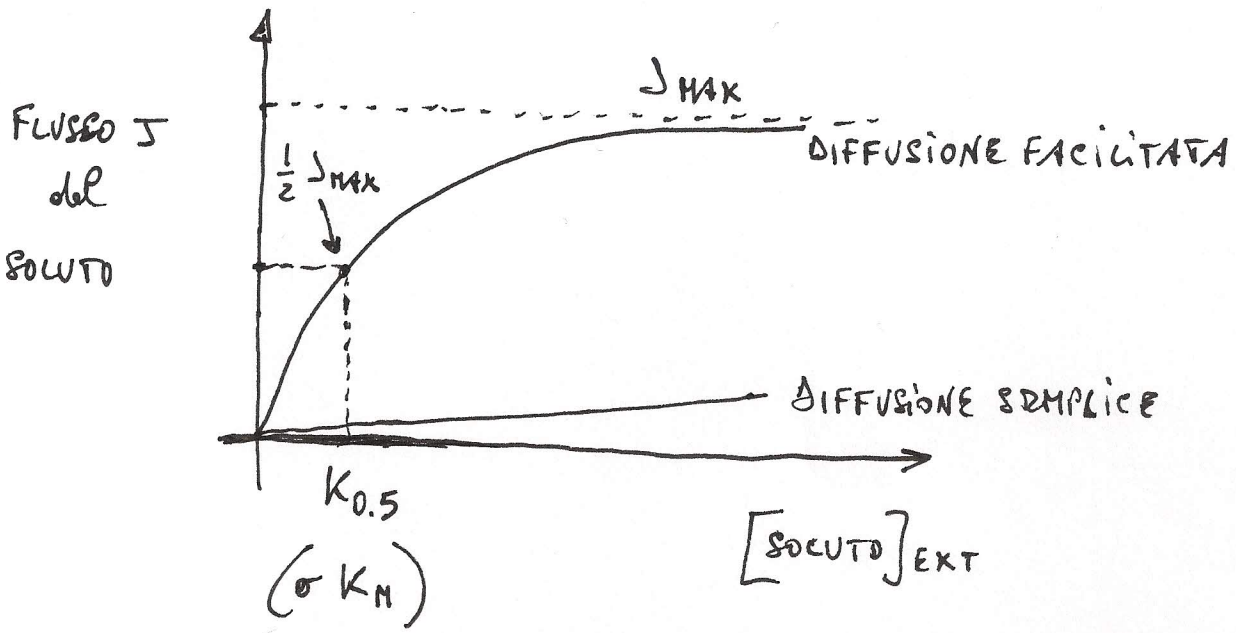
E = Lato extracellulare

i = Lato intracellulare

ASSUNZIONI e DERIVAZIONE ANALOGHE A QUELLE della curva di Michaelis-Menten o enzimologia

$$J_{IN} = \frac{J_{MAX}\,[GLUC]_E}{K_{0.5} + [GLUC]_E}$$

Nel caso più generale, si devono sommare i flussi unidirezionali.


FLUSSO J del SOLUTO
J_{MAX}
$\frac{1}{2} J_{MAX}$
DIFFUSIONE FACILITATA
DIFFUSIONE SEMPLICE
$K_{0.5}$
(σK_M)
[SOLUTO]$_{EXT}$

Pflügers Archiv - European Journal of Physiology (2020) 472:1155–1175
https://doi.org/10.1007/s00424-020-02411-3

INVITED REVIEW

Structure, function and regulation of mammalian glucose transporters of the *SLC2* family

Geoffrey D. Holman[1]

Received: 17 January 2020 / Revised: 27 May 2020 / Accepted: 29 May 2020 / Published online: 26 June 2020

Abstract

The *SLC2* genes code for a family of GLUT proteins that are part of the major facilitator superfamily (MFS) of membrane transporters. Crystal structures have recently revealed how the unique protein fold of these proteins enables the catalysis of transport. The proteins have 12 transmembrane spans built from a replicated trimer substructure. This enables 4 trimer substructures to move relative to each other, and thereby alternately opening and closing a cleft to either the internal or the external side of the membrane. The physiological substrate for the GLUTs is usually a hexose but substrates for GLUTs can include urate, dehydro-ascorbate and myo-inositol. The GLUT proteins have varied physiological functions that are related to their principal substrates, the cell type in which the GLUTs are expressed and the extent to which the proteins are associated with subcellular compartments. Some of the GLUT proteins translocate between subcellular compartments and this facilitates the control of their function over long- and short-time scales. The control of GLUT function is necessary for a regulated supply of metabolites (mainly glucose) to tissues. Pathophysiological abnormalities in GLUT proteins are responsible for, or associated with, clinical problems including type 2 diabetes and cancer and a range of tissue disorders, related to tissue-specific GLUT protein profiles. The availability of GLUT crystal structures has facilitated the search for inhibitors and substrates and that are specific for each GLUT and that can be used therapeutically. Recent studies are starting to unravel the drug targetable properties of each of the GLUT proteins.

Keywords Glucose transport · GLUT proteins · Membrane transport · GLUT1 · GLUT2 · GLUT3 · GLUT4 · GLUT5 · Regulated transport · Insulin · Hypoxia · ATP depletion

Abbreviations

GGAP2	Golgi associated, gamma adaptin ear containing, ARF-binding protein 2
VAMP	Vesicle-associated membrane protein
IRAP	Insulin-responsive aminopeptidase
UBC9	Polyubiquitin-C precursor 9
USP25	Ubiquitin carboxyl-terminal hydrolase 25
TM	Transmembrane segment
p115	General vesicular transport factor p115
MSNBA	N-[4-(methylsulfonyl)-2-nitrophenyl]-1,3-benzodioxol-5-amine
TBC	Tre-2/Bub2/Cdc16
CHC	Clathrin heavy chain
ERGIC	ER-Golgi intermediate compartment
TGN	Trans-Golgi network
MVB	Multivesicular body

This article is part of the special issue on Glucose Transporters in Health and Disease in Pflügers Archiv—European Journal of Physiology

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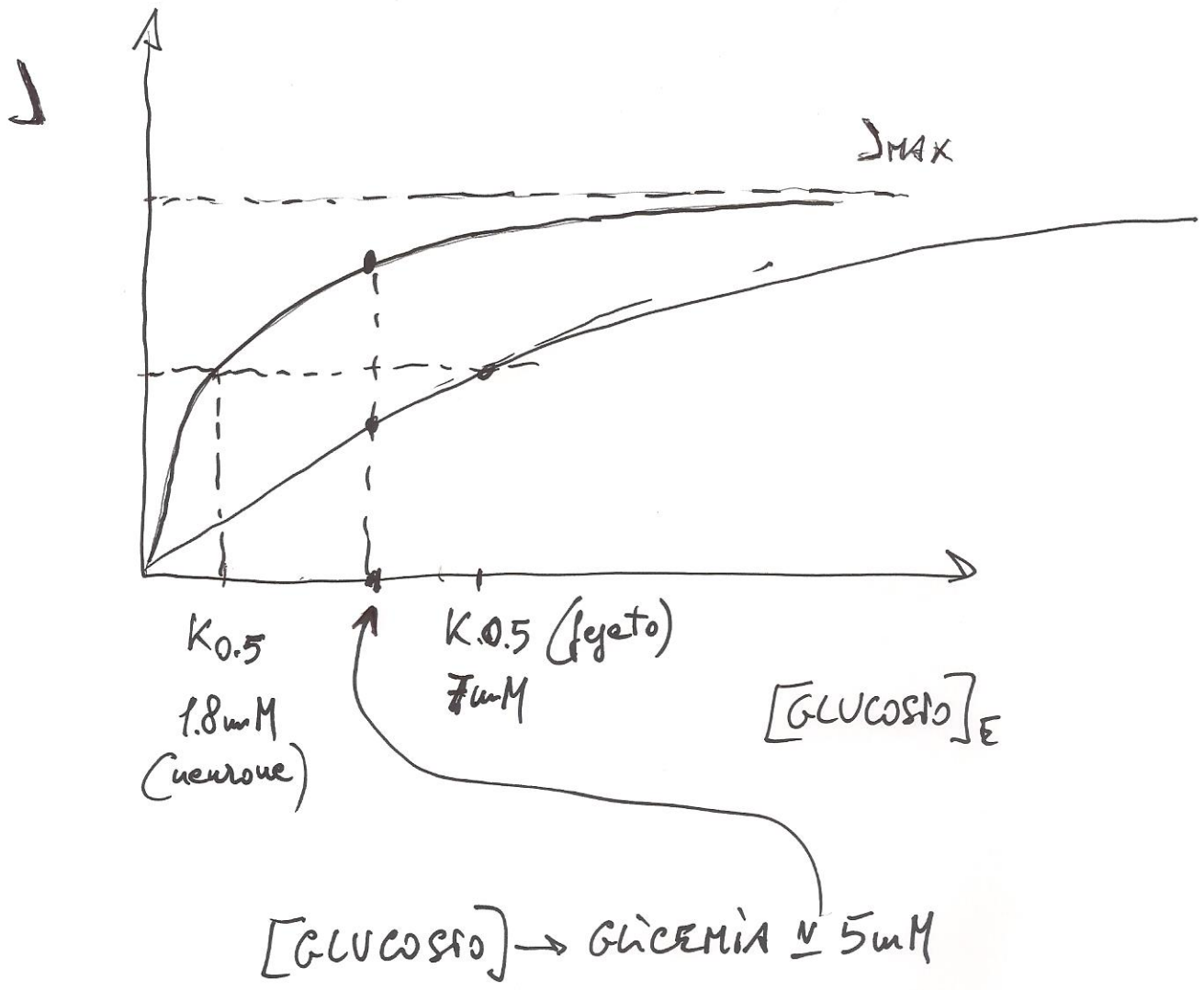
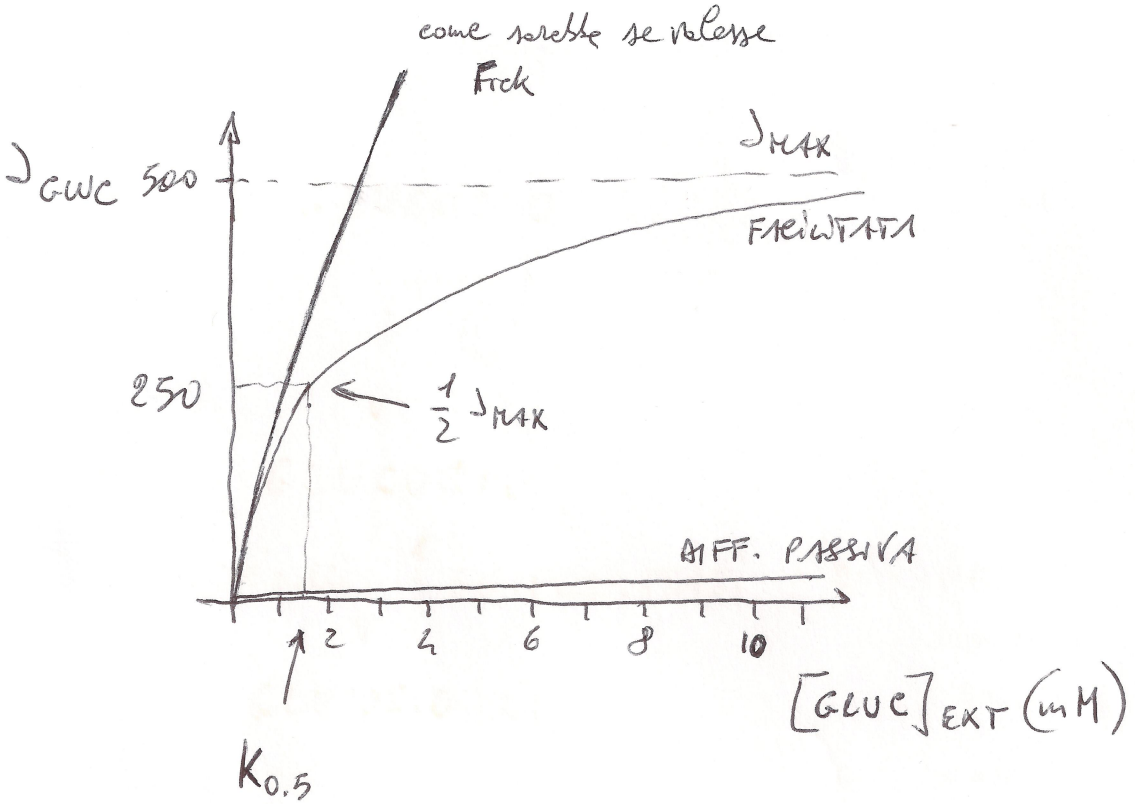
Introduction

The *SLC* (SoLute Carrier) gene family has been classified into 65 sub-families with identities within the sub-family that differ more than 20–25% from other *SLC*s [38, 89]. The *SLC2* sub-families of 14 related genes are thus distinct from the closest relatives (which are the *SLC19* sub-family) and lie within the major facilitator superfamily (MFS) group which codes for proteins whose function is to facilitate membrane transport of substrates [89]. The 14 SLC2 genes code for proteins that are further sub-divided into phylogenetically distinct classes 1-3 of GLUT (glucose transport) proteins [106].

The proteins of the *SLC2* family have 12 transmembrane spans (TMs 1-12) with intracellular N- and C-termini.


J
JMAX
K0.5
1.8mM
(neurone)
K0.5 (fegato)
7mM
[GLUCOSIO]E
[GLUCOSIO] → GLICEMIA ≅ 5mM



CARATTERISTICHE:
- SATURAZIONE
- ALTA V
- SPECIFICITA'
- COMPETIZIONE

J_{MAX} DIPENDE DAL NUMERO DI TRASPORTATORI